RESUMOS DOS TRABALHOS CIENTÍFICOS APROVADOS
SNOLA 2018
Sumário

Áreas Temáticas

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Temos Livres: Modalidade Pôster
Áreas Temáticas

Cuidados paliativos
Neuro Imagem
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Neurologia Oncológica
Neuropatologia
Neuro-Oncologia
Radioterapia e Radiocirurgia
**Código:** 65700

**Modalidade Aprovada:** Apresentação Oral

**Temário:** SNOLA - Neuro Imagem

**Título:** RELATIVE CEREBRAL BLOOD VOLUME AS RESPONSE PREDICTOR IN THE TREATMENT OF RECURRENT GLIOBLASTOMA WITH ANTI-ANGIOGENIC THERAPY

**Autores:** González-Aguilar Alberto; Breda-Yepes Michelle; Reyes-Moreno I;

**Resumo:** Background: Recurrence is the rule in GB, the second line of treatment is the Antiangiogenics of which Bevacizumab (BVZ) is effective. rCBV has been evaluated as a predictor of response. Objective: Correlate response, Measure the Overall Survival (OS) between responders and non-responders and find cutoff for predicting response to BVZ. Patients and Methods/Material and Methods: Patients with GB who progressed according to the RANO criteria treated with BVZ were progressively enrolled, who underwent an MRI perfusion prior to initiation of Bevacizumab and were quantified by the rCBV. The correlation between rCBV and response was analyzed by the correlation coefficient, cutoff point to identify responders and non-responders to BVZ was evaluated by ROC curve and OS using Kaplan Meier curve and log rank. Results: Thirty patients with GB were included. We divided the patients in non-responders (n=17) and responders (n=14), there were differences between the groups (age and KPS). The correlation between the RCBV and the Therapeutic response was r=-0.83, p≤0.0001 (95% CI -0.918 to -0.675). The ROC curve showed 3.7 as the cutoff value with a sensitivity of 100% and specificity of 94% to predict response to BVZ. We divided the groups into non-responders and responders, with OS of 7.7 months vs 14.4 months respectively, p 0.045 (HR 2.3, 95% CI 1.0192 to 5.6192). Conclusion: rCBV is a potential biomarker evaluated by MRI that predicts response to treatment in patients who will be treated with Bevacizumab. Bevacizumab treatment is highly cost-effective and this biomarker would identify who the patients would benefit.

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Resumo: INTRODUCTION: Treatment strategies for patients with craniopharyngioma is still controversial. Currently, quality of life is the goal for all treatment modalities. OBJECTIVE: To analyze the several treatment strategies and outcomes of craniopharyngioma patients in 15 years of experience in a single institution. METHODS: The authors retrospectively evaluated 110 craniopharyngioma patients treated between 2001 and 2016, at IOP/GRAACC/UNIFESP. Data regarding initial clinical presentation, body mass index (BMI), endocrinological complications, treatment modalities and outcomes were collected. RESULTS: From 110 patients treated with craniopharyngioma at our institution, 95 patients were eligible for evaluation and 15 excluded for loss of follow-up. Fifty-five were boys and 40 girls. The mean age at treatment was 10,5 years (range 3,25-25,08). Fifty-six percent of children presented with signs and symptoms of intracranial hypertension, 24% with visual impairment and 38,5% with endocrinological disturbances. At the time of diagnosis, the mean BMI was 20,48kg/m² (range 12,7- 32,8). Predominantly cystic tumors (cystic portion ≥ 60% of total lesion volume) occurred in 38 children and were treated with intralesional interferon-alpha; of these patients, 13 progressed to surgical intervention and adjuvant radiotherapy. Among the remaining 57 patients, 9 were treated with microsurgery only, 29 with microsurgery + radiotherapy, 12 with endoscopic transseptal surgery + radiotherapy and 7 patients, with recurrences tumors after conventional treatment, were treated with intracystic interferon-alpha as alternative therapy. The mean BMI of patients treated exclusively with interferon-alpha was 22,88kg/m² (ideal weight), with interferon-alpha + microsurgery was 31,23kg/m² (grade 1 obesity) and microsurgery + radiotherapy was 29,65kg/m² (overweight). After treatment, 51 cases (65%) progressed to panhypopituitarism. The mean follow up was 7,13 years (range 1-17), and 8 deaths occurred. Currently 41 patients are out of treatment. CONCLUSION: Several efforts have been made to improve the prognosis so unfavorable for these patients. The significant morbidity associated with important recurrence rates require that these patients be treated as having chronic disease. Intracystic therapy with interferon-alpha offers best body mass index control. However, panhipopituitarism is the most common and important complication irrespective of treatment modalities.

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Modalidade Aprovada: Apresentação Oral

Temário: SNOLA - Neurocirurgia

Título: OXIDATIVE DAMAGE, GENOTOXICITY, TP53 AND ING2 IMMUNOEXPRESSION OF HYDROLYZED RUTIN IN Glioblastoma ANIMAL MODEL

Autores: BRUNO CAMPOREZE; Cesar Cozar Pacheco; Ana Carolina Bombardi Duarte; Maycon Giovani Santana; Patrick Moro Mariano; Paula Ribeiro do Prado; Carlos Tadeu Parisi de Oliveira; Denise Gonçalves Priolli;

Resumo: BACKGROUND: Flavonoids are a phenolic compounds group from natural origin. Several biological activities, including anti-tumoral, antioxidant, antiviral and anti-inflammatory are attributed to flavonols, whose have great pharmacological importance. The quercitin is the most abundant flavonoids and found in quercetin-3-rutinoside form in food. It can be transformed in Hydrolyzed Rutin (HR) through breaking the rhamnose molecule by the enzyme alpha-L-rhamnosidase. OBJECTIVE: To evaluate antiproliferative, pro-oxidative and genotoxic potential of HR on human glioblastoma. METHODS: Athymic mice (n=15) were randomly distributed in three groups, control (n=7), HR-Pre (n=4), HR-Post (n=4) regarding the time to start the treatment. Heterotopic xenografts of human glioblastoma cells/U-251 was performed. The tumor volume was monitored daily. The animals of HR-Pre group received gavage with the biocompound prior to tumor implantation, while the animals of HR-Post group were underwent to tumor cells implant and, after the tumor volume reached 100mm³, both groups received gavage for five consecutive days. After anesthesia tumor resection and euthanasia were performed. The conventional histopathological analysis, immunohistochemical study (TP53 and ING2), lipid peroxidation (Monitoring Thiobarbituric Acid-Reactive Substances - TBARS) and genotoxicity assays (comet) were done. The statistical analysis were carried out by adopting a significance level of 5% (p<0.05). RESULTS: RH-Post (p=0.03) and RH-Pre (p=0.01) showed tumor volume decrease when compared with the control group. Pathological analyses showed cellular mitosis reduction (p=0.04) in both treated-groups. Lipidic peroxidation increased in treated-groups (p<0.05). There were no difference in genotoxicity between treated and control groups in ING2 and TP53 immunoexpression. CONCLUSIONS: The HR shows an antitumoral action in xenograft human glioblastoma suggesting that the lipidic peroxidation leads the activation of anti-proliferative pathway.

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Modalidade Aprovada: Apresentação Oral

Temário: SNOLA - Neurologia Oncológica

Título: IDENTIFYING THE MOST FREQUENT VARIANTS IN PEDIATRIC MEDULLOBLASTOMA DRIVER GENES: A SINGLE-INSTITUTION STUDY

Autores: Bruna Mascaro Cordeiro; Indhira Dias Oliveira; Leonardo Caires dos Santos; Renan Paulo Martin; Rafael Filippelli da Silva; Maria Teresa de Seixas Alves; Nasjla Saba-Silva; Sergio Cavalheiro; Patricia Dastoli; Silvia Regina Caminada de Toledo;

Resumo: Medulloblastoma (MB) is a malignant childhood brain tumor from cerebellum. Four principal MB molecular subgroups were established: Sonic Hedgehog (SHH), Wingless (WNT), group 3 and group 4. The present study reports the results of the first Brazilian single-institution investigation of pediatric MB subgroups-related genes. We developed an AmpliSeqTM custom panel for DNA sequencing, comprising CTNNB1, PTCH1, DDX3X, TERT and TP53 genes. We selected 28 MB treatment-naïve tumor samples. DAOY, D283MED and ONS-76 MB cell lines were authenticated and included in the study. We observed two variants in exon 3 of CTNNB1, and two non-described variants in DDX3X gene. PTCH1 gene presented the highest number of variants observed (74% of samples). TP53 variants were present in 15% of samples, occurring concomitantly with PTCH1 mutations, and was related to worst overall survival (p=0.0005). Previous studies about pediatric MB genome were carried out from large cohorts of North American and European populations, resulting in the identification of several genes variants. However, these variants might not be representative for other populations, mainly Brazilian population, due to the history of the current Brazilian population formation, including the interbreeding patterns and several waves of migrations leading to a high degree of admixture. This particularity might contribute to a very specific combination of rare and common variation, making this population interesting and enhancing the importance of the present screening study. MB occurring in pediatric patients requires deregulation of a minimal number of driver genes, and, variants that leads to deregulation of these genes may not be the same between different populations. Finally, we reinforce that new molecular diagnostic approaches involving PTCH1 and TP53 genes screening, concomitantly, can collaborate for the better clinical management of infancy and childhood MB, which emphasizes new therapeutic strategy needs.

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**Modalidade Aprovada:** Apresentação Oral  

**Temário:** SNOLA - Neuro-Oncologia  

**Título:** ALPHA INTERNEXIN: AN ALTERNATIVE STRATEGY FOR DETECTION OF THE 1P19Q CODELETION IN PATIENTS WITH GLIOMAS IN A MOLECULAR ERA  

**Autores:** González-Aguilar Alberto; Rasmussen Astrid; Navarro Bonnet J; Reyes Moreno I;  

**Resumo:** Introduction: Gliomas represent the most common primary malignancy of the central nervous system (CNS). Molecular biology shows us that the 1p/19q is a very specific molecular signature and is strongly associated with an oligodendrogial phenotype. Ducray and cols., identified the expression of Alpha internexin (INA) in patients with 1p19q translocation with strong correlation. The 1p19q codeletion is one of the most important prognostic and the new World Health Organization (WHO) classification it is necessary the knowledge of 1p19q status.  

Material and Methods: We studied INA expression in Gliomas (astrocytoma, oligodendroglioma, oligoastrocytoma and Glioblastoma) samples tumors were analyzed for identification of 1p/19q mutation was achieved by fluorescence in-situ hybridization and correlated INA expression by immune–histochemical staining. We calculated the sensitivity, specificity, Positive predictive value, Negative predictive value and Progression free survival (PFS) and Overall Survival (OS).  

Results: The 154 patients were included; the mean age was 45 years old with predominance in males 76% and women 24%. By grading the 49% were grade 2, the 30% grade 3 and 21% were Glioblastoma. The codeletion 1p19q was presented in 48 cases and negative in 106 patients by FISH for immunostaining INA were presented in 49 cases and negative in 105 patients. Correlation between INA and 1p/19q was statistically significant ($r^2 = 0.834$, $p < 0.0001$; CI 0.7793 to 0.8770). INA expression specificity for 1p19q codeletion was 90%, sensitivity 94%, positive predictive value (PPV) 88%, and negative predictive value (NPV) was 95%; We analyzed alone of Oligodendroglioma with sensitivity was100%, specificity 86%, PPV 96% and NPV 100%. 1p19q codeletion expression was correlated with better PFS and overall survival OS ($p = 0.0001$).  

Conclusions: INA expression has high specificity and sensitivity to predict 1p/19q co-deletion, and it is well correlated with PFS and OS of Gliomas. Therefore, INA expression could be a simple, reliable, and favorable prognostic and surrogate marker for 1p/19q co-deletion and long term survival. With the new classification of WHO it is necessary the determination of 1p19q codeletion, the INA is an option in centers without advanced molecular biology techniques.  

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Resumo: Pilocytic astrocytoma (PA) is the most common glioma in childhood. Usually PA occurs as sporadic disease but, eventually, arises in the heredity context of type 1 neurofibromatosis (NF1). We previously demonstrated the loss of chr9q34.3 region, which encompasses the KCNT1, CAMSAP1, EGFL7, AGPAT2, FAM69B, LCN6 and LCN8 genes, in a series of pilocytic astrocytomas. EGFL7 is related to increased vasculogenesis, tumor growth and proliferation, and the anti-EGFL7 monoclonal antibody Parsatuzumab has been tested in randomized Phase II trials in metastatic colorectal cancer. Therefore, we aimed to assess the expression levels of EGFL7 and evaluate its potential prognostic value in a series of well clinically and molecularly characterized pilocytic astrocytomas. A total of 69 patients were immunohistochemically analyzed for EGFL7 expression, and were grouped according to the percentage of tumor labeled cells (0%, negative; 1-49%, low expression; ≥ 50%, high expression). The clinicopathological features were analyzed according to the experimental groups using chi-square, and survival was analyzed using log rank. High EGFL7 immunostaining was found in 26 patients (37.7%), which was associated with patient gender, namely women (51.6%) vs. 26.3% in men (P=0.03). From the five NF1-PAs patients, four (80%) exhibited a high EGFL7 expression (P=0.04). There was no association between EGFL7 expression and presence of KIAA1549-BRAF fusion. High EGFL7 expression was associated to high FGFR expression (44.9% vs. 20%, P=0.05). High EGFL7 expression patients were also associated with a worse 3-year survival (P=0.04). These results suggest that EGFL7 is overexpressed in a subset of pilocytic astrocytomas, and it can constitute a patient prognostic biomarker. Further studies may be conducted to analyze EGFL7 overexpression as a putative predictive marker response to Parsatuzumab-based therapy. Financial support B.B.B. is recipient of Fundação de Amparo à Pesquisa do Estado de São Paulo fellowship (FAPESP number 2016/23919-8) and L.T.B. is recipient of FAPESP grant (2016/21727-4).

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Resumo: Introduction: Nuclear factor kappa-B (NF-κB) pathway has been demonstrated as constitutively activated in GBM, and it was suggested as a potential therapeutic target. Glycyrrhizic acid (GA) has been shown to reduce cell viability and inducing apoptosis in many human cancer cell lines by NF-κB suppression. However, GA may present toxicity. Dipotassium glycyrrhizinate (DPG), a dipotassium salt of GA, also has anti-inflammatory properties, but no side effects are presented. Aim: This study aimed to investigate the effects of DPG on NF-κB using U87MG and T98G GBM cell lines. Methods: Luciferase assay was performed to determine whether NF-κB could be modulated by DPG. Thus, U87MG and T98G cells were transfected with NF-κB promoter/luciferase reporter plasmid. To identify microRNAs (miRs) involved with the NF-κB signaling pathway, U87MG and T98G cell lines were exposed to 18mM and 24mM DPG for 48h, respectively. Total RNA from GBM cell lines was isolated and miR16 and miR146a expression was evaluated by real-time PCR (qPCR). Also, IRAK2 and TRAF6, known target genes of miR16 and miR146a, respectively, were also evaluated by qPCR. MiR146a is known as a negative regulator of NF-κB signaling. Thus, U87MG and T98G cells overexpressing miR146a were used to investigate whether this miR could influence the inhibitory effect of DPG of suppressing NF-κB pathway by luciferase assay. Next, pcDNA3.3-miR146a transfected cells were treated with DPG (U87MG: 18mM; T98G: 24mM) for 48h. Untreated transfected cells were used as controls. Results: The NF-κB reporter activity was found to be downregulated by DPG in comparison with untreated transfected cells. qPCR results showed that DPG can significantly increase miR16 and miR146a expression in GBM cells (P≤ 0.05). DPG treatment in GBM cells significantly decreased IRAK2 and TRAF6 levels, indicating that DPG up-regulates miR16 and miR146a and down-regulates its target genes (P≤ 0.05). The promoter activity of NF-κB reporter in pcDNA3.3-miR146a transfected cell lines was decreased after DPG treatment compared with untreated transfected cells. IRAK2 and TRAF6 expression presented as down-regulated in both pcDNA3.3-miR146a transfected cells treated with DPG. Conclusions: MiR146a positively inhibits NF-κB through suppressing TRAF6 after DPG action. In this context, IRAK2- and TRAF6-mediating miR16 and miR146a, respectively, might be a potential therapeutic target of DPG. Financial Support: FAPESP

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Modalidade Aprovada: Apresentação Oral

Temário: SNOLA - Neuro-Oncologia

Título: GENETIC PROFILING OF OLIGODENDROGLIOMAS (IDH MUTATED AND 1P19Q CODELETED) TREATED WITH ADJUVANT RADIOTHERAPY OR OBSERVATION INFORMS PROGNOSIS

Autores: FABIO YNOE DE MORAES; Fabio Y Moraes; Jonathan So; Gelareh Zadeh; Ken Aldape;

Resumo: Propose: We sought to analyze The Cancer Genome Atlas (TCGA), 2015 gene expression and copy number datasets on Oligo patients treated with adjuvant RT or those Obs to discover prognostic markers and pathways. Methods: Our cohort consists of patients with Oligo in the TCGA dataset (http://www.cbioportal.org/). mRNA expression, copy number, and clinical information was taken from the TCGA “Brain Lower Grade Glioma (LGG)” provisional dataset. Progression free survival (PFS) modeling and ANOVA analysis was performed using the R packages. Further validation analysis is currently being performed. Results: 164 patients were included in our analysis with LGG, and both IDH mutation and 1p19q codeletion. Out of our cohort of 164 patients, 137 had documentation of treatment (65 receiving adjuvant RT (median dose 5,9Gy) and 62 observed). From the included cohort of 137, 23% of patients who received RT also received chemotherapy (CT) (93% TMZ). A majority of patients who did not receive RT also did not receive adjuvant CT (90% vs. 10%). In the cohort that received adjuvant RT, expression of members of the PDGFRA module (GSTA4, CXXC4, KLRC3, DSCAM, OLIG2, SOX4, SOX8) was associated with shorter PFS (HR=7,p<0.02). This increased risk was not seen in patients who were Obs (HR=0.8,p =0.83). Patients treated with RT and positive for the PDGFRA gene signature had a median PFS of 64 months (m) vs. 120m for those negative for the signature. In addition, expression of circadian clock genes (CSNK1E, CRY2, PER1) was also associated with shorter PFS (HR=4.9, p<0.03) when treated with RT vs. Obs (HR=0.33, p=0.11). Median PFS in the RT cohort positive for the circadian gene signature was 64m vs. 97m for those negative for the signature. Within the Obs cohort, expression of genes in the polycomb repressive complex-2 (EZH1, EZH2, SUZ12, EED, and RBBP4) was associated with poor PFS (HR=1.65, p<0.008). This risk was abrogated in the adjuvant RT cohort (HR=1.03, p=0.55). Decreased expression of genes targeted and down-regulated by this complex also was associated with shorter PFS (Chi=7.4, p< 0.007). Conclusions: We identified genes in the PDGFRA and circadian signalling pathways that are associated with poor PFS in patients with IDH mutated and 1p19q codeleted Oligo treated with adjuvant RT (potential candidates for treatment intensification). We also identified a PRC-2 gene signature for patients who were more likely to progress on Obs. (potential candidates for upfront adjuvant RT).

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Resumo: Introduction: Gliomas represent the largest and most common category of brain tumors. It carry characteristic genetic that may be employed for molecular tumor classification and for target therapies. Next-generation sequencing (NGS) technology enable analysis of a large areas of genome with a fast turnaround time and cost-effective, also a identification of clinically actionable genetic targets. Methods: We report an customized panel NGS assay that analyzes genetic alterations (GAs) in 21 genes (557 amplicons) in 27 glioma samples (Tumor/Normal) and 14 glioma cell lines utilizing Ion Torrent Suite. Results: DNA sequencing were successful in all 41 samples yielding an average of 385 AQ20 Mbases, 110 bp median read length per sample and 1815 mean sequencing depth per amplicon with 500x for minimal depth coverage per locus. Analysis identified 160 GAs in 16 genes with the majority of them distributed in insertion(34.6%), missense(29.6%) and synonymous mutation(17.6%). The most commonly mutated genes across all sample were SETD2 (18.1%), NF1/ATRX (17.4%), and TP53 (12.83%). Only 3/41 (7.3%) of all tumors were negative for all non-synonymous GAs included in the panel. Was observed known GAs in stable cell lines specifically in genes NF1 (K144M; T1589M), RB1 (R579*; V852L), PTEN (L42R; R233*) and TP53 (R273H; M237I). For tumor/normal sample the meanly GAs observed was in IDH1 (R132H), NF1 (H819L), ATRX (V469fs, G795N) and TP53 (M237V, R273C/H). Conclusions: NGS is sufficiently robust for the clinical detection of gene mutations in 74% (tumor/normal) and 93% (cell lines) samples analyzed, indicating glioma panel as a promising diagnostic assay for integrated glioma classification.

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Modalidade Aprovada: Apresentação Oral

Temário: SNOLA - Neuro-Oncologia

Título: IN SILICO ANALYSES OF THE LOCUS CHR9P22.1-P21.3 UNVEILS GENES WITH POTENTIAL PROGNOSTIC VALUE IN GLIOMAS.

Autores: PAOLA GYULIANE GONÇALVES; Rui Reis; Lucas Tadeu Bidinotto;

Resumo: The chr9p22.1-p21.3 is a frequently deleted region in glioblastoma, present in approximately 50% of cases. This region harbors some well-known tumor suppressor genes such as CDKN2A and CDKN2B, yet many other putative important genes lay in this locus, which are less studied. Thus, the aim of the present study was to identify unexplored genes in this region with potential prognostic in gliomas. For this, we analyzed copy number alterations in this region using normalized TCGA data from Low Grade Glioma (LGG) and Glioblastoma (GBM) datasets and correlated to RNA expression data from RSEM-normalized RNA sequencing datasets. For copy number analysis, we considered the thresholds of |0.1| for gains/losses and |0.7| for amplification/deletion for the genes in 591 GBM, 63 lower grade astrocytomas (AA), 54 oligoastrocytomas (OA) and 89 oligodendrogliomas (OD). Then, for mRNA expression, we log10 transformed values of each gene present in the locus for 152 GBM, 194 AA, 130 OA and 191 OD, and compared their expression using ANOVA and Scheffe post hoc statistical test for each gene. Finally, we analyzed survival of GBM patients considering the expression of each gene, using log rank as statistical test. The expression was considered positive when higher than the median in GBM otherwise it was considered negative. The differences were considered statistically significant when P<0.05. We found that the most frequently deleted gene was CDKN2A, with 30% of deletion in AA and 62% in GBM. We found a significant decrease (p<0.01) in the expression of SLC24A2, MLLT3, KIAA1797, KLHL9, MTAP, CDKN2A/2B and ELAVL2 and increased expression of PTPLAD2 in GBM, in comparison to AA, and practically no expression of IFN family genes. Furthermore, we found that loss of expression of SLC24A2, MLLT3, KLHL9, MTAP, CDKN2A/2B and ELAVL2 genes significantly correlated to a worse survival, whereas the loss of PTPLAD2 was found to be correlated to a better GBM patient survival. Interestingly, ELAVL2 presented the most expressive difference in 12-months survival (59% of survival in patients with loss of expression and 83.8% in patients positive for ELAVL2). Besides CDKN2A/2B, our results point to several genes with potential prognostic value in gliomas, such as SLC24A2, MLLT3, KLHL9, MTAP, ELAVL2 and PTPLAD2, which should be the subject of further investigations. Financial support P.G.G. is recipient of FAPESP fellowship (2017/09749-5) and L.T.B. is recipient of FAPESP grant (2016/21727-4).

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Modalidade Aprovada: Apresentação Oral

Temário: SNOLA - Neuro-Oncologia

Título: MOLECULAR CLASSIFICATION OF A BRAZILIAN COHORT OF PEDIATRIC EPENDYMOMA

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Resumo: Recent advances in the biological characterization of ependymomas (EPNs) revealed nine tumors subgroups, which were considered distinct clinical and molecular entities. These findings offer new opportunities to improve ependymoma stratification and to conduct therapeutic decisions based on molecular tumor features. The purpose of this study was to provide a standardized molecular classification for 63 pediatric ependymoma samples and correlate the classification with the clinical data. For the 26 samples of supratentorial (ST) EPNs, we investigated the C11orf95-RELA, YAP1-MAMLD1 and YAP1-FAM118B fusions through RT-PCR and Sanger sequencing. Immunochemistry reactions for LAMA2, NELL2 and TNC were carried out in 37 samples of posterior fossa (FP) EPN. The results showed that, among patients with ST EPNs, eight presented RELA fusion (five were grade II and three grade III), their median age was 6.4 years (range: 1.4-13.7) and a significant portion (7/8; 88%) were submitted to complete surgical resection. The YAP1 fusion was identified in four samples (half grade II and half grade III) from very young children (median age of 1 year; range: 0.5-2 years), being (3/4; 75%) of them submitted to complete tumor resection. Among the PF EPN cases, we identified 32/37 (87%) tumors classified as Group A (LAMA + / NELL-) in children with median age of 4.8 years (range: 0.4-12 years). The other five samples of PF EPN (13%) were negative or positive for both markers and were considered non-A and non-B (median age of 3.2 years; range: 1-8 years). Interestingly, most of older children (> 3 and < 12 years old) classified as EPN Group A presented grade II tumors (92%), while 41% patients EPN Group A below three years old were diagnosed with grade III tumors. Moreover, positive expression of TNC protein was found in 86% of PF EPN cases, most of them were also LAMA2 + (82%), suggesting tumor worse prognosis and disease poor outcome. In summary, we standardized the molecular classification of pediatric EPNs in a Brazilian cohort, in concordance to the procedures described in the literature. In this sense, this reliable data will help to improve EPN diagnostic and prognostic accuracy in our oncology service, bringing perspectives of new therapeutic strategies. Financial Support: FAPESP, CAPES

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Modalidade Aprovada: Apresentação Oral

Título: MOLECULAR PROFILING OF MEDULLOBLASTOMA: A BRAZILIAN MULTICENTER STUDY

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Resumo: Background: Medulloblastoma is the most frequent malignant brain tumor in children. Currently, four distinct medulloblastoma molecular subgroups have been identified: MBSHH, MBWNT, MBGRP3 and MBGRP4. A 22-gene panel employing the NanoString technology was previously developed for classification of medulloblastoma molecular subgroups. The NanoString is a high-throughput platform, highly sensitive, robust and useful for analysis of FFPE tissues. Mutations in KBTBD4 gene were recently reported in medulloblastoma, yet no further studies confirmed such events. hTERT promoter mutations are frequently found in medulloblastoma and are associated with worse prognosis, at variance with IDH1 mutations, which role in these tumors is controversy.

Aim: To apply and to validate the 22-gene panel for molecular classification of Brazilian medulloblastoma using NanoString and to associate the molecular subgroup with the mutational status of driver genes and patient’s clinicopathological features.

Methods: We evaluated 104 medulloblastoma FFPE samples from three reference centers in Brazil. Gene expression was assessed using the nCounter Elements custom panel comprised by distinctive genes for each medulloblastoma molecular subgroup plus hTERT and housekeeping genes. Raw data was normalized by housekeeping genes, followed by PAM method using a large series from Hospital for Sick Children for accurate classification of molecular subgroups. Moreover, hTERT, IDH1 and KBTBD4 hotspot regions were sequenced. The molecular profile was associated with patients’ clinicopathological features. Results: NanoString analysis was conclusive for all 104 patients. Most tumors were MBSHH(n=51), followed by MBWNT(n=19), MBGRP4(n=19) and MBGRP3(n=15). hTERT promoter mutations were detected in 29% of the cases, most of them detected in the MBSHH(77%). Moreover, the presence of hTERT mutations was associated with increased hTERT expression. None of the cases showed IDH1 and KBTBD4 hotspot mutations. The lowest and the highest 5-years cancer-specific overall survival (OS) was found for MBGRP4 and MBWNT, respectively. hTERT expression nor hTERT mutational status were associated with OS. Conclusions: We validated in a Brazilian series a modern approach for classification of medulloblastoma molecular subgroups. The NanoString was helpful to distinguish the medulloblastoma molecular subgroups and can be applied as an effective diagnostic tool.

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**Modalidade Aprovada:** Apresentação Oral

**Temário:** SNOLA - Neuro-Oncologia

**Título:** T-BOX TRANSCRIPTION FACTOR BRACHYURY IS A NOVEL TUMOR SUPPRESSOR GENE IN GLIOMAS

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**Resumo:** The oncogene Brachyury is a T-box transcription factor overexpressed in multiple solid tumors, being associated with tumor aggressiveness and poor patient prognosis. Gliomas comprise the most common and aggressive group of brain tumors, and up to now, Brachyury role has not been explored in these neoplasms. Brachyury expression was assessed in normal brain and glioma tissues (n=675) and cell lines (n=37), and in silico analysis was undertaken using genomic databases totalizing 3115 samples. Brachyury expression was modulated in glioma cell line models and in vitro and in vivo studies were conducted to analyze its functional and therapeutic role. Brachyury showed to be significant downregulated in gliomas compared to normal brain tissues, and was associated with tumor aggressiveness and worse patient outcome. Using in vitro and in vivo studies Brachyury-overexpressing glioma cells exhibited reduced cell viability, due to increase in apoptosis and autophagy. Invasive and migratory capabilities as well as stem properties of gliomas cells were impaired by Brachyury overexpression, with a concomitant increased in cellular differentiation. Moreover, Brachyury reactivation increases temozolomide response. For the first time, we demonstrated that Brachyury exhibit a tumor suppressor gene behavior in gliomas, and its absence constitutes an independent biomarker of worse patient outcome.

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Resumo: Introduction: Chemotherapy resistance is the major obstacle for effective treatment of glioblastoma multiforme (GBM). Glycyrrhizic Acid (GA) is a compound isolated from licorice (Glycyrhiza glabra) with anti-inflammatory and antitumor effects. However, side effects have pointed out the problem of it toxicity. Dipotassium glycyrrhizinate (DPG), a dipotassium salt of GA, also has anti-inflammatory properties, but no side effects are presented. There are no studies showing antitumor effect of DPG in GBM. Aim: This study aimed to investigate the effects of DPG on U87MG and T98G GBM cell lines. Methods: DPG cytotoxicity was determined by MTT assay. Additionally, we assessed DPG as a candidate for combinational therapy in GBM along with Temozolomide (TMZ). The effects of DPG on proliferation of GBM cell lines were measured by proliferation and wound healing (WH) tests. Cellular apoptosis was detected by DNA fragmentation and cleaved caspase-3 activation. Finally, in vitro assay verified whether DPG could reduce clonal sphere formation. Results: MTT assay demonstrated that the survival rate of U87MG and T98G cells significantly decreased in a time- and dose-dependent manner after DPG treatment. Also, cell lines treated using DPG in combination with TMZ revealed synergistic effects. The proliferation and WH tests demonstrated the anti-proliferative effect of DPG on GBM cell lines (P< 0.001). DNA fragmentation and caspase-3 cleavage observed in DPG-treated cells and showed higher apoptotic ratio in than untreated cell lines. The sphere formation assay showed that the treatment with DPG reduces the relative number of brain stem cells capable of forming spheres (P< 0.05). Conclusions: Our findings suggest that DPG can confer inhibitory effects on human GBM U87MG and T98G cell lines including inhibiting proliferation and inducing apoptosis. Furthermore, GBM is characterized by possessing a cancer stem cell subpopulation essential for tumor formation, survival, and recurrence. Therefore, this study may shed the light on identifying agents that target cells subpopulations like brain cancer stem cells is an approach to development chemotherapeutics agents to treat GBM. Financial support: FAPESP.

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Resumo: Medulloblastoma (MB) is a heterogeneous disease, with at least 12 recognizable genetic-molecular subgroups. Patients belonging to the SHH-MB subgroup present somatic mutations of the Sonic Hedgehog pathway genes, which include PTCH1, SUFU, SMO and activation of GLI. TP53 mutations may also be present, particularly in older infants, and confer worse prognosis for SHH-MB. Arsenic trioxide (ATO) has an inhibitory action over GLI, but little is known about its action in MB. We evaluate the potential cytotoxic and radiosensitizing effects of ATO on the pediatric SHH-MB cell-lines (ONS-76:TP53 wild type; DAOY:TP53 mutated c.725GT and UW402). Cell-line subgroups were confirmed by Taqman Low Density array (TDLA); TP53 mutation was validated by Sanger. Cell proliferation, clonogenicity and apoptosis were compared between cells prior and following ATO treatment at different concentrations (1-16uM). Cell clonogenicity assay of ATO alone and combined with irradiation (0.5, 1, 2 and 4Gy at 1.115 Gy/min) was also evaluated. Additionally, we investigated two key proteins (Rad51 and Ku86) responsible for DNA damage repair by Western blotting. Gene expression analysis was performed by QPCR. Genes integrating the SHH pathways and some of their major downstream effectors were also studied. Cell viability was monitored at different endpoints (24 to 120h) by the resazurin assay. Cell apoptosis was measured by annexin and propidium iodide and assessed through flow cytometry. Assays were performed in triplicate and analyzed by One Way, Two Way ANOVA and Bonferroni post-test (p<0.05). We observed a decrease in cell viability for the three SHH-MB cell-lines following ATO treatment at different concentrations. There was a significant decrease in the clonogenic capacity after ATO exposure. Lower cell-colony forming was accompanied by an increase in the apoptotic rate in all cell-lines; Interestingly, cell death was more pronounced (>70%) for the SHH-MB TP53-mutant subgroup (DAOY). Additionally, ATO treatment was able to radiosensitize UW402 cells. No association between time and concentration of ATO exposure and irradiation was seen for DNA-damage repair proteins. Downstream SHH genes showed variable patterns of inhibition. These findings point to a cytotoxic effect of ATO on pediatric SHH-MB cell-lines, with a potential radiosensitizing effect. This study validates the assessment of ATO on SHH-MB, either alone or in combination with radiotherapy, for in-vivo pre-clinical tests.

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Modalidade Aprovada: Apresentação Oral

Temário: SNOLA - Neuro-Oncologia / SLAOP - Biologia e Patologia

Título: IDENTIFICATION OF GENETIC PROFILE ASSOCIATED WITH RESPONSE TO TREATMENT WITH PROTEIN SMOOTHENED (SMO) INHIBITORS IN PAEDIATRIC MEDULLOBLASTOMA PATIENTS.

Autores: Daniel Shoji Hayashi; Isadora Olenscki Gilli; Gabriel Lopes Centoducatte; Iva Loureiro Hoffmann; José Andrés Yunes; Ana Luiza Seidinger;

Resumo: Introduction: Genomic studies have shown that medulloblastoma (MB) is not considered a homogeneous disease, but it has four molecular subgroups called WNT, SHH, group 3 and group 4. This molecular subdivision is based on gene expression profile and each subgroup is associated with different clinical, demographic and prognostic behaviors. The use of molecular classification of MB should direct the risk stratification in future therapeutic protocols. One of the subgroups with great potential to benefit from target therapies is the MB of the SHH subgroup. Currently, several inhibitors against targets that contribute to the tumorigenesis of this subgroup have been tested with promising results. However, patients may present with primary or acquired resistance to treatment with these inhibitors, resulting in transient or absent therapeutic effect. Aim: to investigate genetic changes predictive of response to Smoothened (SMO) protein inhibitors through the identification of alterations in the SHH pathway in samples from patients with pediatric MB. The changes investigated comprised mutations in the SUFU gene, as well amplification of MYCN and GLI2 genes. In addition, we intended to establish if there are and what are the correlations between the genetic profile of these patients and their clinical evolution. Method: Genomic DNA extraction from tumor samples was performed by using Illustra tissue genomic Prep kit. SUFU mutations were screened by PCR amplification of coding exons followed by Sanger sequencing. MYCN and GLI2 amplification were both assessed by real-time PCR amplification followed by analysis with the CopyCaller software. Clinical data were obtained from medical records. Statistical analyses were performed with GraphPad Prism 7.0. Results: Forty-nine patients were screened for genetic changes associated with primary resistance to SMO inhibitors: 2/49 patients were found to harbor SUFU mutations; 1/49 presented MYCN gain; 2/49 presented MYCN amplification and 5/49 presented GLI2 gain; the changes in the SUFU, MYCN and GLI2 genes were not associated with a worse prognosis for patients with MB-SHH (p = 0.5820; p = 1; p = 0.1409, respectively - Fisher’s exact test). Conclusion: The data obtained in the present study showed for the first time the clinical-molecular profile of Brazilian patients diagnosed with MB-SHH. This genetic profile may be a useful tool to help physicians direct therapy for MB-SHH patients.

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**Modalidade Aprovada:** Apresentação Oral

**Temário:** SNOLA - Radioterapia e Radiocirurgia

**Título:** DISEASE OUTCOMES AFTER GAMMA KNIFE RADIOSURGERY FOR SMALL- TO MEDIUM-SIZED BRAIN METASTASES: A PROSPECTIVE INSTITUTIONAL REGISTRY ANALYSIS.

**Autores:** FABIO YNOE MORAES; Fabio Y Moraes; Jeff D Winter; Hamid Raziee; Catherine Coolens; Gelareh Zadeh; Paul Kongkham; Mark Bernstein; Tatiana Conrad; Normand Laperriere; Barbara-Ann Millar; Alejandro Berlin; David B Shultz;

**Resumo:** Background: Marginal tumor dose prescription (DP) from radiosurgery (SRS) for brain metastasis (BM) affects rates of local failure (LF) and symptomatic radionecrosis (RN). In our BM program, we treat lesions adjacent to eloquent structures (e.g. motor cortex) with a smaller DP to reduce the likelihood of adverse side effects. We aimed to determine the effect of DP (15 Gy vs. ≥ 20Gy) on LF and RN for small- to medium-sized BM (≤ 2 cm). Methods: A prospective registry of BM patients treated with gamma knife SRS between January 2008 and September 2016 was reviewed to determine per lesion rates of LF and RN. Each tumor was followed from the date of SRS until LF or RN or at last MRI follow-up. Defined criteria were used to differentiate LF from RN, including pathology, when available. Whole brain irradiation (WBI) was a censoring event. Cumulative Incidence (CI) of LF and RN were estimated using a competitive risks analysis with death as the competing event. Cox regression was performed for univariate analyses. Results: From 1,465 potential subjects, 710 small- to medium-sized BM (≤ 2 cm) were evaluated; of those, 555 lesions (78.1%) were treated with DP ≥ 20 Gy and 155 lesions (21.9%) with 15 Gy. Median radiographic follow-up after SRS was 9.2 months (IQR 3-80 months). Overall, there were 31 local failures (4.37%) resulting in a CI at 2 years of 7.2% (95%CI 0-16.5%) for DP of 15 Gy and 4.8% (95%CI 0-9.7%) for ≥ 20Gy (P=0.45). Overall, CI of LF for lesions ≤ 1 cm, and > 1 cm, were 2.1% (95%CI 0-5.7%), and 10.0% (95CI 0.1-20%), respectively (p=0.0004). Overall, 26 lesions developed RN (3.66%). CI of RN at 2 years was 2.1% (95%IC 0-7.2%) for 15 Gy and 4.8% (95%IC 0-9.9%) for ≥ 20Gy (P=0.02). Overall, CI of RN at 2 years for lesions ≤ 1cm, and > 1 cm, were 1.4% (95%CI 0-4.4%), and 8.9% (95CI 0-19%), respectively (p=0.0014). Conclusion: For lesions ≤ 1 cm, there were no LFs or RN events for DP of 15 Gy. For lesion > 1 cm, there was no significant difference (p=0.344) when comparing DP of 15 Gy (10.2%) versus ≥ 20 Gy (7.7%) for LF, but there was a significantly higher CI of RN for lesions treated with ≥ 20 Gy (9.3% versus 3.8%, P=0.049). Conclusion: Our results suggest that, with respect to LF, 15 Gy is equivalent to ≥ 20 Gy for small- to medium-sized (≤ 2 cm) BM treated with Gamma Knife SRS. However, DP ≥ 20 Gy correlated with a higher CI of RN, especially for lesion greater than 1 cm.

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Resumo: Background At our institution, we commonly treat brain metastases (BM) adjacent to critical structures with a reduced marginal dose prescription (DP) to reduce the likelihood of toxicity. We sought to evaluate the impact of DP on local failure (LF) and radionecrosis (RN) for small-to-medium-sized BM (≤ 2 cm) from non-small cell lung cancer. Methods A prospective registry of BM patients treated with gamma knife SRS between 2008 and 2016 was reviewed to determine per lesion rates of LF and RN. Each lesion was followed until LF or RN or at last MRI follow-up. Defined criteria were used to differentiate LF from RN. Whole brain irradiation (WBI) was a censoring event. Freedom from LF (FFLF) and RN (FFRN) were calculated using the Kaplan-Meier product-limit method. Log-rank test was used as a univariate analysis to compare potential predictive factors of LF or RN events. Results From 1,465 potential subjects, 345 small-to-medium-sized BM from 151 lung cancer patients were evaluated. Median radiographic follow-up was 10.2 months. Median lesion volume and diameter were 0.17 cm³, and 0.81 cm, respectively. Median OS was 17 months (95CI 14.9-19.09) with 1 year OS of 69.13% (95CI 62.9-74.4%). The DP for 71 lesions (21%) was 15 Gy, and ≥ 20 Gy (median 21 Gy; 20-24Gy) for 274(79%). Most lesions were ≤ 1 cm (65%). Median number of SRS courses was 2 (1-4) and 36 patients received salvage WBI. Sixteen lesions (4%) developed LF and 12 (3%) developed RN. Freedom from local failure at 1 year (FFLF) for 15 Gy, and ≥ 20 Gy, was 80%, and 95%, respectively (p<0.05). FFLF for lesions ≤1cm, and >1 cm, was 95%, and 78%, respectively (p<0.01). Freedom from RN at 1-year (FFRN) for DP 15 Gy, and ≥ 20 Gy, was 98%, and 96%, respectively (p=0.3). FFRN for lesions ≤ 1cm, and > 1 cm, was 98%, and 93%, respectively (p<0.05). FFLF and FFRN for lesions ≤1 cm and >1 cm, according to DP, are shown in Table 1. Conclusion Lesions > 1 cm showed improved FFLF improvement with higher DP, although this trend did not reach statistical significance. Prospective randomized evaluation is urged to define the optimal DP.

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Resumo: INTRODUCTION: Depression is a serious and potentially fatal mental disorder, present in 4.4% of the global population (WHO). The symptoms of depression are greater than sadness associated to the diagnosis of a brain tumor and may become very disabling. Patients with brain tumors are at risk for developing depression because, in addition to the psychological distress of adjustment to the diagnosis of a devastating prognosis disease, depression can also be caused by neurophysiological and mechanical effects of the tumor itself and surgery, or the effects of medications used during treatment, or adjuvant therapies. OBJECTIVES: To evaluate the role of depression in patients with brain tumors; prevalence of depression; importance of recognizing depression in the multidisciplinary care; impact of depression as a determining factor in the worsening clinical course of the disease, decreased quality of life (QOL), and reduced survival. Best depression screening instruments. METHOD: Literature review (1955 to 2017) in PubMed/Medline, LiLACS, Cochrane Library and Scopus. RESULTS: High Prevalence: Prevalence of depression in patients with brain tumors may reach 93%, depending on the methodology and diagnostic criteria used. Systematic review and meta-analysis of 2017 estimates a prevalence of 21.7%. Multidisciplinary Care: The QOL is the highest priority and should guide clinical decisions, the multidisciplinary team should be sensitive to distress symptoms and inquire about them in follow-up visits (NCCN-2017). Worsening clinical course: Depressive patients showed less response to chemotherapy and increased rates of deep vein thrombosis, seizures and systemic infections. Decreased QOL: Although scores reflecting depression, fatigue and emotional distress were interrelated, the presence of depressive symptoms was the single most important independent predictor of QOL. Decreased Survival: The survival was shorter among patients who were actively depressed near the time of surgery. Diagnosis: Recommended instruments for depression screening validated in these patients: HADS-D ≥7 (Hospital Anxiety and Depression-Subscale Depression Scale) and PHQ-9 ≥10 (Patient Health Questionnaire-9). CONCLUSIONS: Depression is a common, under-diagnosed and potentially treatable complication in brain tumor patients; it showed a statistically significant negative impact on the course of the disease, QOL and survival in these patients; it should be actively investigated and managed.

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Resumo: Background: Pain is defined as an unpleasant sensory and emotional experience related to actual or potential tissue damage. Chronic pain is a debilitating symptom, which impairs the patient’s quality of life. It is often multifactorial and multidimensional. The International Association for the Study of Pain (IASP) defines neuropathic pain as pain caused by injury or dysfunction of the somatosensory nervous system. There is much less information available on the prevalence of neuropathic pain in children and adolescents. Pain in pediatrics is a subject that is still little discussed, and the incidence of chronic pain in children is underestimated. Conditions that may be the cause of this type of pain are increasingly recognized in pediatrics and include complex regional pain syndrome, HIV-associated neuropathy, post trauma, and phantom limb pain, and it is commonly reported in cancer patients. The study of neuropathic pain is already justified by its high prevalence, but it is the effect on the patient’s quality of life that makes it even more significant. Not only is neuropathic pain more debilitating than nociceptive pain, but it is also more challenging to diagnose and treat. Part of this is due to the difficulty of assessing pain in the pediatric age group, either because of the complexity of children expressing their pain or because of the limitation of validated instruments to evaluate this population. Objectives: To evaluate the child’s pain through his perception and collaboration - using the diagrams. Methods: a retrospective study through the evaluation of medical records of patients who attended the outpatient clinic of pain in Hospital of childhood cancer. Results: Patients with neuropathic pain from 3 to 21 years through the diagram locate, indicate their score and describe their pain. In our children, the primary cause of neuropathic pain was central nervous system tumors, followed by cases of amputation by bone tumors and neuropathic pain caused by chemotherapy. Conclusion: Neuropathic pain has been detected from very young children to adolescents. To better approach this symptom, a correct diagnosis is necessary for early treatment, so it is essential to evaluate the pain with instruments that allow the child to describe his/her pain; we believe that the diagram can help children to express better their pain leading to treatment and optimal care.

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Modalidade Aprovada: Pôster

Tema: SNOLA - Cuidados paliativos

Título: ESTUDO DE CASO – ATUAÇÃO DO TERAPEUTA OCUPACIONAL EM ONCOLOGIA PEDIÁTRICA

Autores: Fabiana Yumi Takatuzi; Walkyria de Almeida Santos; Silvia Wasserstein;

Resumo: Estudo de Caso – Atuação do Terapeuta Ocupacional em Oncologia Pediátrica
Apresentação do caso: Estudo de caso sobre acompanhamento de paciente (R.O.P.) portador de Neurofibromatose tipo 2 (NF2), Schwannoma bulbo cervical, Meningiomas, Neurinoma de acústico bilateral, Polineuropatia relacionada à NF2 e atual tetraparesia, pelo serviço de Terapia Ocupacional em um serviço especializado em oncologia pediátrica, desde 2015. R.O.P., atualmente com 18 anos de idade, passou por diversas intervenções cirúrgicas. Apresentou períodos de total dependência nas atividades de vida diária básica e instrumental, uso de cadeira de rodas para locomoção e uso órteses de posicionamento de membros superiores (MMss). Apresentou também períodos de independência funcional, em fases de estabilidade clínica.Discussão: Em sua última internação (agosto/17 à jan/18) manteve assistência pelo serviço de Terapia Ocupacional, onde foram realizadas intervenções visando orientações aos familiares em relação a mudanças de decúbito no leito, posicionamento e prevenção da síndrome do imobilismo. Foram realizados estímulos perceptivos visando melhora e manutenção da qualidade de vida, além de confecção, treino, acompanhamento e orientação do uso de dispositivos de tecnologia assistiva, entre eles órteses de posicionamento de MMss e “adaptação” para o uso de smartphone de maneira funcional e independente. Para a confecção das órteses de MMss foram utilizadas placas de material termomoldável a baixa temperatura e velcros para fixação. Para a composição do dispositivo para acessar o smartphone foram utilizados: protetor bucal de borracha duplo, pedaços de placa de material termomoldável e ponteira específica para uso de equipamentos com display touch screen (tela sensível ao toque). Considerando sua efetividade funcional e prevenção de qualquer prejuízo orgânico futuro, foram feitas consultas e discussões com a dentista da equipe, que realizou avaliação clínica e orientação relativa aos cuidados na higiene oral, além de modelar o protetor bucal à arcada do paciente, para posterior confecção do aparato adaptativo. Comentários Finais: A atuação do terapeuta ocupacional dentro de um serviço especializado em oncologia pediátrica contribui não só no processo de reabilitação do paciente, mas também permite seu acesso aos meios sociais e de comunicação de maneira independente, através de recursos de tecnologia assistiva.

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Resumos do SNOLA 2018
Código: 65620

Modalidade Aprovada: Pôster

Temário: SNOLA - Cuidados paliativos

Título: NURSING INTERVENTIONS IN PALLIATIVE CARE IN CHILDREN AND ADOLESCENTS WITH CANCER: INTEGRATIVE REVIEW

Autores: AMANDA DANIELLE RESENDE SILVA E SOUSA; Liliane Faria da Silva; Claudia Christy de Oliveira Tenório;

Resumo: Palliative care for children is a specialty in itself, consisting of active total care of the body, mind and spirit of the child and support the family. Data from the World Health Organization in 2017 show that globally, of all people requiring palliative care, only 14% have access, proving the importance of new research in this area. Nursing interventions in palliative care should begin at the time of diagnosis along with curative care and perpetuate throughout the treatment, managing pain management and all the overall symptoms presented. The child and adolescent diagnosed with cancer will probably only achieve an excellent quality of life with early recognition and the implementation of palliative care. Objective: to identify, in scientific productions, nursing interventions in the development of palliative care in children and adolescents with cancer. Method: integrative review of the literature in the databases: CINAHL, MEDLINE, IBECS, LILACS and SCIELO, conducted in October and November 2017. Results: 18 articles were analyzed that met the inclusion criteria. The synthesis of knowledge was made by two categories of analysis: integral nursing interventions in palliative care and nonpharmacological nursing interventions in palliative care. The results showed that, among the articles selected, Brazil is the country with the largest number of publications and nonpharmacological interventions have appeared in greater numbers divided into: music therapy, massage, play application, early consultation of palliative care, social and a meta-analysis that brought exercise as the most effective intervention in reducing fatigue in children and adolescents. In the integral interventions, it was observed the search for comfort, communication and relationship team, child and family. We conclude that greater emphasis should be given to palliative care in nursing and academic training, that further studies in the search for the best evidence should be performed to support interventions in nursing practice.

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Temário: SNOLA - Cuidados paliativos

Título: O USO DE TÉCNICAS DE CONSERVAÇÃO DE ENERGIA EM ONCOLOGIA PEDIÁTRICA

Autores: WALKYRIA DE ALMEIDA SANTOS; Fabiana Yumi Takatuzi; Sílvia Wasserstein;

Resumo: O Uso de Técnicas de Conservação de Energia em Oncologia Pediátrica

Introdução - As técnicas de conservação de energia são recursos empregados para melhoria no manejo de sintomas relacionados ao tratamento oncológico e pediatria, assim como a fadiga. Consistem em orientações e treinos específicos para redução do gasto energético durante a realização de atividades básicas de vida diária, visando à manutenção ou à retomada da funcionalidade destes pacientes. Objetivos - Este estudo tem como objetivo relatar a experiência do emprego das técnicas de conservação de energia pela terapia ocupacional, no ambulatório de reabilitação oncológica em hospital de especialidade, através do trabalho de orientação ao paciente e cuidadores, visando o controle da FADIGA decorrente dos tratamentos. Métodos - Trata-se de um relato de experiência de caráter descritivo, com base nos casos atendidos pela terapia ocupacional em setor de reabilitação oncológica, em hospital de câncer infantil em São Paulo, capital. Resultados - Como resultado verificou-se que a utilização das técnicas de conservação de energia foi adequada e eficaz, no sentido de conscientizar pacientes e cuidadores sobre a eficácia do planejamento das atividades funcionais diárias (ABVD e AIVD) , e no sentido de controlar a fadiga vigente durante o tratamento oncológico, preservando condições de independência motora e autonomia dos pacientes.

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Resumo: CONTEXT: According to the World Health Organization-WHO, "palliative care consists of the assistance promoted by a multidisciplinary team, aiming at improving the quality of life of the patient and their relatives, in the face of a disease that threatens life, through prevention and alleviation of suffering, early identification, assessment and treatment of pain and other physical, psychological and spiritual symptoms." This modality of treatment is important in several health fields, making it necessary to know and apply these care in a way supported by professionals dealing with terminal patients. Among these patients, the neurosurgical patient occupies a prominent position, since the severity and the great frequency of neurosurgical diseases that require palliative medicine as a form of treatment is well marked in tertiary hospitals. OBJECTIVES: To identify the level of knowledge about palliative care in neurosurgical patients of the professionals of specialized units in Neurosurgery of a tertiary hospital (Dr. José Frota Institute-IJF-Fortaleza-CE), as well as to analyze the relationship of sociodemographic variables and complementary training with knowledge in palliative care. METHODS: A descriptive and cross-sectional study was carried out in a probabilistic sample composed of 88 health professionals (neurosurgeons, nurses, nursing technicians, physiotherapists, psychologists). The data were standardized following the Knowledge Questionnaire on Palliative Care-QCCP (Lopes & Ribeiro, 2012), which was adapted to the reality of neurosurgical patients after literature review. RESULTS: We found that 35.3% of the professionals have insufficient knowledge about palliative care in neurosurgical patients. Extracurricular training in palliative care is still rare in our midst, 10% of the sample had this type of education. Most of the professionals revealed knowledge about the concept, communication, family support and organization of palliative care, however, there is a significant deficit on specific aspects of palliative intervention in neurosurgical patients (ie pain control pathways, wound care). CONCLUSION: From the results obtained, we have seen that the dissemination of knowledge about palliative medicine in terminal neurosurgical patients is of paramount importance. Even professionals who have neurosurgical patient care routines present deficits in the knowledge and practices of care in this group of patients, corroborating the need for actions aimed at qualification in this specific area.

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Modalidade Aprovada: Pôster
Temário: SNOLA - Cuidados paliativos

Título: PERCEPÇÃO MÉDICA SOBRE CUIDADOS PALIATIVOS, OBSTINAÇÃO TERAPÊUTICA E TERMINALIDADE EM UM HOSPITAL ONCOLÓGICO PEDIÁTRICO NO INTERIOR DO ESTADO DE SÃO PAULO

Autores: LETÍCIA MIRANDA; Dileiny Geronutti Antunes; Érica Boldrini;

Resumo: O câncer não consiste em uma doença única, com causa única. É um grupo de doenças distintas, com diferentes causas, manifestações, tratamentos e prognósticos. Na infância e na adolescência o câncer é a primeira causa de morte por doenças em todas as regiões do Brasil. Apesar dos avanços técnicos e científicos alcançados pela oncologia e do empenho dos profissionais da saúde, muitas doenças ainda ameaçam a continuidade da vida e o objetivo do tratamento passa a visar não somente a cura, mas também melhorar a qualidade de vida, prevenir e aliviar o sofrimento do paciente e de sua família. JUSTIFICATIVA: A equipe médica está familiarizada em lidar com a doença, no entanto nota-se uma grande dificuldade em lidar com as particularidades dos indivíduos que não podem ser curados; junto com a doença, os pacientes trazem consigo seus medos, dúvidas, expectativas, juntamente com as de suas famílias. Tratar desses pacientes como um todo, atendendo todas suas necessidades, vai além do cuidar, torna-se um desafio. OBJETIVO: apreender a percepção médica sobre cuidados paliativos, obstinação terapêutica e terminalidade, em um hospital oncológico pediátrico, no interior do Estado de São Paulo. MATERIAIS E MÉTODOS: Trata-se de um estudo qualitativo descritivo exploratório. O referencial utilizado para a análise dos dados qualitativos será o Método de Análise de Conteúdo proposto por Bardin. RESULTADOS: Os dados coletados foram organizados nos seguintes temas: Cuidados Paliativos na formação acadêmica; A falta de conhecimento e a busca por informações; Conceções sobre Cuidados Paliativos; Obstáculos enfrentados para realização dos Cuidados Paliativos; Obstinação terapêutica; Terminalidade e uma boa morte. CONCLUSÃO: Fica evidenciado que temas como cuidados paliativos, obstinação terapêutica e terminalidade são pouco abordados na formação dos profissionais da saúde, transformando em uma dificuldade ao se deparar com determinadas situações no decorrer de sua vivência profissional.

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Temário: SNOLA - Cuidados paliativos / SLAOP - Biologia e Patologia

Título: THE PREVALENCE AND MANAGEMENT OF BREATHLESSNESS AT THE END OF LIFE IN CHILDREN WITH CANCER

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Resumo: Background: Dyspnea is one of the most frequent symptoms in children with advanced cancer requiring palliative care to manage this symptom. Although it is a subject of high importance, there has been little research on dyspnea in children at the end of life. Dyspnea is a common and distressing symptom, which causes intense suffering when present at the end of life; it is usually progressive and is challenging to manage. This symptom is present mainly in the advanced stages of primary or metastatic cancer in the lung, and also in the presence of pleural effusion or carcinomatous lymphangitis. It is widely accepted that opioids are safe and effective for treating dyspnea. Nevertheless, no opioids have the authorization to treat shortness of breath. Objective: The purpose of this review is to investigate the prevalence and causes of dyspnea in children with cancer at the end of life and to identify the measurements, treatments, and the evaluation of therapeutic interventions. Methods: It was reviewed all the data in the available electronic medical records of patients attended at the palliative care service of the Institute of Pediatric Oncology from April 2012 to April 2017. Results: Dyspnea was the first most common symptom in our group of patients followed by pain. The primary cause of dyspnea is pulmonary metastases. Moreover, the dyspnea has been classified as an extremely distressing symptom by patient and family Many of these patients received opioids for schedule and rescue dose for shortness of breath. Opioid therapy was considered useful for most patients who suffered from dyspnea; they had an improvement in this symptom, and besides the opioid, many of these patients received corticosteroids and oxygen therapy. Conclusion: Dyspnea is a frequent symptom at the end of life that causes suffering, and opioids positively influence it. However, there is a need for further studies and follow-up of children and adolescents with dyspnea to assess the response of opioid to improve symptom control and quality of life.

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Temário: SNOLA - Neuro Imagem

Título: BRAIN METASTASIS IN REFRACTORY HEPATOBLASTOMA. CASE REPORT AND LITERATURE REVIEW.

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Resumo: Hepatoblastoma is the most frequent malignant liver tumor in children, occurring especially in premature infants with extremely low weight. The world incidence rate is only 3.8:1.000.000. This study reports a case of high risk hepatoblastoma in a twin female, 4 year old patient with previous history of prematurity, low weight admitted at a Cancer Center in Sao Paulo for diagnosis and specialized treatment. After first-line chemotherapy and a liver transplant, the patient relapsed with multiple and bilateral pulmonary nodules. After the two cycles of second-line treatment the pulmonary lesions persited and the patient evolved with neurological symptoms such as vomits, hyporeflexia and seizures. A brain computed tomography identified metastatic lesions. The neurological status worsened rapidly and the family opted for palliative care, and the patient passed away. Most often, hepatoblastomas are seen as restricted to the liver or with locoregional extension damaging lymph nodes in the hepatic hilum. When talking about distant metastatic disease, pulmonary damage is most frequent, followed by bone metastasis, more rarely. Other sites are even rarer and unexpected, such as brain metastases with case descriptions in medical literature. Reports of rare cases in medicine are essential, since the act of sharing such experiences may lead to a better approach in diagnosis and treatment for future patients.

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Título: NEUROPLASTICIDADE E RESSECÇÃO TUMORAL

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Resumo: O estudo consiste no relato de caso do paciente masculino, com 15 anos atualmente. Este fora admitido em nosso serviço pelo pronto atendimento da pediatria com queixa de cefaleia intensa de caráter inespecífico. Em vista disso, iniciou se o manejo clínico do paciente e investigação diagnóstica. Realizado o estudo de imagem, observamos os seguintes achados positivos: Ressonância Nuclear Magnética de crânio: área hipointensa em T1 e hiperintensa em T2 localizada na topografia de lobo frontal esquerdo com aparente atenuação discreta após injeção de contraste. À difusão, apresenta importante restrição. Ressonância Nuclear Magnética de crânio com espectroscopia: lesão expansiva em lobo frontal esquerdo com pico de colina e perfusão aumentada em duas vezes, sugerindo glioma. Em vista disso, programou se uma biopsia estereotáxica cerebral, acusando um anatomopatológico característico de glioblastoma multiforme. Ao exame clínico pré-operatório, o paciente se encontrava se afásico e hemiparético à direita. Realizamos uma primeira abordagem por craniotomia frontotemporoparietal para remoção parcial do tumor. Uma segunda abordagem foi programada, contou com inspeção microcirúrgica para obtenção da maior ressecção possível e programação para acompanhamento ambulatorial, radioterapia em 60cGy e quimioterapia com Temozolamida. Em acompanhamento ambulatorial, notou se uma recuperação das funções da fala e motoras. Por conta da inesperada recuperação, fora aventada a hipótese de que este paciente tenha apresentado um evento neuroplástico que permitiu essa recuperação funcional. Embora não tenham sido realizados testes que comprovaram a dominância esquerda da área de Broca, como o habitual, podemos confirmar esta hipótese pela correlação clinicorradiológica: o paciente apresentava uma lesão, macroscopicamente visível, em lobo frontal esquerdo, acometendo giros frontais superiores, médio e inferiores. Neste momento, o paciente já apresentava afasia, sugerindo a presença habitual da área de Broca. Para identificar este evento fora realizada uma ressonância funcional, acusando a migração da área de Broca. Após as ressecções, o paciente teve a amputação de toda área acometida pela neoplasia, se estendendo desde o lobo frontal até o giro pré central. Após os procedimentos, nosso paciente apresentou uma melhora gradativa de suas funções, atualmente, comunica se normalmente e não apresenta prejuízos na qualidade de vida, mantendo um KPS DE 100%.

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**Título:** ULTRASONOGRAPHY DURING SURGERY TO APPROACH CEREBRAL METASTASES: EFFECT ON KARNOFSKY INDEX SCORES AND TUMOR VOLUME

**Autores:** MARCELO DE LIMA OLIVEIRA; Marcelo de Lima Oliveira; Helder Picarelli; Marcos Roberto Menezes; Robson Luis Amorim; Manoel Jacbsen Teixeira; Edson Bor-Seng-Shu;

**Resumo:** Background: The main objectives of treating a cerebral metastasis (CM) are to reach local control of the disease and to improve patients' neurological status. Objective: The objective of this study was to analyse the effect of conventional surgery supported by intra-operative ultrasound (IOUS) during CM resection. To perform this analysis, we determined Karnofsky post-operative scores (KPS) and the grade of residual tumor in surgical bed. Methods: Patients with a CM diagnosis were included in this study. Surgical treatment was either supported or not by IOUS. Pre- and post-operative KPS was determined by oncology team and cerebral tumor volume was estimated through pre- and post-operative MRI; surgical team determined whether it was possible to perform a total CM resection. Results: 78 patients underwent to surgical treatment (35 with and 43 without IOUS); in IOUS group post-operative KPS was higher (80 versus 70, p=0.045) and KPS evolution was superior (p=0.036), especially in the following patients subgroups: a difficulty of tumor resection ranking score<4 (p=0.037), tumor in an eloquent area (p=0.043), tumor not associated with vessels or nerves (p=0.007), and solitary lesions (p=0.038). The residual tumor volume was lower in the IOUS group (9.5% and 1.6 mm3 versus 30.8% and 9 mm3, p=0.05). In patients with a KPS≥70, the residual tumor volume was categorized as <10% or ≥10%, and 62% of patients had <10% residual tumors (76% in the IOUS group and 45% in the non-IOUS group; p=0.032 and OR=3.8). Conclusion: IOUS may improve post-operative KPS and in decreasing residual tumor volumes in CM surgical treatment.

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Título: A RARE CASE REPORT: EPIDERMOID CYST IN THE FOURTH VENTRICLE

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Resumo: Epidermoid tumors are dysontogenic lesions and relatively rare tumors that comprise 0.2 to 1.8% of intracranial tumors. They are generally located off the midline, and arise from ectodermal inclusions during neural tube closure. The most common location for epidermoid cysts (EC) is the cerebellopontine angle (40%-50%), with the fourth ventricle being a less frequent location (approximately 17%). We report a case of an EC that arises from the fourth ventricle. LFSS, 47 years old, male, admitted to the hospital reporting “difficulty to walk”, that progressing for one year. He presented progressive tetraparesis, worse to the left, speech impairment and moderate I headache. He denied having nausea, emesis or visual disturbances. Upon examination: awake and oriented; dysarthria, ataxic gait; no cranial nerves affected; power: graded 4 to musculature of right arm and leg and 3 to the left. Normal sensitivity; intention tremor and dysmetria to the left; normal deep reflexes; Hoffman and Babinski signs were absent. CT imaging demonstrated a hypodense mass in the fourth ventricle (isodense in relation to cerebrospinal fluid), without calcifications. MRI imaging revealed a hypointense mass in T1, without contrast uptake and hyperintense in T2, with diffusion restriction. Intraoperatively, the lesion had a pearled aspect and was not infiltrative of surrounding tissues. The lesion was successfully resected microsurgically, with no intraoperative complications. The patient was transferred to the ICU postoperatively. He developed sepsis and respiratory failure, subsequently progressing to death. Later histopathological analysis confirmed the hypothesis of EC. The appearance of a EC in the fourth ventricle is a rare presentation. ECs can be asymptomatic for many years as they grow slowly from the desquamation of cells and from the breakdown of keratin. The average age of symptom onset is from 20 to 60 years. Symptomatic EC are rare in children. There is no predominance of gender. The symptoms depend on the location of the lesion. Headache and cranial neuropathy (especially nerves V, VII and VIII) are common findings. EC resembles cerebrospinal fluid imaging studies. Due to extrinsic complications, this patient had an undesirable outcome. Nevertheless, in the management of such tumors, the literature suggests that early diagnosis and complete excision or near total excision of this benign tumor can be curative, with good prognosis and little morbidity.

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**Título:** ANTERIOR MIDLINE MAGNUM FORAMEN MENINGIOMAS: SURGICAL PROCEDURE, COMPLICATIONS AND PITFALLS ON 21 CASES

**Autores:** Paulo Henrique Pires de Aguiar; Bruno Camporeze; Mariany Carolina de Melo Silva; Webster de Oliveira Vitoria; Giovanna Matricardi; Fábio Jundy Nakasone; Maick Fernandes; Tatiana A. Vilasboas; Daniel A. Gripp; Renata Simm; Marcos Vinicius Calfat Mauldaun

**Resumo:** BACKGROUND: Meningiomas of foramen magnum has been described associated to an uncommon frequency and yet they have been considered a challenge with regards the adequate surgical management. Therefore, this tumor requires special considerations about the technique pitfalls, detailed anatomy of region and the landmarks for this procedure aiming the total resection and good outcome. OBJECTIVE: Discuss the complications and pitfalls surgical technique used for resection of foramen magnum meningiomas based on our experience in comparison to previously reported data. CASUISTIC AND METHODS: Twenty-one patients affected by magnum foramen meningiomas located medially and anteriorly were included in this study. All the patients were submitted at surgery by our surgical team during the period from 2004 to 2016. All of them were surgically approached by far lateral approach with resection of occipital condyle, associated to neurophysiological intraoperative monitoring. The Simpson grade of meningioma resection as well as the non visual morbidity and the mortality rates were analyzed. RESULTS: The study was performed with 15 female and 6 male, whose average age was 43.4 years. Regarding the complications, the presence of CSF (Cerebrospinal Fluid) leak (28%, n=6), hemorrhage (4.7%, n=1), and lesion of lower cranial nerves (9.5%, n=2) were observed during the procedure. Furthermore, meningitis after management of CSF leak (4.7%, n=1), worse of spasticity of lower bilateral limbs (9.5%, n=2) and thromboembolism (19%, n=4) was observed as complications in the postoperative. The grades of resection were Simpson I (47.6%, n=10), II (38%, n=8) and III (14.2%, n=3). During the follow-up, whose average was 48 months, was observed four recurrences in 18 cases, which were treated by radiotherapy devices. Preoperative tumor embolization was utilized in just one case of our casuistic. CONCLUSION: Based in the experience of authors and literature, the main conclusion about the surgical approach of foramen magnum meningiomas is about the side of procedure, which is based on the vertebral artery’s location and sigmoid sinus venous dominance. More studies are necessary to define the prognostic factors for patients in this scenario.

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Título: ARTERIOVENOUS MALFORMATION ASSOCIATED WITH A GLIAL NEOPLASM: CASE REPORT

Autores: RAFAEL PEREIRA MONTEIRO; RAFAEL PEREIRA MONTEIRO; Ricardo Lourenço Caramanti; Raysa Moreira Aprígio; Marcos Devanir da Costa; Kleber Gonzales Echeverria; Helbert Palmiero Manuca; Hugo Leonardo Dória; José Maria Campos Filho; Suely Melo; Carmen Lúcia Pent

Resumo: CASE REPORT: A 26-years-old man was admitted on the Emergency Department referring sudden headache and seizures 7 hours before admission. His past medical and familial history were unremarkable. On neurological examination, the patient presented a left side grade four hemiparesis. Laboratorial blood tests were found within normal range. Cranial computed tomography on admission revealed right temporal lobe hematoma. Encephalic T2 weighted magnetic resonance imaging (MRI) showed a hypointense lesion in the right temporal lobe with mass effect and perilesional edema. The angiography showed a temporal nidus with middle cerebral artery feeders and venous drainage to internal cerebral vein and sylvian vein. The patient underwent an avm microsurgical resection. The biopsy revealed the association between an avm and a high grade astrocytic glioma with positive S100 and GFAP testing. DISCUSSION: The association between brain tumors and arteriovenous malformations is rare, with 0,1% of frequency. The most common associated tumor is high grade glioma. This association pathophysiology is uncertain. There are speculations about secondary changes in the glial tissue caused by chronic isquemic injury generated by the arteriovenous malformation. The association between AVM and tumor can present more commonly with mass effect or bleeding, sometimes requiring emergency surgery to treat intracranial hypertension. Cases in wich a highly vascularized lesion is suspected, we considerate a pre operatory angiography to exclude AVM association. The most common surgical complications involve intraoperatory bleeding also intra and post operatory edema. FINAL COMENTS: The association between brain tumors and arteriovenous malformations is rare and needs to be confirmed by brain angiography. The best surgical strategy can be defined by MRI and angiography analysis. In general, we advise to use a large craniotomy to avoid intraoperative edema complications.

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Resumo: BACKGROUND: The astroblastoma is a primary brain tumor originated from the neuroepithelial tissue. This neoplasm has been described epidemiologically associated to a bimodal distribution, histopathologically little characterized and clinically unpredictable. OBJECTIVE: The authors report a case of an intra-axial astroblastoma mimicking an extra-axial neoplasm showing bone remodeling and review the literature about this rare type of tumor. CASUISTIC AND METHODS: This paper was based in one case of an astroblastoma retrospectively reviewed associated to bibliographical consultation based on indexed databases, using language as selection criteria, choosing preferably recent articles in Portuguese, Spanish or English. CLINICAL PRESENTATION: The authors present a case of a 3-year-old boy admitted with generalized seizures without neurological deficits. The imaging investigation with CT and MRI showed an intra-axial contrast enhanced mass with 20 mm in diameter located in the right frontal lobe associated to ipsilateral frontal calvarial remodeling. The patient was treated with successful total tumor resection. In the histological study, the features were suggestive of low-grade astroblastoma. In the immunohistochemical analysis, the neoplastic cells exhibited high expression for GFAP and S100; focal staining for EMA and Ki67; and absence of significant staining Sinaptofisina and CAM 5.2. Currently, the patient is without neurological deficits or seizures, 3 months postoperatively. RESULTS AND DISCUSSION: Although the histopathological and immunohistochemical features of this case are in agreement with the literature, the radiological characteristics shows extra-axial neoplasm features such as bone remodeling ipsilateral to the lesion. Based in the literature only 2 other reports (Eom et al., 2008 and Yunten et al., 1996) showed extra-axial findings in astroblastomas, described as calvarial erosion associated or not with bulking of the cerebral cortex by peripherally located well circumscribed, highly enhancing masses. CONCLUSIONS: Astroblastoma has been described as a rare brain tumor, potentially, curable. However, the unclear clinicopathological correlation and absence of optimal management defined in the literature makes this tumor a neurosurgical challenge, incorporating the differential diagnosis of intra axial tumors in the childhood presenting with extra-axial mass features.
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Temário: SNOLA - Neurocirurgia

Título: ASTROCITOMAS INTRACRANIANOS: EXPERIÊNCIA PESSOAL INTERINSTITUCIONAL

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Resumo: OBJETIVO: Analisar experiência pessoal da assistência neurocirúrgica a 89 pacientes portadores de astrocitomas intracraniianos diagnosticados e tratados durante os anos 2002-2014. MÉTODOS: Cento e três pacientes com lesões cerebrais suspeitas de glioma foram tratados por técnica microcirúrgica padronizada entre janeiro de 2002 e dezembro de 2014. RESULTADOS: Dos 103 pacientes operados com a suspeita inicial, 89 (86%) se tratavam de astrocitomas, confirmados por histopatologia: astrocitoma pilocítico grau I (cerebelar, 6 casos); astrocitoma difuso grau II (9 casos); astrocitomas grau III (5 casos) e astrocitomas grau IV (69 casos), distribuídos entre 75 homens e 14 mulheres com idade variando entre 14 e 78 anos. O principal critério para indicar cirurgia foi a presença de efeito volumétrico significativo, identificado nos exames de imagem pela perda de sulcos, fissuras e cisternas próximos a massa, distorção do sistema ventricular, com ou sem desvio da linha media e déficit neurológico em progressão (hemiparesia / alteração de fala). EVOLUÇÃO: Todos os casos operados retornaram à primeira consulta ambulatorial no primeiro mês após a intervenção, momento em que foram avaliados do ponto de vista clínico e cirúrgico e encaminhados para tratamento adjuvante, quando indicado (Grau III e IV). Nos seis meses seguintes, 90% dos pacientes retornaram para seguimento, entretanto, essa taxa despencou para menos de 10% a partir do primeiro ano, sendo que apenas 4 dos casos inicialmente tratados retornaram para avaliação no segundo ano após a cirurgia, todos Grau II, em estado de progressão da doença. Por outro lado, quase a totalidade (~96%) dos astrocitomas grau III e IV (74 pacientes) inicialmente submetidos a cirurgia agressiva, deixaram de receber tratamento adjuvante, em razão da dificuldade de acesso a consultas, a exames de imagem e devido a problemas operacionais. CONCLUSÕES: A divulgação dos resultados individuais e institucionais possui relevância para o progresso da especialidade, uma vez que ao se partilhar detalhes relacionados a assistência, dificuldades técnicas, estratégias de tratamento, complicações, morbidade/mortalidade e soluções individualizadas, oferece subsídios para a comunidade científica acerca da realidade regional e nacional, promovendo o debate dos aspectos desfavoráveis na assistência medica a esse universo de patologias, e a possibilidade de gerar soluções duradouras para promover a melhoria da especialidade como um todo.

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Título: AWAKE CRANIOTOMY FOR BRAIN MAPPING IN LOW GRADE GLIOMA PATIENTS - AN INITIAL EXPERIENCE

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Resumo: Introduction Grade II gliomas are diffusely infiltrative and evolutive tumors. They are often related to eloquent brain areas and they spread beyond the hyperintensity T2-FLAIR image in MRI. Therefore, anatomical limits are not sufficient, the resection should be extended until functional boundaries. Objective To demonstrate our initial experience with awake craniotomy in the treatment of Low Grade Gliomas (LGG). Methods Between April 2017 (when we performed our first case) and January 2018 a total of 22 patients underwent awake craniotomy. We excluded from this analysis 6 patients with high grade glioma and 2 patients with very disseminated tumors (>3 lobes involved). This is a prospective study of 14 consecutive patients with LGG submitted to an awake craniotomy for brain mapping by direct electrical stimulation (DES) to the brain. Results From 14 patients, 8 (57.1%) were male. The mean age was 38.2 years-old (range 24-55 years-old). The mean time of symptoms before surgery was 1238 days (range 29-7300 days). The most common symptom was seizure (85.7%), followed by headache (14.3%) and behavioral disorder (14.3%). The mean pre-operative Karnofsky Performance Status (KPS) was 90 (range 70-100). The mean volume of the tumors was 77cc (range 3-320cc) and the frequency of lobe involvement were: frontal (85.7%), insular (21.4%), temporal (14.3%), parietal (14.3%) and occipital (7.1%). Supratotal resection was possible in 14.3% of patients, total in 14.3% of patients, subtotal (>90% of resection) in 42.8% of patients and partial in 28.6% of patients. The mean hospitalization time after surgery was 7.2 days (range 6-17 days). The mean KPS at discharge was 84.2 (range 70-100). Three patients (21.4%) presented new deficits at hospital discharge, but only 1 patient (7.1%) had a permanent moderate deficit at the last follow up. There was no death. Four patients in this series were previously under conservative treatment because of the risk of surgery without awake brain mapping. Conclusion: Awake craniotomy with brain mapping in LGG resection is safe, it leads to the extension of indications of LGG surgery within eloquent areas; to a decrease in the risk of sequelae; and to improvement of the quality of tumor resection. And it is also resource-sparing, as it leads to a reduced hospitalization time and substitute other more expensive technologies. With fewer sequelae we may also expect fewer expenses in rehabilitation and faster return to work.

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Título: AWAKE SURGERY FOR PEDIATRIC BRAIN TUMOR - SURGICAL AND ANESTHETIC CONSIDERATION OF A CHALLENGE PROCEDURE

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Resumo: CASE PRESENTATION: A 12-year-old male patient presented to neurosurgical ambulatory with her mother who reported neuropsychological delay especially concerning his speech. During neurological evaluation it was noticed the presence of a left superior temporal gyrus and insular lesions that did not enhance in MRI, so it was made the hypothesis of a low grade tumor. Because of it this lesion was symptomatic it was proposed neurosurgical approach. However the lesion was in a eloquent area and surgery could worse the symptoms. Aiming to reduce the risk of neurologic sequelae it was proposed an awake surgery for performing a better brain mapping and avoid complications. The surgery was successful with gross total removal, allowed a proper cortical mapping and no neurological deficits happened. He improved of his previously symptoms after some weeks. DISCUSSION: Awake surgery nowadays is a common neurosurgical procedure especially for low grade tumors located in eloquent areas. However not every patients could undergo to this procedure. Neuropsychological evaluation is mandatory since patient collaboration is essential. Few studies have referenced the psychological impact of this event in the pediatric population. Surgeon and anesthesiologist collaboration is crucial for performing an effective awake procedure specially in childhood that constitute a group in which there are only few cases and the neurosurgical experience is scarce. COMMENTS: Awake neurosurgery in childhood could be safely performed for eloquent lesions if proper evaluation and collaboration among surgeon and anesthesiologist is performed. Despite only few cases have been reported, this type of oncological procedure should become more popular.

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CASE REPORT A 56-year-old, caucasian man, with a three-month progressive frontal headache, weight loss and dizziness, presented clinical worsening with nausea and mental confusion two days before admittance. He showed no pupillary changes or focal signs. The biochemical tests were normal and the MRI showed a left frontal lobe 5 cm nodular/cystic lesion with great edema area, isointense in T1 and T2 enhancement contrast and restriction of nodular part in the diffusion. On spectroscopy there was high choline/creatine and choline/N-Acetylaspartate ratios. Due to the important mass effect and size we performed an uneventfully complete microsurgical resection. The patient evolved with complete neurological improvement and was subjected to screening in search for other sites of metastases. Liver nodules were observed on the CT of the abdomen and he received treatment using radiotherapy and chemotherapy. Unfortunately, after 3 months of treatment he passed away due to liver complications. DISCUSSION: Merkel cell carcinoma (MCC) is a rare neuroendocrine tumor characterized by small cells with round nuclei, monomorphic, with basophilic nucleus and cytoplasm minimum associated with high mitosis number and apoptotic bodies. The Immunohistochemical is critical to differentiation of the MCC, showing cytokeratins 8,18 and 20 positive, with sensitivity greater than 90%. The cytokeratin CK20 is mainly used to differentiate lung small cell carcinoma and was positive in 87% of MCC. The cromogranin -A, is present in 52% and enolase in 50% of cases. We can still find somatostatin, neurofilament, CD56 and synaptophysin positives. It typically affects elderly caucasians with light skin types with a mean age of 69 years, but can occur in immunosuppressed young people including: organ transplant recipients, HIV-infected individuals and those with B-cell malignancies, with local recurrence tendencies. Cerebral metastases from MCC are extremely uncommon with less than 20 cases published in the literature. When it is possible to locate the skin lesion, it can be a fast growing, painless, firm, non-tender, shiny, flesh-colored or bluish-red, intradermic nodule. In addition to brain, are common metastasis to liver, lung and the skin itself. FINAL CONSIDERATIONS: The encephalic Merkel cell carcinoma is a very rare metastasis which needs to be differentiated from small cell lung and salivary cell carcinoma. The Brain metastasis needs to be resected to avoid intracranial hypertension.

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Resumo: This article presents a case report of an atypical localization of infantile myofibroma (IM), an uncommon mesenchymal tissue tumor that may present at all ages, normally at birth or in early infancy. A one and a half-year-old male child reported in the Department of Neurosurgery of Brasilia Children Hospital with the only complaint of a slow growing nodulation on the left frontosphenoidal area since 5 months, without any history of pain, trauma, fever, weight loss, or other constitutional symptoms. On palpation, it was well located, firm, fixed to the underlying bone and non-adhered to the superficial skin, measuring 2.5 x 2.5 cm, without associated lymphadenopathy. A CT scan revealed a well circumscribed, homogeneous, isodense soft tissue lesion inside the frontal bone with underlying erosion, without necrosis or peripheral edema. Many differential diagnoses were considered, including benign tumors as histiocytosis, glioma, lymphanghioma, and also malignant tumors as neuroblastoma, rhabdomyosarcoma, and leukemic masses. After group discussion about the tomography and the clinical examination, it was decided do to enucleation for resection of the lesion with established myofibroma in post-operative histopathological study. There was no signs of recurrence after a follow up period of 4 months. Even though rare, this neoplasm is the most common fibrous tumor of infancy without defined cause, although familial and post traumatic cases have been reported. This case was unusual because the solitary IM lesion was in an atypical location, inside bone tissue, and according to the literature, the solitary form of myofibroma occurs most often in the dermis and subcutis. To the best of our knowledge, the present case is among rare reported cases located in this area and with bone involvement. Since the rarity of the lesion and the leak of symptoms lead to misdiagnosis, and the prognosis of this tumor is variable, although mostly good, the early and surgical treatment and the histopathologic confirmation are mandatory.

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Título: CAVERNOUS SINUS EWING’S SARCOMA FIVE YEARS FOLLOW UP

Autores: ANDRÉ SIMIS; Samuel Simis;

Resumo: Ewing's Sarcomas (ES) are malignant tumors mostly found in children and young adults and located in the limbs and axial skeleton. Similarities between ES and Peripheral Primitive Neuroectodermal Tumors (pPNET) in light microscopy, immunohistologic and genetic findings are found, thus ES and pPNET are considered a single group with varying degrees of neuroectodermal differentiation. There are few intracranial case reports and only five Cavernous Sinus ES in the literature. A 21-year-old male patient presented with diplopia. Examination revealed a left VI nerve palsy. Cranial magnetic ressonance imaging revealed a contrast enhancing ovoid lesion in the left cavernous sinus. Pre temporal craniotomy with cavernous sinus was performed with partial resection and symptomatic recovery. The tumor consisted of small round cells at histopathological examination positive for CD99, CD56, BCL-2 and Ki 67 positive in 10% of the cells. Patient returned five years later with small lesion growth and diplopia.

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**Resumo:** Introduction: Functional MRI has been recognized as a valuable adjunct to improve the safety of brain surgery in eloquent areas, but there are controversies regarding its sensibility and specificity in patients with low grade gliomas. Methods: we studied 12 patients with supratentorial low grade gliomas in which awake surgery with brain mapping was indicated. We performed language fMRI with three different protocols (nomination, word discrimination and verb generation) in addition to motor fMRI. We processed fMRI images as a 3D model with superposed areas of activation, and utilized neuronavigation and the sulcal anatomy of the patient to identify areas of activation intraoperatively. We then compared those areas of activation with the findings of surgical brain mapping with direct cortical stimulation (DCS). Results: We had complete concordance in the motor mapping between fMRI and DCS, but in language mapping we found one case of false negative (area detected by surgical brain mapping but no by fMRI) and one case of false positive (posterior left temporal area detected by fMRI but with negative surgical mapping). Conclusions: fMRI in patients with gliomas has several caveats. Areas with compensable functions can show hyper metabolism and increase blood flow without inducing a deficit if resected, and areas that are critical for a certain functions may not show on fMRI due to the particular nature of MRI signals and blood flow around and inside gliomas. Direct cortical stimulation continues to be the gold standard for brain mapping in this population.

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INTRODUCTION: Alterations of plasmatic sodium are alterations frequently found in the neurosurgery postoperative period and are associate with the worsening of the these patients neurological state. Sodium disorders may manifest as hyponatremia or hypernatremia, being the first, most frequent in neurological patients. These alterations can be explained by three different syndromes: Cerebral Salt Wasting Syndrome (CSWS), Syndrome of the Inappropriate Secretion of Antidiuretic Hormone (SIADH) e Diabetes Insipidus (DI). And these disorders are common after brain tumor surgeries. OBJECTIVES: The goal of this study is assess the impact of the sodium disorders in prognostic after brain tumors surgeries. METHODS: 59 patients were analyzed, submitted to tumor resection in 2017. This is a retrospective, quantitative, transversal and descriptive study. Were analyzed age, gender, tumor type, sodium level, neurological deficits and Glasgow Outcome Scale (GOS) Statistical analysis was considered the significance p less than 0.05 and the confidence interval of 95%. The software SPSS V17, Minitab 16 and Excel Office 2010 were used for statistical analysis. RESULTS: The first outcome is that the cumulative variation of sodium level was (-2,29%). Also our analysis suggest that posterior fossa tumors caused a greater fall in sodium level (33,82%). Our finding demonstrated that motor neurological deficits and those of consciousness are associated with higher levels of sodium (19,76%). Finally, it is important to note that the patients who had worse performance in GOS were precisely those who presented higher variation of sodium levels in the postoperative period. CONCLUSIONS: The changes in sodium levels in the postoperative period seem to impact the prognosis of surgeries for brain tumors.
Código: 65703

Modalidade Aprovada: Pôster

Temário: SNOLA - Neurocirurgia

Título: EPIDEMIOLOGICAL ANALYSIS OF 1546 SURGICAL BRAIN TUMORS IN A PERIOD OF 15 YEARS - PECULIAR FEATURES OF A BIG CASE SERIE

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Resumo: INTRODUCTION: Brain tumors have increased incidence in the past years especially because of the availability of neuromaging methods. Early diagnosis has influence in extent and quality of life mainly in high grade tumors. Epidemiology knowledge helps to predict risk factors and guide screening and treatment of these patients. Oncology is a dynamic science with peculiar features. The newest WHO brain tumor classification of 2016 brought some new information that could help improve treatment. All aspects should be evaluated aiming to increase quality of life and overall survival. OBJECTIVE: Describe a fifteen years experience of a oncological neurosurgery hospital concerning peculiar features of patient epidemiology.

METHODS: Data about gender, age, familiar history, histological type, topography and surgery performed of all operated brain tumor during 15 years (January 2002- July 2017) were collected through the Neurosurgery discipline database of a huge tertiary hospital. The most common neoplasms were better studied and an epidemiological profile concerning the data collected was performed.

RESULTS/CASE SERIE: In this period 1546 patients were diagnosed and submitted to neurosurgical procedure in this hospital. Among them 13,5% were younger than 18 years, 47,8% were male patients and 52,2% female. Supratentorial tumors were more common (84,3%). Considering histologic subtypes brain metastasis corresponded to 17,8%, followed by meningiomas with 17,7% and high grade glioma (anaplastic astrocytoma and glioblastoma) with 16,2%. CONCLUSION: This analysis allow to delineate an oncological profile and by this way optimize screening and treatment. It could be noticed that more and more pediatric patients are diagnosed with brain tumors and so nowadays this must be considered as an important differential diagnosis in childhood. Furthermore it could be noticed an early and increased diagnosis of brain metastasis that few days ago were not considered to neurosurgical approach.

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Resumo: Introduction: Pituitary adenoma is usually benign and is the third most common intracranial tumor (10-15%), mainly affects the adenohypophysis, being rare in neurohypophysis. Among the pathologies that affect the pituitary gland, it is the most common. The classification is based on size, hormonal function, clinical findings and histology. According to their function they may be divided into non-functioning and functioning. The functioning tumors may be: prolactinomas (40%), GH (20%), ACTH (5-10%), LH and FSH (1%) and TSH secreting adenoma (1%). Objective: to perform an epidemiological study on pituitary tumors, with emphasis on immunohistochemical exams in a Cancer Hospital in the city of João Pessoa - PB. Method: Epidemiological, retrospective, observational and transverse study of the descriptive type, based on medical records from January 2015 to November 2017. The data were submitted to anatomopathological and immunohistochemical results. Results: 27 pituitary tumors were found, representing 20.45% of the tumors operated in the neurosurgery department of the hospital, being 17 in men (62,9%) and 10 in women (37,1%). 16 tumors were not submitted to immunohistochemical exams. The remaining 11 tumors were distributed in 2 prolactin and ACTH producing tumors (18.2%), 3 prolactinomas (27.3%), 5 ACTH secreting tumor (45.45%) and 1 non-functioning (9.09%), being the less frequent tumor. Concerning the 27 patients, the mortality rate was 0 (0%), 5 patients had liquoric fistulas (18,5%), 2 hypocortisolism (7,4%), 8 transient diabetes insipidus (29,6%) and 2 permanent diabetes insipidus (7,4%). Conclusion: Considering the presented data, among the pituitary tumors that had their immunohistochemical analysis concluded, the ACTH secreting adenoma was the most predominant corresponding to 45,45%, diverging from the literature, which appoints prolactinoma as the most common. Pituitary adenomas are frequent intracranial tumors, and represent a significant portion of the total number of tumors submitted to surgery at the service of the present study. The increased incidence in men (62,9%) also requires attention, since both prolactinomas and corticotropinomas are more prevalent in women. Therefore, it is expected that this study may contribute to strengthen the critical readings regarding the subject, aiming to contribute to optimize approaches and services provided to these patients.

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Resumo: Introduction: Spinal tumors can be classified as intramedullary, intradural extramedullary, extradural and primary spinal tumors. Spinal cord tumors are rare, but may account for up to 10% of tumors of the central nervous system, which may be primary or secondary, the latest being more prevalent. The most frequent symptom is back pain that worsens at night, which progresses to paraesthesia, analgesia and paresis. In children, such tumors may remain asymptomatic for long periods. The most frequent tumors are metastasis, meningiomas and schwannomas. Looking at tumors derived from nerve cells, ependymomas and astrocytomas are the most common. Surgical treatment of these tumors is usually difficult and carries a significant risk of postoperative neurological complications. Objective: To present a statistical analysis of spinal tumors submitted to neurosurgery at a cancer hospital in João Pessoa – Paraíba, from January 2015 to November 2017 and to compare the local incidence with information found in the literature. Method: Retrospective, observational and cross-sectional epidemiological study, carried out through the search of medical records of patients submitted to neurosurgery at a cancer hospital in João Pessoa - PB between January 2015 and November 2017. Results: Of the 148 tumors operated, 21 (14.2%) were spinal surgeries. Of these 132, 13 were secondary tumors (62%), where 11 were metastasis (84.6%), 1 was an hemangioma (7.7%) and 1 a sarcoma of Ewing (7.7%). Eight primary tumors (38%) were found, 4 of which were multiple myeloma (50%), 3 schwannomas (37.5%) and 1 neurofibroma (12.5%). No ependymoma or astrocytoma was found, although they were found with relative frequency in the literature. Secondary tumors were more frequent in comparison to primary tumors, which corroborates the data found in the literature. Conclusion: This study is important for exposing relevant epidemiological data related to spinal tumors in Paraíba. It is important to develop new epidemiological work in the region, with a larger number of patients and analyzing other variables, in order to consolidate the incidence of these disorders in João Pessoa and in Paraíba.

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INTRODUCTION: The hospital under study is a reference center in the fight against cancer in the Northeast, serving 72.2% of all patients with cancer in the state of Paraíba. According to data presented by the hospital, there was an increase of 43.11% on the new cases of cancer in a comparison to 2014 and 2015, going from 5,137 to 7,352. Among the cases presented, there is a prevalence of breast tumors in women and prostate cancer in men.

OBJECTIVE: To present an epidemiological profile with general statistical analysis of tumors with neurosurgical involvement in the last 3 years in a reference hospital of cancer in Paraíba.

METHODS: Retrospective, cross-sectional, descriptive and observational study with a survey of patients with tumors undergoing neurosurgery from August 2015 to November 2017. RESULTS: A total of 148 patients were referred to the neurosurgery service and 132 surgeries occurred due to tumors. The sex distribution was 75 women and 57 men (56.8% and 43.2%, respectively). Considering the primary tumors, 83 cases (56%) were found, among them 27 pituitary adenomas (18.24%), 15 meningiomas (10.13%), 14 glioblastomas (9.45%), 7 diffuse astrocytomas grade II (4.73%), 5 schwannomas (3.38%), 2 anaplastic grade III astrocytomas (1.35%), 2 hemangioblastomas (1.35%), 02 medulloblastomas (1.35%), 2 oligodendrogliomas grade II (1.35%), 1 craniopharyngioma (0.67%), 1 degree pilocytic astrocytoma (0.67%), 1 neuroblastoma (0.67%), 1 neurofibroma (0.67%), 1 oligoastrocytoma (0.67%), 1 oligodendroglioma grade III (0.67%) and 1 solitary fibrous tumor (0.67%). Among the secondary tumors, 49 tumors (33.11%) were submitted to surgery, 13 of which came from the breast (8.78%), 8 lung (5.4%), 4 multiple myeloma (2.7%), 4 who are still under pathological study (2.7%), 2 colon-rectum (1.35%), 2 prostate (1.35%), 2 thyroid (1.35%), 2 uterus (1.35%), 1 acute myeloid leukemia (0.67%), 1 bladder (0.67%), 1 B-cell non-Hodgkin’s lymphoma (0.67%), 1 cholesteatoma (0.67%), 1 Ewing’s sarcoma (0.67%), 1 hemangioma (0.67%), 1 hip (0.67%), 1 mediastinum (0.67%), 1 skin (0.67%), 1 stomach (0.67%) and 1 uterus-ovary (0.67%). CONCLUSION: Pituitary tumors represent 10% to 15% of primary brain tumors on the literature, but the data obtained reveals a larger number than expected. The neurosurgery service in this hospital started in 2015, which corroborates the relevance of this study, given that it establishes a general parameter of visualization of the tumors submitted to surgery.
Código: 65585

Modalidade Aprovada: Pôster

Temário: SNOLA - Neurocirurgia

Título: EXTRAVENTRICULAR CENTRAL NEUROCYTOMAS IN THE SELRAR/SUPRASELLAR REGION: CASE REPORT AND SYSTEMATIC REVIEW

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Resumo: BACKGROUND: Central neurocytomas (CN) are neuronal neoplasms with little aggressive behavior. Epidemiologically, they represent lower than 1% of central nervous system neoplasms, and sellar/suprasellar extraventricular CNs are extremely rare, with only 12 reported cases in the literature. OBJECTIVE: We describe a case of an extraventricular CN in the sellar/suprasellar region, as well as analyze the epidemiological, clinical, radiological, pathological, and treatment features of previous case reports in the literature. CASUISTIC AND METHODS: This paper was based in one case of extraventricular CN in the sellar/suprasellar region retrospectively reviewed associated to the systematic review, using indexed databases. CLINICAL PRESENTATION: The authors report a case of male patient, 27-year-old, who presented with progressive vision loss during the last 4 years and serious bilateral keratoconus. The patient developed left amaurosis and right temporal hemianopsia after undergoing bilateral corneal transplantation, which was detected during campimetry testing, and subsequently underwent magnetic resonance imaging, which revealed a hypophyseal neoplasm. The endocrinological evaluation showed a global loss of the pituitary function. The patient underwent a successful gross total resection by a two-stepwise surgery (transsphenoidal approach and cranio-orbital zygomatic approach) that showed to be in the histopathological and immunohistochemical analysis an extraventricular CN. Currently, the patient has improvement of right temporal hemianopsia after 18 months of surgery and control MRI shows absence of tumor recidive. RESULTS AND DISCUSSION: After analysis of the 12 cases previous described in the literature, we showed no sex-specific tendency in these lesions with a mean age of presentation of 49.75 years. Regarding the initial symptoms of such tumors in this region, the visual impairment occurred in 91.7% of the cases, and all cases presented in the literature show invasion of the cavernous sinus. Although the initial clinical features have been mainly described in the literature, we showed that half of the studies did not describe properly patient’s hormonal status, approach and follow-up. CONCLUSIONS: Although extraventricular CN are rare, careful preoperative consideration of its anatomy, pathophysiological and radiological features can enhance the treatment outcomes. We believe that further studies are needed to understand such a rare pathology.

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**Título:** FLUORESCEN GUIDED SURGERY FOR AN INTRAVENTRICULAR GRADE II EPENDYMOMA: CASE REPORT.  
**Autores:** RENAN MAXIMILIAN LOVATO; JOÃO LUIZ VITORINO ARAUJO; ALINE LARIESSY CAMPOS PAIVA; JOSÉ CARLOS ESTEVES VEIGA;  

**Resumo:** Introduction Ependymomas are rare tumors corresponding to 3-5% of adult intracranial gliomas. Ventricular tumours usually grow along the surface of the lateral ventricle of the septum pellucidum. The extent of resection is the most consistent factor affecting outcome and second-look surgeries have been proposed with the aim of achieving gross total resection. Surgery should also aim for preservation of a good quality of life. Sodium fluorescein has been used in neurosurgery and is a drug with a safe profile. The use in high grade gliomas and in brain metastasis has shown to be of great value and increase significantly the rates of gross total resection. The use of fluorescein in low grade lesions, and in all ependymomas is still not established. This is the first report of its use in an intraventricular grade II ependymoma.  

**Methods** A 3D printed device was designed with light filters that could fit any microscope. It is possible easily alternate during the surgery between the white light and the fluorescence mode. The excitation filter for the light source is a band-pass filter with high transmission rate and that allows only wavelength between 425 and 490nm, and, as a barrier, a longpass filter that cuts of light under 520nm, enhancing the fluorescence contrast. Results A 53-year old female patient with history of treated breast cancer was referred to neurosurgical department with progressive headache and a brain MRI revealing a ventricular lesion with unilateral right ventricle ectasia. She did not present metastatic lesions and had a controlled disease. Just before skin incision it was administrated 5mg/kg of sodium Fluorescein. A transcallosal transforaminal approach was performed with gross total resection and proper functional preservation and good recovery. The tumor showed fluorescence after the attachment of the device. The patient did not presented any complication related to the drug administration. Conclusions Ependymomas are rare tumors of the central nervous system, and gross total resection is the most consistent factor affecting the outcome. This is the first report of the use of fluorescein guided surgery for a grade II intraventricular ependymoma. The tumor showed a low fluorescence, unlike the high grade tumors, but it was easily differentiated from the surrounding normal neural tissue. It is necessary to have a bigger number to know the exact value of this technique for these lesions.  

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**Título:** IMPLEMENTATION OF A DAILY ALGORITHM FOR EARLY DISCHARGE AFTER BRAIN TUMOR SURGERY: A RETROSPECTIVE COHORT STUDY

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**Resumo:** Purpose: The routine of postoperative patient care in specialized cancer centers has undergone significant advances in the last decades. Almost universally, the protocols adopted by hospitals have sought to reduce length of stay (LOS) after surgery through programs to improve the quality of care and optimize postoperative recovery. Recently, one neurosurgeon of our institution has adopted a daily algorithm for hospital discharge (DAHD). Thus, we designed a retrospective cohort study to evaluate whether there was a difference in LOS after the introduction the DAHD compared to the traditional postoperative management of patients who underwent brain tumor resection by a single surgeon at a single institution. Methods: All consecutive patients who underwent brain tumor resection in 2017 were analyzed. Demographic and procedure-related variables, complications, and clinical outcomes within 30 days after surgery were collected and compared in patients before (pre-implementation) and after (post-implementation) the DAHD. Results: 47 patients who had been submitted to brain tumor resection in 2017 were analyzed. The baseline demographic characteristics were similar between the groups, except for a American Society of Anesthesiologists (ASA) score that were 1 or 2 in 19 (59.4%) patients in the control group and in 14 (93.3%) patients in the intervention group, p=0.020. After the DAHD implementation, LOS after surgery in days decreased significantly (5.30 versus 3.24 days; p=0.034). The number of patients who were discharged within day 1 or 2 after surgery was significantly higher after DAHD protocol (3.1% versus 33.3%; p=0.009). The number of performed imaging tests were significantly reduced after the implementation of the algorithm (4.5 versus 2; p=0.046). Major and minor complications rates, readmission rate, and unplanned return to hospital in 30-day follow-up were comparable between the groups. Conclusion: Our results indicated a reduction of the LOS after the implementation of a DAHD compared to the traditional postoperative management (control group). The number of performed imaging tests was also lower in the post-implementation group. The DAHD seems to be a safe and cost-effective management of the patients after brain tumor surgery.

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Título: INDICATIONS OF 5-AMINOLEVULINIC ACID AND INTRAOPERATIVE MRI IN GLIOMA SURGERY: FIRST CASES IN LATIN AMERICA IN A SINGLE REFEREE CENTER

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Resumo: Introduction: The benefits of the extent of resection in gliomas improved with the combination of 5-aminolevulinic acid (5-ALA) and intraoperative magnetic resonance imaging (iMRI) have been demonstrated in previous studies. Objectives: To establish the indications of 5-ALA and/or iMRI for brain gliomas. Methods: we demonstrate 63 cases of intracranial gliomas who underwent image-guided surgery using 5-ALA or with iMRI. All patients were also subjected to postoperative MRI to evaluate the extent of resection (EOR). Other adjuvant intra-operative techniques utilized (awake surgery, electrophysiological stimulation and monitoring) were performed according to tumor location. Results: 18 tumors were 5-ALA fluorescence negative (2 grade I, 14 grade II, 1 grade III and 1 grade IV) and 45 tumors were 5-ALA fluorescence positive (3 grade II, 3 grade III, 37 grade IV and 2 high grade astroblastoma - undetermined due to rarity). In 27 of the 45 positive cases, a safe 5-ALA free resection was achieved. In 5-ALA negative cases, the iMRI findings oriented the resection, were 11 cases of complete resection. Incomplete tumor removal occurred to avoid neurological impairment due to infiltration of eloquent areas. Conclusions: The use of iMRI and/or 5-ALA showed an improved result in glioma surgery, offering a safer maximum extent of resection. In 5-ALA positive cases (mostly high grade), the fluorescence was a better tool. In 5-ALA negative cases (mostly low grade), the iMRI was decisive to determine the extent of tumor removal.

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Título: INTRACRANIAL SOLITARY FIBROUS TUMOR: A CASE REPORT.

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Resumo: Case report: a 27-year-old female presented to the Department of Neurosurgery of a cancer hospital in the city of João Pessoa - PB in 2016 with progressive headache and vomiting, one year after being operated on in another service, with magnetic resonance imaging showing falcina lesion in the middle third of the superior sagittal sinus. Surgery was performed with biopsy material sent to the pathology service, which resulted in fusocellular neoplasia permeated by vessels of hemangiopericytic pattern, which together with the immunohistochemical study that revealed CD34 (QbEnd / 10) and BCL-2 (124) positive, S-100, EMA (E29) and HUC-1 negative, the diagnosis of intracranial solitary fibrous tumor (SFT) was confirmed. Patient progressed without neurological deficit. Discussion: SFT are rare spindle-cell mesenchymal neoplasm with frequent pleural site. Extrapleural involvement is uncommon and of the central nervous system is even rarer, with the first reported case in the literature in 1996. The few cases reporting central nervous SFT usually describe location in the spinal cord. The literature reports that SFT of the central nervous system correspond to about 0.09% of meningeal tumors. Intracranial STF can be confused with meningioma and hemangiopericytoma due to radiological and histological similarities, which makes the immunohistochemical study mandatory when suspected. While SFT has a strong and diffuse positivity for CD34 between 80-100% of cases, with frequent positivity for BCL-2 and negativity for S-100 and EMA, the intensity and extent of positivity for CD34, when present, among hemangiopericytomas is usually weak and patchy. In addition, meningiomas are often (80%) positive for EMA and negative for CD34. Although the case presents a histological pattern of hemangiopericytoma, it presents a typical immunohistochemical profile of SFT, essential for diagnosis. Conclusion: SFT is a relatively new entity and our knowledge about it is still limited. The diagnosis of SFT is based mainly on the immunohistochemical profile, since it makes differential diagnosis with meningioma and hemangiopericytoma.

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Resumo: Introduction: Tuberculum sellae and medial sphenoid ridge meningiomas may involve or infiltrate the internal carotid artery (ICA) and the optic apparatus (OA). Radical resection of these tumors is related to the grade of involvement of these structures. A classification based on the grade of involvement of the ICA and OA as well as the surgical techniques used to remove these tumors is presented. Material and Methods: The involvement of ICA and OA was evaluated in a surgical series of 176 sellar and parasellar meningiomas (51 olfactory groove, 38 tuberculum sellae, 3 dorum sellae, 12 anterior clinoid and 72 medial sphenoid ridge). Medial sphenoid ridge meningiomas were classified in three types: “En masse A” - no involvement of the ICA and OA, “En masse B” – with involvement of the ICA and OA and “Invasive” - tumors with invasion of the cavernous sinus and orbital fissure. Surgical approaches used were: fronto-lateral, pterional and fronto-orbito-zygomatic. High flow bypass was done in four patients due to infiltration of the ICA. Results: In 18 cases of tuberculum sellae meningiomas the optic canal was involved and the cavernous sinus in three. Radical removal (Simpson 1) was possible in 34 cases. In 4 cases due to infiltration of cavernous sinus a Simpson 3 removal was achieved. Postoperative visual deterioration (one blindness) occured in 3 cases. Simpson’s resections grades 1&2 was possible in all cases of tumors type “En masse A” (20 cases), in 20 out of 22 patients with type “En masse B” and in 4 cases with invasive sphenoid ridge meningiomas Conclusion: Grade of involvement of ICA and OA in sellar and parasellar region meningiomas is the most important factor for radical surgical removal. The proposed medial sphenoid ridge meningiomas classification in three types showed high correlation with the grade of resection.

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Título: IS AWAKE CRANIOTOMY AN IDEAL APPROACH TO GLIOMA RESECTION IN MOTOR AREA? ANALYZES OF FUNCTIONAL OUTCOME
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Resumo: BACKGROUND: The awake craniotomy (AC) for neoplasms in language area has been showed higher rates of success when compared to general anesthesia (GA). However, a question still remains regarding its real indication in glioma resection in motor cortex when compared to GA surgery associated to intraoperative monitoring. OBJECTIVES: Discuss the complications, results and prognosis of glioma resection in motor cortex through GA and AC. CASUISTIC AND METHODS: The authors selected retrospectively, from 2014 to 2017, patients affected by gliomas in motor cortex, associated or not to language area, that were surgically treated by GA or AC. The included patients were analyzed for the categorical variables: age, gender, tumor grade, anatomopathological examination, preoperative and postoperative complications, surgical technique performed, side of procedure, functional area affected by tumor, resection level and Karnofsky score. The authors adopted a significance level of p<0.05 in the statistical analyzes. RESULTS: The authors showed 65.9% (n=29) male and 34.1% female (n=15) in the study, whose the average of age was 47.2+14.6 years, and average of follow-up was 14.4+10.1 months. The tumor grade was were classified in low-grade (40.9%, n=18) and high-grade (59.1%, n=26). The gross total resection (GTR) were performed in 65.9% (n=29). The intraoperative and immediate postoperative complications were presented in 30% and 5% of AC and GA group, respectively. The Karnofsky score evaluated during outcome showed statically significant improvement (p<0.00 in postoperative evaluation of 12 months) in patients underwent to AC when compared to GA group. Fisher’s test showed statically significant association (p=0.01) between the tumor resection adjacent to motor cortex alone in right hemisphere in both of surgical approaches. While AC was statically significant (p<0.00) in the resection of motor cortex, associated or not to language area, in left side when compared to GA. CONCLUSION: The AC showed lower rates of GTR and significant higher rates of intraoperative and immediate postoperative complications. However, the significant higher rates in the long-term functional outcome (12 months) in patients underwent to AC when compared to GA. Lastly, based in the brain hemisphere, the indication of AC may be implying only in enhance of complications and mortality rates in disturbs adjacent or in right motor area.

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Case presentation: A 33-year-old woman developed progressive headache, nausea and vomiting in August of 2016, subsequently progressing to cerebellar syndrome with disequilibrium and locomotor ataxia, so the patient was referred to the otorhinolaryngologist. Magnetic Resonance Imaging (MRI) was requested, which revealed an expansive lesion in the posterior fossa, with epicenter in vermis and right cerebellar hemisphere and total collapse of the IV ventricle, suggesting a medulloblastoma. After 45 days, the patient sought evaluation of neurologist, and the lesion was admitted as a supposed primary neoplasm. The patient was referred to referral hospital to perform microsurgery for intracranial cerebellar tumor on 2017. Anatomopathological exams revealed cerebellar tissue with multiple granulomas involving eggs and larvae of Schistosoma mansoni. After diagnosis, she was treated with anthelmintic and physiotherapy for rehabilitation. Post-surgical MRI demonstrated reduction of the lesion, and the patient progressed with improvement of headache, cerebellar syndrome and other symptoms. Discussion: Neuroschistosomiasis can be classified as acute, chronic or pseudotumoral. The case reported showed granulomas involving eggs with great immune reaction, therefore, being classified as pseudotumoral form of neuroeschistosomiasis, which, like only other 14 cases described in the literature and histologically proven, reported from 1984 to 2009, was not associated with other severe forms of visceral presentation, thus evidencing the rarity of the case. Cerebellar schistosomiasis manifests clinically with increased intracranial pressure and mass effect in the posterior cranial fossa with different degrees of headache, ataxia, dizziness, and emesis. However, signs of meningeal irritation, loss of muscle strength at the extremities and disturbances of consciousness may be found due to increased intracranial pressure. Generally, the prognosis is good, once adequate treatment is instituted, which consists, as in the other cases, of both total surgical excision of the lesions and treatment with specific anthelmintic. Conclusion: The suspicion of tumor in the cerebellar region should be accompanied by detailed anamnesis in endemic areas for a possible diagnosis and best conduct. The early treatment of this neuroparasitosis through surgical excision, corticosteroid therapy and antihelmintics may lead the patient to a good recovery.

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Título: METASTASIS OF THE MOTOR AREA - ANALYSIS OF THE MOTOR DEFICIT IN THE IMMEDIATE POSTOPERATIVE PERIOD AND MOTOR RECOVERY IN 30 DAYS

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Resumo: Brain metastasis is the most common intracranial tumors in adults and is five to ten times more common than primary brain tumors. With this, lesions located in the motor area are increasingly frequent and are feared by neurosurgeons and patients. The treatment options are multiple but must be individualized for each patient. Surgery is still the main method of treatment, but data in the world literature on the risks of motor deficit in the immediate postoperative period and the chances of recovery of strength are scarce. This study presents the experience of the author and co-authors, makes a database analysis of 150 patients with motor area metastasis treated with surgery. In the series presented by the authors, patients who have an injury to the motor area and who are operated on according to the modern micro neurosurgical technique present an overall risk of motor deficit in the immediate postoperative period or worsen from a previous motor deficit of 18%. However, the vast majority of these patients (79%) will show improved strength in the first 30 days and will be without a motor deficit (strength V degree) or better than in the preoperative period (strength IV). Only 5.3% of the patients remained with motor power worse than the preoperative state after 30 days of surgery. These data are the results of a general analysis, where the motor area was considered as a single location, not taking into account the proposed subdivision. The authors propose a subdivision of the motor area and present a clear, objective and specific data on the risks of motor deficit and the outcomes after the surgical treatment of these lesions for each of the proposed motor areas.

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**Título**: METASTATIC DISSEMINATION TO PARASELLAR REGION OF PAPILLARY RENAL CELL CARCINOMA: CASE REPORT AND SYSTEMATIC REVIEW

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**Resumo**: BACKGROUND: Metastasis of renal cell carcinoma to the sellar region is rare, such that it represents lower than 1% of the cases of metastasis to the sellar region of which only 10% are of the papillary histological subtype. OBJECTIVE: This paper aims to describe a case report of metastatic dissemination of renal carcinoma to the parassellar region, as well as analysis the clinical and pathological features. METHODS: A case report based on retrospective analysis of patient’s medical records associated to systematic review of similar cases described in the literature, using the databases LILACS, SciELO, MEDLINE, BIREME, PubMed. CLINICAL PRESENTATION: The authors reported a clinical case of male patient, J.C.C., 59-years-old, affected by left palpebral ptosis after five years of surgical approach with left total nephrectomy due to papillary renal cell carcinoma diagnosed. In the complementary investigation, we showed the presence of parassellar expansive process resulting from renal cell carcinoma on computed tomography and magnetic resonance imaging of sinuses, orbits and brain. Based in the chest computed tomography that showed the presence of pulmonary and pre-tracheal metastasis, the neurosurgical team chose not to perform the surgical treatment. RESULTS AND DISCUSSION: After tabulation and analysis of the 50 cases described in the literature, we showed that 62% (n=31) of cases occurred in males, whose mean age and mean metastatic diagnosis time were 58 years and 40.2 months, respectively. Regarding the initial symptoms, the visual impairment occurred in 70% (n=35) of cases, diabetes insipidus in 28% (n=14), hypopituitarism in 58% (n=29) and absence of symptoms in 26% (n=13) of cases. Although the initials clinical features have been described adequately, we showed that 46% (n=23) of the studies did not describe disease-free survival, whose average was estimated at 15 months based on 54% (n=28) of the described cases. CONCLUSION: Metastasis sellar is a rare variant of renal cell carcinoma poorly described in the literature, mainly regarding the prognosis of these patients. However, it should be considered as differential diagnosis of pathologies in this anatomic region.

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Título: MINIMALLY INVASIVE APPROACH TO INTRAMEDULLARY SPINAL METASTASIS - A CASE SERIE AND A REVIEW

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Resumo: INTRODUCTION: Nowadays metastatic disease is more frequently because of screening programs are more efficient and the diagnosis could be done earlier. Central nervous system (CNS) is more and more affected mainly when there are metastases in other systems. Spine is rarely affected and when this occur, the implants compromise the vertebral bodies in almost all cases. A primarily intramedular lesion with metastatic origin is very uncommon specially if there is not bone commitment. OBJECTIVE: Describe a case serie of intramedullary metastasis emphasizing clinical and radiological features besides a literature review about this theme. METHODS: All intramedular metastasis operated by the Neurosurgery Discipline in a huge tertiary hospital during a period of one year were analyzed. Clinical manifestation, image and surgery details were described. Also a literature review was performed. RESULTS/CASE SERIE: 3 cases were included in this study. It was one male patient and two female. The first was secondary to a kidney cancer and the others are manifestations of breast neoplasm. All patients presented thoracic intramedular lesion with clinical picture of weakness in inferior limbs that had a quickly progression. Minimally invasive neurosurgical approach through laminoplasty was performed to access these lesions and multidisciplinary oncological treatment. CONCLUSION: Intramedullary metastasis are very rare, although should be considered as a differential diagnosis of patients whom presented with a known cancer diagnosis and neurological deficits with quickly progression. Neurosurgical approach should be considered according to neurological status and disease control. Multidisciplinary treatment for a proper decision should be a priority.

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Título: MULTIPLE MENINGIOMA AFTER BREAST CANCER AND RADIOTHERAPY: CASE REPORT

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Resumo: Case presentation: A 54-year-old woman was diagnosed with breast cancer in 2004 and submitted to treatment based on right breast mastectomy, whose pathological results revealed infiltrating ductal carcinoma. Chemotherapy and radiotherapy sessions were performed in referral hospital. 10 years later, scintigraphy showed lesions in the Central Nervous System with a suspicion of metastasis. Intracranial lesions were diagnosed by computed tomography on 2015 and confirmed by Magnetic Resonance Imaging (MRI), which quantified the three largest in volume in the left regions: temporal, parieto-occipital and frontal. The lesions were treated with daily radiotherapy sessions for a month without response, manifesting adverse reactions to treatment, such as focal seizures, and cerebral edema. On 2015, the first surgery was performed, with the removal of the lesions in the frontal and temporal regions. Immunohistochemical exams revealed histological aspects of meningioma grade I with areas of necrosis. The second surgery, on 2016, removed lesion in the parietal-occipital region, demonstrating the same histological grade. Post-surgical MRI showed no signs of residual/relapsed neoplastic lesion. Discussion: Multiple meningioma are defined as "two spatially separated meningiomas in a patient with no signs of neurofibromatosis.", they are rare conditions, corresponding to about 1 to 9% of patients with meningioma. The relationship of these tumors to breast cancer and radiotherapy is defined. Radiation-induced meningiomas (RIM) have different characteristics from non-radiation-induced meningiomas (RIM), they tend to be more aggressive, recurrent and histologically atypical. Therefore, one can understand the necrosis found in the anatomopathological examination, at the same time being a benign tumor. To be considered radiation-induced, meningiomas must comply with five criteria, such as: be located in the irradiated bed, to have no previous lesion to radiotherapy, be histologically different from the primary tumor, five-year interval between the first exposure and onset of the tumor and absence of favorable conditions for the onset of meningioma. The patient does not fit all criteria, thus suggesting a greater attention to other risk factors. Conclusion: The interaction of the multiplicity of the patient risk factors, such as those included in radio-induction and breast cancer, are possibly associated with the acquisition of the meningiomas.

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Resumo: OBJECTIVE: The ommaya reservoir plays an important role in the treatment of many patients, especially in those who require intrathecal chemotherapy. Although simple, the ommaya system must be perfectly placed in the lateral ventricular system. Otherwise, serious complications may occur after chemo administration. This study aims to describe the surgical technique for Ommaya placement using advanced methods of neuronavigation and immediate postoperative tomography; analyze the surgical results and compare with the results of the freehand technique, described in the literature. METHODS: The authors systematized the surgical technique using neuronavigation and immediate postoperative tomography in 49 consecutive patients. All surgeries were to place reservoir of ommaya with ventricular catheter precisely placed with all holes in the ipsilateral ventricle. All patients had meningeal carcinomatosis. RESULTS: The surgical technique presented by the authors presented lower rates of surgical complications (6%), mainly, lower rates of reoperation due to an inadequate positioning of the ventricular catheter. The literature presents up to 60% of complications rates in the freehand placement of ommaya reservoir. CONCLUSIONS: This surgical protocol described minimizes the number of reoperations, and decreases chemo complications. The positive results give credibility to this surgical protocol. We believe this a good technique to offer for our patients in the face of such a complex and debilitating disease.

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Título: OCCIPITAL DERMAL SINUS ASSOCIATED TO INFECTIOUS TERATOMA IN AN ADULT PATIENT AFFECTED BY KLIPPEL-FEIL SYNDROME: RARE CASE REPORT
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Resumo: BACKGROUND: The dermal sinus (DS) are defined as epithelium-lined tracts that result from incomplete separation of cutaneous ectoderm from the underlying neuroectoderm. The association of DS, infected teratoma and Klippel Feil syndrome (KFS) with initial symptoms in the adulthood has not yet been described in the literature. OBJECTIVE: This case report aims to describe a cranial DS associated to KFS and infectious teratoma of the cerebellum reported in the same patient, as well as analyses the epidemiological, clinical, pathological and treatment features. CASUISTIC AND METHODS: This report was based in one case of DS associated to KFS and infectious teratoma retrospectively reviewed associated to the bibliographical consultation, using indexed databases. CLINICAL PRESENTATION: We present a case of an adult male patient, 24-years-old, admitted in our service presenting fever and meningeal irritation as initial symptoms. In the patient's past clinical history, he was diagnosed with an occipital DS in his childhood which was previously instructed to be operated on by another neurosurgical team, but the patient did not want to perform the procedure. The MRI investigation showed a DS associated to a cerebellar infected mass with 2cm on its main diameter. The patient was treated with antibiotic therapy for 10 days, and underwent gross total surgical resection of the tumor as well as DS correction, confirmed in the histopathological examination as a teratoma. After surgery, further CT scan analysis showed the presence of cervical vertebrae fusion, compatible with KFS diagnosis. RESULTS AND DISCUSSION: Teratomas comprise less than 1.5% of all intracranial tumors, while KFS presents an incidence of one in 42,000 births and DS affects lower than 1% within the neonatal population. Although DS are easily identifiable and curable lesions, their pathological importance rests on its risk of intracranial infection and the variable association with a dysembryogenetic tumors (dermoid or epidermoid lineage) and neurological syndromes, such as KFS. CONCLUSIONS: The association of DS, infected teratoma and KPS presenting with initial symptoms in the adulthood is quite rare. Proper management of this pathology should consider not only the treatment of the associated meningitis but also tumor resection and DS tract resection to avoid further recidive of infection. Genetic markers encompassing association between DS, KPS and teratomas are still lacking in the literature.

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Resumo: Introduction: Meningiomas are uncommon childhood tumors, accounting for 0.4–4.6% of central nervous system tumors in this population, and differ in various clinical and biological aspects from their adult counterparts, reflecting different tumor dynamics. Management approaches have been drawn from reports and extrapolated from the treatment of adult meningiomas, without clear, statistically validated guidelines for the management of child and adolescent meningiomas. Objective: The goal of this study was to determine the epidemiology, clinical presentation, associated factors, pathological features, and treatment outcome of pediatric meningiomas in a single-center institution, and attempt to evaluate such features in the context of published literature. Methods: Clinical data of 19 patients under 18 years of age operated on for meningiomas from January 1994 to July 2017 were reviewed. Results: The group included 10 males and 9 females (mean age of 12.9 years at surgery). The most common symptoms at presentation were headaches in 9 out of 19 (47%), raised intracranial pressure, seizures and cranial nerves palsies in 3 out of 19 each (15% each). Sole operated tumors were found in 16 out of 19 (84%), whose location is as follows: parasagittal in 4 out of 16 (25%), 4 in the convexity (25%), 2 at the skull base (12%), 2 intraventricular (12%) and 4 in other sites (25%). 3 patients (15%) had multiple meningiomas, all of which had Neurofibromatosis type 2 (NF2). 6 children presented with radiation induced (RT) meningiomas and 5 had evidence of NF2. Simpson’s grade I excision was achieved in 14 out of 19 (74%). On histopathology, 14 out of 19 (74%) were grade I and 5 (26%) were grade II. 6 tumors (31%) recurred, 4 of which had RT or NF2. During the mean follow-up period of 5 years, 16 out of 19 (84%) had a good outcome (GOS05). Conclusions: Meningiomas are relatively rare lesions in the pediatric population. Although there are several known risk factors, many of which were observed in the patients in our study, sporadic meningiomas can be observed in children. They show higher rates of atypical features when compared with adult meningiomas, so it should be thought of as an entity separate from its adult counterpart as it behaves more aggressively on the whole. Location, associated factors (such as RT and NF2), and extent of excision appear to be more important than histology in predicting outcome. Early treatment should be considered, and close follow-up is mandatory.

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Resumo: Introduction: The awake craniotomy (AC) for low grade glioma is a well described and safe technique and such a technique has a great potential to improve the surgical results, from both oncological and functional perspectives. However, only few centers in the world use this technique routinely. Objective: To describe the main challenges in our initial experience performing invasive cerebral mapping in an asleep-awake-asleep (AAA) technique. Methods: Between April 2017 (when we performed our first case) and January 2018 a total of 22 patients underwent awake craniotomy. We excluded from this analysis 6 patients with high grade glioma and 2 patients with very disseminated tumors (>3 lobes involved). This is a prospective study of 14 consecutive patients with LGG submitted to an awake craniotomy for brain mapping with an AAA technique. The parameters for direct electrical stimulation on the brain of awake patients were made with a bipolar electrode with 5 mm spaced tips delivering a biphasic current - pulse frequency 60 Hz; single pulse phase duration 1 ms; amplitude 1.5–4 mA (Ojemann cortical stimulator). Results: From 14 patients, 8 (57.1%) were male. The mean age was 38.2 years-old (range 24–55 years-old). The mean time of surgery was 283 min (range 210-365 min). The anesthesia induction and the perioperative awakening were performed with the patient in the lateral position. The first airway phase was with laryngeal mask and there was no complication. The mean time of awake brain mapping was 98.5 min (range 50-143 min). There were 2 cases of focal seizure not related to cortical stimulation and 2 cases of generalized seizure related to cortical stimulation; in one case venous medication was necessary and the brain mapping was interrupted. We had 2 cases of cooperation problems that limited the brain mapping performance (1 patient presented a panic attack and 1 patient stayed drowsy during all the procedure). Some postural discomfort was reported in 35.7% of cases, but it did not limit the surgery. The second airway phase was with fiberscope (9 cases) or video laryngoscopy (5 cases) and there was no intubation failure. No other major complications or mortality. Conclusion: There are many challenges starting a new technique full of peculiarities. However, the results of this study suggest that it may be feasible, reproducible, and relatively safe in the context of a standardized protocol involving a multidisciplinary team.

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Título: PROPOSAL OF A METHOD OF CONTINUOUS NEUROPSYCHOLOGICAL EVALUATION WITH AN ANDROID-BASED APPLICATION IN AWAKE SURGERY FOR FRONTAL GLIOMAS

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Resumo: Introduction: awake surgery and brain mapping are important tools in the resection of gliomas in eloquent areas. Although cortical mapping is widely used in tumors that are suspected to involve language and motor areas, its use in the evaluation of other frontal functions (i.e. working memory, attentional control, cognitive inhibition and inhibitory control) is less studied. It is not clear if it is possible to prevent cognitive worsening in these areas with traditional techniques of brain mapping by direct cortical stimulation. Methods: We propose a method for evaluating frontal functions in patients with low grade gliomas with a custom made Android-based application, to be used with a tablet during awake surgery in frontal gliomas. Based on the diffuse neural networks that are the anatomical substrate of these functions, we propose an alternative approach in which instead of cortical stimulation, continuous neuropsychological testing is performed while resecting the tumor, utilizing alternating blocks of tests customized according to the location of the tumor and pre operatory neuropsychological testing. We analyze in real time possible decline in selective cognitive domains to determine the extent of surgical resection. Conclusion: frontal functions can be evaluated during awake resection of frontal gliomas. Resection of the tumor often leads to a intraoperative decline in these functions. It remains to be seen if monitoring these functions during resection can prevent cognitive worsening in the long term.

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Título: PSEUDOPROGRESSION METASTASIS OF ELOQUENT AREA ON IMMUNOTHERAPY: A CASE REPORT

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Resumo: CASE: Male patient, 65 years, hypertension, with metastatic renal tumor for central nervous system and spinal metastasis, underwent radiosurgery, began treatment with immunotherapy last month. He was admitted reporting abnormal sensation in the left arm and three previous episodes of dystonic posturing in the same arm, lasting for a few minutes in a period of two days. Being the last episode, followed by loss of consciousness and epileptic seizure. A patient have significant clinical decline and was conducted a Brain Magnetic Resonance Imaging that showed expansive lesion, with heterogeneous enhancement after gadolinium administration, delimiting the central area of necrosis and extensive hyperintense area on T2 / FLAIR, located in the centrum semiovale extending the subcortical white matter and other lesion in anterior right parietal lobe. A focus marked by low signal transition on right pontomesencefálica with a slightly contrast enhancement and signal on FLAIR. In the thoracic spine CT, showed bone expanding process in T4 and T5 spinal metastasis. The parietal brain metastatic lesion on the right was submitted to partial resection and the material was sent for histopathological identifying pseudoprogression. DISCUSSION: Metastases are the most common brain malignancies neoplasms and increased morbidity and mortality rate. Therapeutic methods have been developed for treatment in these tumors, including immunotherapeutic treatment. Reaching important progress in the treatment of brain metastases, including within the renal cell carcinoma, increasing the survival rate of patients. However, during treatment, tumor growth may occur, known as pseudoprogression. Immunotherapy stimulates the host antitumor immunne response. The immunne response mechanism that leads to pseudoprogression being it associated only with inhibition of an immune checkpoint, but unclear. The pseudoprogression after immunotherapy considered unusual in metastatic brain tumors. Pseudoprogression cases of metastatic renal tumor to the brain was not described. COMMENTS: In short, the presentation of this case is relevant to advise on the recognition of similar cases and reiterate the need to conduct studies to elucidate the mechanism pseudoprogression after immunotherapy treatment.

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Título: SAFETY AND EFFICACY OF STEREOTACTIC BIOPSY OF BRAINSTEM IN CHILDREN: A SINGLE INSTITUTION EXPERIENCE.

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Resumo: Brain tumors are a second most common neoplasm in pediatrics and the most common solid tumor. Brainstem gliomas account for 10% to 20% of all Central Nervous System (CNS) tumors in childhood and about 80% of these tumors involving pons are low grade gliomas (WHO grade 1 and 2). As in adults, high-grade gliomas in children can occur anywhere in the CNS. However, in pediatric patients trend to occur more in deep gray matter, cerebellum and brainstem, the latter being rare and treated based on imaging diagnosis and without histopathological diagnosis. However, the diagnosis by magnetic resonance imaging (MRI) appears to be erroneous in 10 to 20% of the cases, leading patients without prognosis. The growth patterns observed in neuroimaging studies are suggestive of histological classification, although there are no more patterns. A stereotactic biopsy in these tumors has proven to be safe, accurate, and much more used in adults. However, in the pediatric population it still generates controversy. We report our experience and aim to contribute to improve the analysis of the subject and to emphasize the importance of histopathologic diagnosis in these tumors.

OBJECTIVE: The objective of this study is to report a series of biopsies of brainstem lesions in 9 children, conducted between 2000 and 2017. We report in order to better classify these lesions for more appropriate treatment and to contribute to the subject of stereotactic pediatrics.

METHOD: Performed by a review of medical records at HCFMUSP. All the surgeries were performed in patients between 2 and 18 years old between 2000 and 2017. RESULTS: Among the 9 cases analyzed, 3 were high grade gliomas, 1 low grade glioma, 1 germ cell tumor (GCT) non-seminomatous, 1 anaplastic ependymoma, 1 subacute demyelinating lesion, 1 infiltrative granulomatous lesion and 1 inconclusive. In none of the analyzed patients complications as bleeding or additional neurologic deficit occurred. CONCLUSION: In our series, stereotactic biopsy showed to be a safe technique even in the pediatric range, allowing better classification of lesions for strategic treatment planning, aiming at a better patient survival, since a better diagnostic characterization allows more assertive treatment and reduction of toxicity.

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Título: SPHENOID WING DIFFUSE LARGE B-CELL LYMPHOMA MIMICKING A MENINGIOMA: A RARE DIFFERENTIAL DIAGNOSIS

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Resumo: CASE PRESENTATION: A 67-year-old female patient presented to neurosurgical department complaining of progressive left exophthalmos and left non-pulsatile frontotemporal headache. A brain MR was indicated and disclosure a left sphenoid ring hyperintense lesion with orbital invasion and adjacent hyperostosis. The diagnosis of meningioma was the initial hypothesis and surgical approach was performed. During histopathological evaluation, however, it was disclosure that in fact the mass was a diffuse large B cell lymphoma of germinal center classified was Ann Harbor I-E. Chemotherapy was administrated and she evolved with tumoral volume reduction. DISCUSSION: Primary dural lymphomas are rare and correspond to 1% of all CNS lymphomas. They have a slow growing pattern when compared to the other lymphomas. Radiological features are very similar to meningiomas and in most cases is a low-grade B cell marginal zone lymphoma. This differential diagnosis is very important because in cases of brain lymphoma, maximal surgical resection is not a fundamental principle as in meningioma surgeries. It is described a case of a patient with typical image of sphenoid ring meningioma although histopathological analysis revealed that was the rare entity of a diffuse large B cell primary dural. COMMENTS: Despite of meningioma is the most common dural tumor; there are several differential diagnosis that should be considered for proper therapeutic approach. A primary dural lymphoma is more indolent and has a better prognosis than parenchymal primary CNS lymphoma or systemic lymphoma with CNS metastasis.

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Título: SURGICAL TECHNIQUES IN TUBERCULUM SELLAR MENINGIOMA: CURRENT PERSPECTIVES OF THE INDICATIONS, COMPLICATIONS AND PITFALLS

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Resumo: BACKGROUND: Tuberculum sellae meningiomas is a serious challenge for neurosurgeons. It accounts for up to 10% of all intracranial meningiomas. The difficulty in surgically excising a Tuberculum sellae meningioma comes from its anatomical relationship to the optic nerves and chiasm and to the anterior cerebral and internal carotid arteries and their perforators. OBJECTIVE: Discuss the complications and pitfalls of each main surgical technique used for resection of tuberculum sellae meningiomas based on our experience in comparison to previously reported data. METHODS: The authors report a personal case series of senior authors composed by 38 patients with tuberculum sellae meningiomas submitted at surgery during the period from 1995 to 2016. All patients was underwent evaluation by CT scan and MRI. The radiological parameters included tumor size, brain–tumor interface, perilesional edema, arterial encasement, optic canal extension, and hyperostosis. The patients was underwent an endoscopic endonasal approach or conventional craniotomy for tumor resection by bifrontal, pterional, supraciliary, unilateral frontal, or fronto-orbito-zygomatic surgical access. The Simpson grade of meningioma resection as well as the non visual morbidity and the mortality rates were analyzed. RESULTS: The study was performed with 30 female and 8 male, whose average age was 52 years. Regarding the surgical procedure, 94.7% (n=36) patients was underwent craniotomy for tumor resection (31.5% bifrontal, 31.5% pterional, 15.8% supraciliary, 10.6% unilateral frontal, and 5.3% fronto-orbito-zygomatic access), while in two patients excision was performed through an endoscopic endonasal approach. Thirty one patients had Simpson grades 1 and 2 excisions, while seven had Simpson grade 4 excisions. The overall rate of non visual morbidity was 13.15% (5 of 38 patients) and mortality was 5.2%. The pterional access was associated to the worse inadequate visualization of optic nerve and carotid artery, as well as higher rates of visual deterioration and high degree of difficulty in cases invasion of the optic canal and intrasellar extension of the tumor. CONCLUSION: The primary symptom leading to the diagnosis of a tuberculum sellae meningioma was visual compromise and the main goal of surgery was to achieve improvement of vision. Favorable outcomes were achieved with appropriate selection of surgical approach.

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**Título:** THE USE OF SODIUM FLUORESCINE TO IMPROVE THE ACCURACY OF TISSUE DIAGNOSIS DURING STEREOTACTIC BIOPSY: A CASE REPORT.

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**Resumo:** Introduction Stereotactic biopsy is a very important tool in the diagnosis on intracranial lesions, specially in cases of tumors in deep seated regions, eloquent areas, or when there is doubt in the diagnosis of some lesions. Intraoperative frozen section assessment helps to minimize sampling errors, but it depends of a neuro-pathologist, that might not be always available during the surgical procedures. This technique is also time demanding. Fluorescein accumulates in high grade gliomas, metastasis and other lesions that disrupt the blood-brain barrier and has shown a good correspondence with the gadolinium enhancement areas. The use of fluorescein to guide biopsies has been published with some goon initial results. We present our first case of a glioblastoma biopsy. Methods Patient was submitted to a standard stereotactic biopsy, and after the beginning of the anesthesia received a dose of 5mg/kg sodium fluorescein intravenously. Each fragment of the biopsy was immediately assessed for the presence of fluorescence using a fluorescence device attached to a surgical microscope, or other techniques such as the previously reported “fluoropen” or a UV light source and a custom made yellow barrier filter on a cellphone camera (fig ). Results A 57 year old male patient presented with mental confusion and headache, the MRI showed a lesion in the splenium of the corpus callosum, a stereotactic biopsy was performed. The fragments were immediately assessed and showed fluorescence, confirming that the area of the biopsy was in the lesion and not in the normal surrounding brain. Histopathological analysis confirmed the diagnosis of a glioblastoma. Previous results were published using this method and up to 100% of the fluorescent samples contained diagnostic tissue adequate for tumor diagnosis and grading. Conclusion Fluorescein sodium fluorescence might be a helpful tool to improve accuracy of tissue diagnosis in stereotactic biopsy. It allows a cheap and rapid intraoperative assessment of the samples.

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Título: USE OF FLUORESCENCE FOR MALIGNANT BRAIN TUMOR SURGERY USING A CUSTOM MADE DEVICE

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Resumo: Introduction Fluorescein is an organic dye widely and safely used in humans. It requires a blue light source and an interposition of a yellow filter to see it properly. It is a highly fluorescent molecule and is excited by light with a wavelength between 465 and 490nm and has a peak emission between 520 and 530 nm. This substance accumulates where the blood brain barrier is broken. It has been used in central nervous system such as metastasis, high grade gliomas and skull base tumors. Studies have shown good results using fluorescence for the resection of malignant brain tumors, increasing cases that achieved gross total resection, reaching 80% or even more, including brainstem lesions Methods A 3D printed device was designed with light filters that could fit any microscope with a removable part. It was possible to easily alternate during surgery between the white light and the fluorescence mode. The excitation filter for the light source is a band-pass filter that allows only wavelengths between 425 and 490nm, and, as a barrier, a longpass filter that cuts of light under 520nm enhancing the fluorescence contrast. Just before skin incision the injected dose was 5mg/Kg of fluorescein. We present a sample of our cases. Results In all cases the tumor showed a high fluorescence in contrast with the normal surrounding brain. None of the patients presented with any complication related to fluorescein administration. The first case was a 61-year-old female patient who presented with a single right temporal metastasis. Her primary situs was ovary and she had a controlled disease and a KPS of 80%. Gross total resection was achieved. Another case was of a 50 years old female patient with a right temporal recurrent Glioblastoma with headache and mental confusion. A fluorescence guided surgery was performed with gross total resection. A 68 years old male with a temporal glioblastoma. Awake craniotomy was performed with intraoperative monitoring. The tumor showed high fluorescence, but not the surrounding brain. Total resection was not possible due to worsening of speech. Conclusions Fluorescence guided surgery increases the rate of gross total resection of malignant brain tumors. This is an important tool with a potential impact on overall survival of the patients. This is a low cost option that could make this technology available in low resources areas. This is a universal device that could be attached to any surgical microscope.

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Título: ALTERAÇÕES MOTORAS EM CRIANÇAS E ADOLESCENTES PÓS-CIRURGIA DE TUMOR INTRAMEDULAR: ESTUDO RETROSPECTIVO

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Resumo: Ependymomas (EPN) are primary tumors in the central nervous system (CNS). In children, 90% of EPNs occur intracranial, with two-thirds being located in the posterior fossa (PF) and one-third within the supratentorial (ST) compartment. Despite the development of new molecular classifications and increasing understanding of the underlying EPN mechanisms, management and treatment remain challenging. We investigated the expression of genes involved in EPN molecular rearrangements (YAP1, RELA, MAMLD1 and FAM118B), in 27 EPN patients from Pediatric Oncology Institute – GRAACC, Brazil. Gene expression levels were quantified using qPCR. Molecular findings were correlated to clinicopathological characteristics of patients. Significant results were considered when p<0.005. Overall survival was significantly lower in patients with PF tumors than ST tumors (p=0.0109), and high YAP1 expression was related to worst overall survival (p=0.0488). ST tumors presented higher RELA expression than PF tumors (p=0.0089). Expression of YAP1 and FAM118B genes significantly correlated (r=0.917, p<0.0001). All investigated genes are partners in fusion genes recently described for EPN and the levels of expression observed were in agreement with findings in the literature. Additional studies are in progress to collaborate with the characterization of EPN genetics, once development of targeted therapies will require the understanding of tumor biology and its effect in the clinical outcomes. Based on recent molecular findings, and after the actualization of WHO classification of tumors of the CNS in 2016, it is becoming evident that, in the near future, histologic criteria alone might be insufficient to direct treatment, to predict outcomes and refine EPN treatment.

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Resumo: Background: Navigated Transcranial Magnetic Stimulation (nTMS) has been used as a valuable tool in preoperative brain mapping for brain tumor surgeries. In addition to this important feature, nTMS can also be used to study the integrity of corticospinal projections, and these parameters are collectively referred to as cortical excitability (CE) measurements. However, little is known about CE behavior in this population. The aim of this study is to report a descriptive analysis of the CE in patients with brain tumors located in the frontal lobe. Methods: nTMS and CE evaluation were performed in 7 patients consecutively recruited with single brain tumor located at frontal lobe. We used a circular coil of nTMS to apply simple and paired pulses on the motor area (M1) of both cerebral hemispheres (healthy and ill). The measured CE parameters measured on all 14 cerebral hemispheres were: resting motor threshold (RMT), suprathreshold motor evoked potential (MEP), short interval intracortical inhibition (SIICI) and intracortical facilitation (ICF). We performed comparisons between the healthy and ill cerebral hemispheres. Results: Patients were 55.14±8.47 years old, 5 female (71.4%), and with median Karnofsky Performance Scale (KPS) of 80. The most common histopathological diagnosis was high grade glioma (5 patients; 71.4%) and 4 patients (57.1%) presented with preoperative motor deficit. The ill cerebral hemisphere was the right side in 6 patients (85.7%). Our data showed higher values of MEP (2096.14±2394.52 versus 868.00±461.65) and ICF (mean 2.507±1.628 versus 1.598±0.989) on ill hemispheres, despite no statistical significance was found (p=2.248 and p=2.306, respectively). On a general comparison to normative data, even patients’ healthy hemispheres parameters showed most values already considered abnormal. These abnormalities are comparable to those found in other neurological conditions such as stroke, traumatic brain injury, and movement disorders. Conclusion: The CE study provides valuable information on the functional status of the corticospinal system of patients with brain tumor. Thus, nTMS may be a valuable tool in the neurophysiological assessment in this population. Although we did not find statistical significance, we verified changes in the assessed CE parameters. A larger sample may have sufficient power to detect such differences.

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Título: CLUSTER HEADACHE IN A PATIENT WITH HODGKIN’S LYMPHOMA

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Resumo: Case presentation: A 41-year-old male patient with Hodgkin’s lymphoma diagnosed in 2006, under control, who underwent chemotherapy and radiotherapy in the past, presented with a ocular, frontal and parietal headache, with intense left stab pain, during 15 to 30 minutes, 15 times a day, with associated behavioral changes and dysautonomic symptoms, such as tearing, left conjunctival hyperemia and left nasal congestion. Investigation with CT (computer tomography) scans or MRI (magnetic resonance imaging) was negative and there was no sign of cancer recurrence. Complete resolution of symptoms 30 days after initiation of preventive therapy with Diltiazem, Clonazepam and Sertraline. Discussion: Cluster headache belongs to the trigeminal autonomic cephalalgias, which involve unilateral, severe headache attacks and typical accompanying autonomic symptoms. Prevalence is < 1% and mostly affects men. Occasionally, patients have a potential secondary cause, such a structural brain lesion. 98% have normal skull image exams. Treatment include oxygen, triptans, lidocaine, ergotamine for acute treatment and verapamil, carbolitium and glucocorticoids for preventive therapy. Final comments: Consider the diagnosis of cluster headache in cancer patients even without structural lesion or cancer recurrence that meet the diagnostic criteria.

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Título: GAIT DISTURBANCES - VESTIBULAR AND CEREBELLAR COMPLICATIONS OF CHEMOTHERAPY: THE IMPORTANCE OF NEUROLOGICAL EXAMINATION.
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Resumo: Case presentation: Case 1: A Female patient of 58 years-old, with leukemia, was undergoing chemotherapy with HDAC, which included cytarabine (Ara-C). Brain nuclear magnetic resonance and liquor was normal. Neurologic examination revealed dysphonia, severe ataxia that evolved to inability to ambulate, dysmetria and decomposition movements of lower and upper limbs. The patient was diagnosed with cytarabine cerebellar toxicity. The patient evolved with evolutionary improvement after physical therapy rehabilitation. After diagnosis change of the chemotherapeutic drugs was made and patient continued treatment. Case 2: A male patient of 75 year-old with hypertension, diabetes, dyslipidemia, prostatic hyperplasia and rectal adenocarcinoma was treated with XELOX regimen chemotherapy, which included oxaliplatin (platinum). Neurologic examination revealed no cerebellar abnormalities, but gait instability, imbalance, tinnitus and nystagmus. Brain nuclear magnetic resonance was normal. The patient was diagnosed with platinum vestibular toxicity. The patient evolved with evolutionary improvement after vestibular rehabilitation and anti-dizziness medications. After diagnosis change of the chemotherapeutic drugs was made and patient continued treatment.

Discussion: Neurologic complications of anticancer therapy may result from direct toxic effects on the nervous system. A wide range of neurologic complications are associated with antineoplastic drug treatment. Their recognition is important because of potential confusion with metastatic disease, paraneoplastic syndromes and other neurologic disorders. Neurologic exam and knowledge about neurologic complications of the drugs may help the diagnosis. Discontinuation of the offending agent may prevent irreversible injury. In the discussed cases, gait disorders had different neurologic examination. High doses of citarabine are associated with an acute cerebellar syndrome in 10 to 25 percent of patients. Ototoxicity is the second most common cisplatin-related neurotoxic effect. Final comments: The gait disturbances in the discussed cases resulted from vestibular and cerebellar toxic complications of chemotherapy. Correct identification of the agent um the medical record and adequate neurological examination allowed discontinuation of the agent and correct treatment.

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Resumo: CASE: A patient, male, 70 year-old, hypertensive and former smoker, was admitted after complaining of epigastric aura and olfactory hallucination succeeded by loss of consciousness, tonic posturing and sphincter release. Neurological physical examination revealed Glasgow 15, isochoric and isofotorreagentes pupils, extraocular motility were present and focal deficits was absent. It was performed a Brain Magnetic imaging in which showed lesion in the right parahippocampal gyrus, annular impregnation of gadolinium, infiltrative, central necrotic core, with about 1.3 cm and extending up to the amygdaloid body, temporal pole adjacent the isthmus. Spectroscopy and perfusion studies showed an increased tumor microvasculature and capillary permeability as well as an increase in peak choline, respectively. Favoring the possibility of diffuse glial neoplasm high grade. On the complementary tests, it was evidenced infiltrated perihilar, leukocytosis with lymphocytosis, obstruction between 50 and 69% of the right carotid artery, mild mitral and aortic insufficiency, paroxysmal atrial fibrillation, and no malignant cells in the cerebrospinal fluid (CSF). And positive immunophenotype for Chronic Lymphocytic Leukemia. Patient submitted a neurosurgical procedure subjected to gross total resection, the material was sent for histopathological in which confirmed glioblastoma. The patient developed arrhythmia in the postoperative and with no neurological deficits.

DISCUSSION: Glioblastoma is the most frequent primary malignant neoplasm of the central nervous system in adults accounting for approximately 45-50% of these. And the Lymphocytic Chronic Leukemia is the most common leukemia in the same age range. The simultaneous occurrence of the two neoplasms, although rare, two cases had been reported and one study was conducted in patients with Chronic Lymphocytic Leukemia with neurological symptoms, where 5% had these brain tumors. It has not been elucidated the relationship between chronic Lymphocytic Leukemia and glioblastoma development, but studies show that the Lymphocytic Leukemia as anti-tumor immunity is impaired, it may occur to favor the development of other primary tumors.

COMMENTS: Summarizing, the presentation of this unusual case is important to orient about the recognition of similar cases and reiterate the need to conduct studies aimed to provide information about the correlation between these two conditions.

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Resumo: Case report: A 66-year-old male patient with multiple myeloma and plasmacytoma in the sacrum submitted 3 months before the onset to autograft bone marrow transplantation (autologous transplantation). No clinical signs of Graft-versus-host disease (GVHD). Clinical presentation of generalized and symmetrical fatigue, polymyalgia, palpebral ptosis, without diplopia, dysphagia and dysphonia of gradual evolution 20 days before initial evaluation. Patient presented reduction of proximal force greater than distal, reduced reflexes and tonus, without sensory alterations. Research revealed small increased muscle enzymes, negative serologies, negative rheumatic markers, electroneuromyography without signal of myoneural plaques diseases but suggesting myopathy. He underwent physiotherapy and speech therapy, submitted to immunoglobulin therapy, followed by glucocorticoids for 8 months with complete regression of symptoms. Muscle biopsy confirmed Inclusion body miositis. Discussion: Inclusion body miositis is a rare sporadic inflammatory idiopathic myopathy. Causes muscle weakness with an insidious onset. The distribution of weakness can be either symmetric or asymmetric and both proximal and distal muscle groups can be involved. Dysphagia occurs in about one-third of patients. Prevalence is 5-9 cases per million adults. Affects men more often than women. The optimal treatment is not known. The disease is relatively resistant to standard immunomodulatory therapies. Nonpharmacologic interventions are indicated, creatine monohydrate can be supplemented. Patients usually progress to disability over a period of years. Final comments: The correlation of oncologic disease and bone marrow transplantation with the development of Inclusion body miositis is not well known. GVHD after haematopoietic stem cell transplantation has similarities to some idiopathic autoimmune diseases. Muscle may be a target tissue for GVHD. The favorable response to immunosuppressive therapy in this patient, may suggest underlying autoimmune mechanism, perhaps correlated to bone marrow transplantation.

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**Título:** ISCHEMIC STROKE INTRAVENOUS THROMBOLYSIS IN LARYNGEAL CARCINOMA PATIENT

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**Resumo:** Case presentation: A 62-year-old male patient with laryngeal carcinoma T4N0M0E3 (relapsed ameloblastoma) during an outpatient visit at the hospital presented sudden right hemiplegia, hypoesthesia and dysarthria. He had undergone laryngectomy 15 days before. He underwent brain computer tomography (CT) that revealed left middle cerebral artery occlusion in M1 segment. Neurological examination revealed NIHSS scale 15. Submitted to intravenous thrombolysis (IV) without intercurrences, with complete reversal of the deficits after 24 hours. Investigations revealed no major abnormalities. Discussion: Stroke presents rapidly evolving signs of focal, sometimes global, brain function lasting more than 24 hours or leading to death with no apparent cause other than vascular origin. It is the leading cause of death in Brazil. The association of stroke with cancer is high, autopsies reveal 15% cancer patients with cerebral stroke, half symptomatic. Stroke determined by unconventional mechanisms occurs in large numbers of cancer patients and coagulation disorders have important role. IV Thrombolysis in cancer patients does not have a higher rate of bleeding. Hematologic neoplasms had a better outcome than solid neoplasms. IV thrombolysis in caucasians with cancer, by the exception of chemotherapy and ongoing radiotherapy can be safe and effective. The risk of bleeding and life expectancy should be considered. About half of patients with stroke and cancer die in the first 3 months and the 3-month functional outcome is poor in 50% of patients despite acute therapy. Final comments: IV Thrombolysis of patients with ischemic stroke with cancer should be considered, and may be safe and effective, considering the risks and life expectancy of each patient.

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Resumo: Case presentation: a 18 year-old, male was admitted with a history of seizures for one year, and adequate control with carbamazepine. No neurological complaints were present. Previous medical history was uneventful. No motor or sensory deficits were observed at physical exam. Brain MRI showed a right occipital expansive lesion suggestive of neoplasia. Patient was submitted to complete tumor resection without complications. Histopathological findings of the specimen: diffuse neuroepithelial neoplasia comprising of monomorphic architecture of glial cells with discrete atypia, rounded nuclei, basophilic chromatin and inconspicuous nucleoli; cells showed granular, eosinophilic cytoplasm with imprecise limits. The neoplasia diffusely infiltrated the cortex and cerebral white matter. No figures of mitoses or areas of necrosis were observed. Focally, a few remaining neurons were noted which exhibited several nuclei with prominent nucleoli and broad cytoplasm. The immunohistochemical profile (IH) showed positivity for GFAP and Ki67<1%. These findings were consistent with isomorphic astrocytoma (IA). Patient remains free of residual lesion or recurrence (2 years of follow-up) and with adequate seizure control. Discussion: the isomorphic subtype is a unusual histopathological variant of diffuse astrocytomas (classified as WHO grade II lesion); yet, IA shows an extremely favorable prognosis, with a clinical behavior similar to WHO grade I tumors. Approximately 27 cases of IA were described in the literature to date, the majority associated with epilepsy initiating at childhood or adolescence. The histopathological findings that characterize IA are isomorphic architecture with highly differentiated astroglial cell elements amid small, rounded nuclei, residual neuronal elements and absence of mitotic or necrosis figures; IH strongly positive for GFAP, lack of CD34 and MAP2 expression in addition to Ki67<1% contribute to the differentiation between the “classical” variants and other tumor histologies associated with epilepsy. Ongoing studies suggest molecular similarities of IA with angiocentric gliomas. Fusions involving MYB/MYBL-1 seems common for both, although methylation profile of IA clusters as a distinct subgroup. Final comments: multicenter studies are needed for a better clinical and molecular characterization of these lesions. The scant data currently available support the categorization of this variant as a novel entity within brain tumors.

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Título: ISOMORPHIC ASTROCYTOMA: AN EXCEEDINGLY RARE SUBTYPE OF DIFFUSE ASTROCYTOMAS.

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Título: OPSOCLONUS-MYOCLONUS-ATAXIA SYNDROME ASSOCIATED WITH NEUROBLASTOMA – CASE REPORT

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Resumo: Case Presentation. A 3-year-old female patient presented to the hospital with nausea and vomits. Treated two years earlier from a neuroblastoma, the patient was using azathioprine, immunoglobulin and clonazepam. The psychomotor development was normal, with loss of marks after Opsoclonus-Myoclonus-Ataxia Syndrome, diagnosed after neuroblastoma detection. On the admission, the patient had an important ataxia of the trunk and limbs, tremor of the extremities and “dancing eyes” (opsoclonus). The computed tomography scan of the abdomen performed on the admission showed a paravertebral mass extending from L1 to L3 vertebræ. As the symptoms remained, the patient underwent surgical removal of the mass, which later resulted in fibroadipose and lymphoid tissue without neoplasm detection by the pathological analysis. In the postoperative, patient remained with opsoclonus, even after introduction of prednisone, but improved from ataxia and myoclonia, being discharged five days later.

Discussion. The Opsoclonus-Myoclonus-Ataxia Syndrome is a rare neurological disease, often chronic, composed by three main symptoms: opsoclonus, myoclonus and ataxia. It is usually a paraneoplastic or parainfectious manifestation, being associated with neuroblastoma in 50% of the cases. Neuroblastoma surgical removal may be helpful in some cases but the sequelae of the syndrome improve slowly and incompletely. Therefore, symptomatic treatment is frequently needed. Medications include: corticosteroids, adrenocorticotropic hormone, intravenous immunoglobulin and immunosuppressors; new therapies such as rituximab and cyclophosphamide can also be used. Since the recovery is slow and as recurrence causes permanent neurological damage, prognosis remains poor.

Final Comments. The persistence of the syndrome’s symptoms in the 3-year-old patient lead to an investigation for an occult neuroblastoma, being found the paravertebral mass. The mass removal did not improve the symptoms, since it was not neoplastic, suggesting a parainfectious etiology for the recurrence of the syndrome. The treatment given to the patient was made as recommended by the literature, apart from the adrenocorticotropic hormone, which was not used. With the reintroduction of the corticosteroid producing partial control of neurological symptoms, the patient was able to be discharged. Even though outcome is not favorable, follow-up care is relevant for improving patient’s quality of life.

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Título: PRIMARY CENTRAL NERVOUS SYSTEM GERM CELL TUMORS: A SINGLE CENTER INSTITUTION EXPERIENCE

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Resumo: Background: Primary Central Nervous System Germ Cell Tumors (CNSGCT) are a rare type of cancer in childhood responsible for 2-3% of brain tumors. They are classified into two main groups which are considered heterogeneous in presentation and treatment outcome. Objective: To describe an institutional review of epidemiological, clinical characteristics and survival of children and adolescents with diagnosis of CNSGCT. Material and Methods: Retrospective assessment obtain by medical records. Results: Between January 2000 and December 2017, 68 patients with diagnosis of CNSGCT, confirmed by tumor markers and/or surgery were admitted at IOP/GRAACC/UNIFESP. Median age was 12,5 years (range 3 months to 30 years), 53 (77,9%) male. The main signs and symptoms at diagnosis were: 62% headache, 54% DI, 47% vomiting, 19% Parinaud Syndrome, 9% seizures and ICH in 50%. Primary sites were 44% pineal, 26% suprassellar, 25% bifocal with 19% disseminated at diagnosis. Germinoma (G) was observed in 75%, 22% non germinomatous germ cell tumors (NGGCT) and 3% cases of mature teratoma. Treatment regimen occur as followed: 10 patients were treated by the 3rd international CNSGCT study from 2001 to 2003 (group 1); 33 patients from 2004 to 2014 were treated with carboplatin/cyclophosphamide/vepesid, followed by 21-30Gy ventricular field irradiation (VFI) (group 2) and 23 patients since 2013 by the CNSGCT brazilian consortium with reducing dose of VFI and ABMT for slow responders (group 3). In all three protocols, toxicity occurred mostly as GIII/IV neutropenia with cyclophosphamide and thrombocytopenia with carboplatin cycles. Recurrence occur in 4 of 8 (50%) G and none NGGCT in group 1; 5 of 26 (19%) G and 4 of 8 (50%) NGGCT in group 2 and none in group 3. Event free (EF) and Overall survival (OS) for the all group was 73,5% and 79,4% respectively in a median follow-up of 49,7 months. According the treatment group the EF and OS was 50% and 60% (group 1), 63,6% and 69,7% (group 2), 95,7% (group 3). Conclusion: Chemotherapy followed by RT seems to promote best response for CNSGCT, specially Germinomas. Chemotherapy followed by 18Gy VFI and ABMT for slow responders seems effective but further follow-up is warranted once late recurrence seems to occur in this group of patients.

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Resumo: Case presentation: Case 1: A 69-year-old female patient with colon IIIB adenocarcinoma, previous colectomy, chemotherapy with modified FLOX and XELOX, evolved with subacute and progressive progression in 20 days to severe tetraparesis (grade 1-2/5 strength), dysphagia and arreflexia. Hospitalized due to neurological worsening and respiratory insufficiency. Negative image investigation, cerebrospinal fluid (CSF) with albumin-cytological dissociation. Treated with 2 cycles of Immunoglobulin (IVIG) with improvement. After 1 year of follow-up, motor improvement with distal right dysesthesia and hypoesthesia. Case 2: A 67-year-old male patient with mucoepidermoid carcinoma diagnosed in 2004, previously submitted to parotidectomy and radiotherapy, is hospitalized due to respiratory insufficiency and pneumonia. The patient presented 30 days before non-specific self-limited infection, with subacute evolution of severe tetraparesis (strength of 1/5 arms and 2/5 legs), ptosis, bilateral facial paresis, reduction of ocular movements, dysphagia and arreflexia. Negative image investigation, CSF with albumino-cytological dissociation. Submitted to 2 cycles of IVIG and 1 corticoid cycle with partial improvement, persisting cranial pairs paresis and dysphagia. Eletrodiagnostic studies (ES) after discharge revealed axonal sensory-motor polyneuropathy. Antibodies for myasthenia gravis were negative. After 7 months of follow-up, motor improvement with dysphagia persistence. Discussion: The Guillain-Barre Syndrome (GBS) is an acute monophasic illness causing a rapidly polyneuropathy with weakness or paralysis. The cardinal clinical features are progressive, most symmetric muscle weakness and absent or depressed tendon reflexes. Usually progress over a period of about 2 weeks. GBS is a heterogeneous syndrome with several variant forms. Diagnosis is supported with cerebrospinal fluid analysis and ES. Treatment include plasma exchange and IVIG. After 1 year after onset and treatment, full motor recovery occur in about 60% of patients. Final comments: We report 2 cancer patients with severe presentation of GBS, whether or not related to their disease and complementary oncologic treatments. Both patients despite the oncological disease and severe presentation presented satisfactory evolution, suggesting that similar therapeutic interventions can be done in cancer and non cancer patients.
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**Temário:** SNOLA - Neurologia Oncológica

**Título:** SECOND AUTOLOGOUS HEMATOPOIETIC STEM-CELL TRANSPLANT FOR RELAPSED BRAIN TUMORS, SINGLE CENTER EXPERIENCE.

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**Resumo:** Introduction: autologous hematopoietic stem-cell transplant (aHSCT) can improve OS and avoid or postpone radiotherapy (RXT) in pediatric brain tumors (BT). Relapsed tumors after HSCT, however, present few therapeutic options and dismal prognosis. Methods: Description of three cases submitted to 2nd aHSCT. Results: three patients underwent new HSCT for relapsed BT after prior HSCT. Conditioning regimen included Cyclophosphamide and Melphalan (CYMel).

Discussion: Patient 1: male, 3 yo, high-grade neuroepithelial tumor (HGNET) - primary cerebellar BCOR submitted to complete resection (CR) and three cycles of chemotherapy (HeadStart protocol - HS). Peripheral blood stem cells (PBSC) were harvested after 2nd cycle. He underwent 1st HSCT with Carboplatin, Etoposide and Thiotepa and tumor bed RXT. Disseminated tumor relapse occurred four months later. Three cycles of Temodal, Irinotecan and Ciclophosphamide plus intrathecal (IT) Topotecan were performed, and new PBSC harvesting after 2nd cycle. New HSCT (CYMel) was performed. Patient died four months after 2nd HSCT of tumor progression.

Patient 2: 18 months, male, classic medulloblastoma (R0M1) submitted to CR and three cycles of chemotherapy (HS), and PBSC harvesting after 1st cycle. Tandem transplantation (three HSCT) with Carboplatin and Thiotepa (C-TT) was performed with no further RXT. Eleven months after HSCT tumor relapsed. Thus, he received five cycles of Temodal, Irinotecan, Cyclophosphamide and Topotecan IT, with 2nd PBSC harvesting after 2nd cycle. A new HSCT (CYMel) was performed. After HSCT patient underwent RXT in tumor bed and neuroaxis. He has been out of treatment in remission for six months. Patient 3: 2 yo, male, medulloblastoma (R0M0). CR was followed by three cycles of chemotherapy (HS) and PBSC harvesting. Tandem HSCT (C-TT) was done with no RXT. Tumor relapsed 14 months later. Three cycles of Temodal/Carboplatin, Irinotecan and Cyclophosphamide were given and PBSC harvested again. Patient underwent new HSCT (CYMel) and he is alive after two months and under RXT. There were no delays in engraftment and major complication included grade 3 mucositis in all patients. Conclusion: A new PBSC harvesting after aHSCT is feasible. Despite poor prognosis, patients with relapsed BT after HSCT may benefit from alternative treatments with mild toxicity. Although longer follow-up and number of patients are required, 66.6% OS in this small sample is encouraging.

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Título: A SINGLE CENTER REGISTRY OF PEDIATRIC CENTRAL NERVOUS SYSTEM TUMORS: REPORT OF 405 PATIENTS.

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Resumo: INTRODUCTION: central nervous system tumors as a group are the second most common solid neoplasia of children and adolescents. Our center is the only one caring for these patients in a region the size of England and with a population of more than nine million. We have been constructing a database of information from cases of pediatric patients with central nervous system tumors for the last three years. This report presents its results. OBJECTIVE: report on a single center hospital based registry of pediatric central nervous system tumors. METHODS: after IRB approval, de-identified data was retrieved from patients charts and used to inform a web based database. Patients 0-18 years diagnosed between 2000-2014 were included. Data quality assessment was performed. Data cleansing was used to ensure standard performance. RESULTS: three hundred, and ninety five patients were included, 216 (55%) male and 179 female, median age at diagnosis 7.3 years (range 28 days to 17.9 years). One hundred and thirty one (33%) of the patients were from the same city of our center, and the rest was from another 118 cities in a 150,000 square kilometers region. Median follow-up time was 1.7 years (range a month to 15.3 years). Eighty patients (20.2%) were diagnosed with medulloblastoma, 67 (17%) were diagnosed with low grade astrocytomas, 41 (10.4%) were diagnosed with ependymoma, 22 (5.6%) were diagnosed with glioblastoma or anaplastic astrocytoma, 16 (4.1%) were diagnosed with oligodendrogiomas or other gliomas, 14 (3.5%) were diagnosed with germ cell tumors, 10 (2.5%) were diagnosed with other embryonal tumors, 40 (10.1%) were diagnosed with miscellaneous other tumors and 105 (26.6%) had no histologic diagnosis (75 with brainstem tumors and the rest with other midline tumors). One hundred and forty five patients (36.7%) had cerebellar tumors, 92 (23.3%) had brainstem tumors, 77 (19.5%) had hemispheric tumors, 66 (16.7%) had midline supratentorial tumors, 11 (2.8%) had spinal tumors and 4 (1%) had tumors in other locations. CONCLUSIONS: this hospital-based registry of central nervous system tumors in pediatric patients has information on all cases treated in a wide region of our country and can be used to inform public health strategies, funding policies and clinical trial designs.

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**Temário:** SNOLA - Neuro-Oncologia

**Título:** ADAM23 GENE EXPRESSION CONTROLS PROLIFERATIVE PHENOTYPE AND ASSOCIATES WITH HIGH RISK GROUP IN DIFFUSE ASTROCYTOMAS

**Autores:** ELISA HELENA FARIAS JANDREY; ELISA HELENA FARIAS JANDREY; NATÁLIA CRISTINA SANTOS; LILIAN TIEMI INOUE; CARMEN LUCIA PENTEADO LANCELLOTTI; ANAMARIA ARANHA CAMARGO; ERICO TOSONI COSTA;

**Resumo:** INTRODUCTION: Astrocytic tumor cells are prototypical examples of invasive, proliferative and life threatening cells. They diffusely colonize brain structures and clinically emerge as devastating masses that lead to a progressive neurological dysfunction and patient morbidity. The aim of this study is to examine the potential role of the ADAM23 gene as a new prognostic marker and a regulator of proliferative phenotype in astrocytomas. METHODS: Gene expression levels and clinical data for 346 astrocytoma patients were obtained from TCGA and visualized with Gliovis portal. Human astrocytoma cells were cultured in vitro and knocked down for ADAM23 expression using small-hairpin RNA (shRNA). To model human disease, these cells were surgically transplanted into the brain of immunocompromised mice. Tumor growth in vivo was monitored weekly by intravital imaging and the histopathological characteristics of the engrafted tumors were evaluated post-mortem by an experienced neuropathologist. RESULTS: We demonstrated a significant correlation between high ADAM23 levels and a shorter OS of grade II-III astrocytomas patients (ADAM23high = 44.0 versus ADAM23low = 93.2 months, HR=0.48, CI 0.28-0.82, p=0.008), but not for grade IV (13.0 versus 14.5 months, HR=0.79, CI 0.54-1.13, p=0.1879). We noticed that our experimental rodent system strongly recapitulate relevant aspects of the human pathology, including histological (e.g. high cellularity, presence of mitosis, extensive invasion) and clinical features. Analyses of tumor growth kinetics, mitotic activity and brain midline shifting index (BMS) revealed that proliferative rates and mass-effect associated with BMS are life-threatening conditions strongly dependent of high ADAM23 expression in astrocytomas cells. As observed in patients, we found that high ADAM23 expression reduced the overall mice survival (ADAM23high = 70.0 vs ADAM23low = 96.5 days, HR=3.70, CI 1.98-61.77, p=0.006). CONCLUSIONS: We provide integrative analysis of clinical and experimental data that strongly indicates that high ADAM23 expression in human astrocytoma cells could be causally linked to short patient survival, mainly due to the positive effects of ADAM23 expression on cell proliferation programs. In this context, development of new drugs for blocking ADAM23 or related pathway could be new strategies to improve astrocytoma treatment.

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Título: AMELOBLASTOMA WITH INTRACRANIAL INVASION. AN UNCOMMON PRESENTATION AND LITERATURE REVIEW.

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Resumo: CASE REPORT: A female patient, 19 year old presenting moderate holocranial headache associated with nausea, vomit, left facial hypoesthesia and low visual acuity. She presented initially with Glasgow Coma Scale 15, bilateral papilledema, low visual acuity, left facial hypoesthesia and vomit reflex absent. Magnetic Resonance Image presented expansive formation heterogeneous solid in clivus with neoplastic aspect with dissemination signs by contiguity and invasion of skull base structures especially cavernous sinus and internal carotid artery, determining still compression of the brainstain. An endoscope skull base biopsy first that was fulfilled with otorhinolaryngology service. The pathology study evidenced histologic section with evidence of neoplasia represented by basaloid-like cells with hyperchromasia and peripheral palisade. Presenting plexiform and microcytic disposition, presence of squamous metaplasia with giant foreign body type reaction. These characteristics defined Ameloblastoma as diagnosis. After the patient was submitted to endoscopic surgery for cranial base tumor at September of 2017 with neurosurgery service. DISCUTION: Ameloblastoma is a locally invasive behavior benign lesion that accounts 1% of all oral tumors. Epidemiological characters are variable in the literature. The most recurrence sites are Mandible and Maxilla. In special, the posterior mandible is the site responsible for 66% of all cases. Usually asymptomatic and with low growth, Ameloblastoma can be found incidentally on routine dental examinations. Rarely presents metastasis, but the Skull Base, Lymph nodes and the Lung are described how sites. Low recurrence rates were reported in few authors when the surgical treatment present underwent tumor resection including the dentoalveolar structures. CONCLUSION: Ameloblastoma with intracranial involvement is a rare presentation with few literature reviews. The long time disease course and multiple surgeries approaches are the characteristics presents in majority of described cases. The Surgical with wide margins is the treatment of choice and Endoscopic transnasal resection is a viable option.

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**Título:** ATUAÇÃO DO ENFERMEIRO NEURO-CLÍNICO ESPECIALISTA NO ACOMPANHAMENTO DE PACIENTES COM TUMOR DE SNC.

**Autores:** DANIELA BARBOSA; Daniela Barbosa;

**Resumo:** Introdução: Os tumores de Sistema Nervoso Central (SNC) são considerados os tumores sólidos mais frequentes nas crianças, sendo apontados como a causa mais comum de morte por câncer na infância. Considerando a gravidade dos tumores de SNC, faz-se indispensável à presença do Enfermeiro Neuro-Clínico Especialista (ENCE) em seu quadro de gerenciadores do cuidado, como profissional competente e qualificado para atuar com este grupo distinto de pacientes. Objetivo: Relatar a experiência da atuação do Enfermeiro Neuro-Clínico Especialista (ENCE), no acompanhamento de pacientes com tumores de SNC. Metodologia: Estudo descritivo, do tipo relato de experiência do ENCE. Resultados: Em 2010 um centro especializado brasileiro incorporou em seu quadro de profissionais o ENCE, este profissional age de forma crucial através do conhecimento, bem com o estreitamento das relações interpessais. Cabe a este profissional organizar os agendamentos clínicos, o gerenciamento de sinais/síntomas, orientação referente Protocolos Quimioterápicos validando as possíveis intercorrências e intervenções durante o tratamento, orientação sobre a forma de aplicação dos diversos medicamentos, apoio psicológico, encaminhamento para outras especialidades e educação permanente através de aulas e treinamentos específicos da área de atuação. O ENCE, portanto, funciona como a "teia de aranha" coordenando e monitorando todo o cuidado do paciente, tornando possível inclusive identificar as necessidades deste público e agir de forma a minimizar riscos e intervir nas demandas levantadas. As competências deste profissional são baseadas em quatro pilares: assistência qualificada; educação/ensino; pesquisa e gestão, a fim de garantir melhoria na qualidade da assistência. Ao identificar cada individuo como único, o ENCE favorece o levantamento de pontos relevantes, incorporando ações à terapêutica, objetivando uma melhor qualidade de vida durante o período do tratamento. O ENCE facilita a comunicação entre membros da equipe médica e demais profissionais da equipe multiprofissional, sendo o ENCE identificado como o profissional que presta cuidado centrado na família. Conclusão: O ENCE assume a responsabilidade do cuidado aos pacientes e suas famílias, estreita sua relação com os referidos e com os demais profissionais da equipe multidisciplinar, favorecendo um cuidado holístico, tornando-se referência para instituição e pacientes com suas famílias.

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Temário: SNOLA - Neuro-Oncologia

Título: AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION IN PATIENTS WITH RETINOBLASTOMA, SINGLE CENTER EXPERIENCE.

Autores: VICTOR GOTTARDELLO ZECCHIN; Ana Cristina Mendonça; Renata Fittipaldi da Costa Guimarães; Virgínio Climaco de Araujo Fernandes Junior; Carla Renata Donato Pacheco Macedo; Paula Gracielle Guedes Granja; Adriane da Silva Santos Ibanes; Cintia Monteiro; Letic

Resumo: Introduction: Retinoblastoma (RB) is the most common ocular tumor in childhood. Early stages carry good prognosis. Advanced stage disease (IV or trilateral stage), however, usually presents dismal prognosis and enhanced disease free survival (DFS) can be attained employing hematopoietic stem cell transplantation (HSCT) as consolidation therapy. Objective: To describe the experience and results with the use of HSCT for RB in a single pediatric oncology center. Methods: Retrospective cohort study of patients submitted to autologous HSCT from March 2005 to December 2017. Results: Fifteen HSCT were performed. Nine patients were female and median age was 4.2 yo. Eight patients (53%) were in 1st remission, of whom six had an initial stage 4 B and two stage 4 A disease; six patients were in 2nd remission and one patient was in 3rd remission. Conditioning regimen included Carboplatin, Etoposide and Thiotepa. Peripheral blood hematopoietic stem cells (PBSC) were used for post-chemotherapy rescue n all but one patient. Engraftment average was D+16 (11-22). Median follow-up was 191 days. Nine patients are alive (60%), of whom two were transplanted in 2nd remission and seven in 1st remission (four stage 4 B, two stage 4 A and one trilateral). Of the six (40%) patients who died, only one had undergone HSCT in 1st remission (stage 4B); one patient was in 3rd remission and the others were in 2nd remission. Transplant related mortality (TRM) was cause of death in two and the others had recurrence of RB after HSCT. Discussion: Despite the modest casuistry, the number of patients undergoing HSCT for advanced stage RB in our institution is higher to that found in literature for single center studies. TRM of 13% was relatively high, however, both patients had disease beyond second remission and were heavily treated prior to HSCT. In this study, we did not observe a trend of better survival in cases of metastatic tumors without central nervous system (CNS) involvement, possibly due to the small number of patients. Conclusion: Autologous HSCT has been shown to be effective in improving DFS mostly in patients in first remission (7 of 8 patients are alive and in remission). TRM was observed in two heavily treated patients. Longer follow-up time and greater numbers of patients are needed to confirm whether the difference in survival reported in the literature in favor of patients with metastatic disease without CNS involvement will be confirmed in this group of patients.

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**Título:** BILATERAL OPTIC GLIOMA ASSOCIATED WITH NEUROFIBROMATOSIS: A CASE REPORT

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**Resumo:** Case report: A 17-year old male patient with a family history of NF-1 and leukemia, referred by the ophthalmologist after the visualization of Lisch nodules. He presented a complaint of headache, pain in the left abdomen, acute, stabbing, attenuated by prolonged walking and arthralgia in the right knee, aggravated by movement (pseudarthrosis under investigation). At physical examination: diffuse spots of coffee-milk staining, dorsal scoliosis present, slight dysmetria when closing the eyes, predominating right upper limb, antalgic gait. Absence of motor deficit. Absence of neurofibroma. MRI of the skull revealed images of hypersignal in FLAIR and T2 in pale globe topography on the right, knee and trunk of corpus callosum and pulvinar of thalamus (myelin vacuolization). Thickening of optic nerves, chiasm and optic pathways (optic pathway glioma). Image suggestive of arachnoid cyst in the bilateral middle cranial fossa. Oriented to make clinical follow-up every six months. Discussion: NF-1 is a relatively common autosomal dominant disease occurring in 1:3000 of the born. Glioma is a proven condition in NF-1, usually in the form of pilocytic astrocytoma, with a prevalence of 15-20%, in the majority of cases and asymptomatic, with indolent evolution and in only 14.8% of treatment cases. A pre-chiasmatic location (64.4%) is more common, chiasmatic (28.2%) and post-chiasmatic (7.4%), being in these last two situations more frequent a presence of symptoms and need for intervention. The bilateral presentation of glioma is found in 34.8% of patients with NF-1 and 50% of patients presenting with problems. Arachnoid cysts are reported rarely in NF-1 and may explain the patient’s headache. One review of the neurological presentation in found that headache was the primary symptom in 61 percent. Conclusion: Finally, we emphasize the need for continuous reassessment of the patient reported in this case, since its type of glioma is much related to the need for therapeutic intervention.

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Título: BIOLOGICAL ACTIVITY OF EUPHOL FROM EUPHORBIA TIRUCALLI ON HUMAN GLIOMA CELLS.

Autores: Viviane Aline O Silva; Marcela N Rosa; Vera Miranda-Gonçalves; Angela M Costa; Aline Tansini; Adriane F. Evangelista; Olga Martinho; Adriana C. Carloni; João Paulo Lima; Luiz F Pianowski; Rui Manuel Reis;

Resumo: Introduction: Euphorbia tirucalli L. (Euphorbiaceae) is a subtropical and tropical plant, used in Brazilian folk medicine against many diseases, including cancer, yet little is known about its true anticancer properties. Aim: To evaluate the antitumor effect of the tetracyclic triterpene alcohol, euphol, the main constituent of E. tirucalli on glioma cell lines. Results and Discussion: Euphol treatment showed a similar cytotoxicity effect against glioma primary culture derived from glioblastoma surgical biopsies (HCB2 and HCB149) compared to commercial glioma cell lines panel (GAMG, SW1088, U251, SNB19, U373, SW1783 and U87MG), pediatric human glioma cell lines (UW479, RES186, RES259, KNS42, SF188). Concentration-dependent cytotoxicity effects of euphol were seen in all cancer cell lines tested, with up to a more than five-fold difference in the IC50 values (IC50 range: 5.98 – 31.05 μM). Also, the treatments with euphol afforded the highest selectivity indexes, from 0.64 to 3.36 compared to temozolomide, which selectivity indices ranged from 0.11 to 1.13. Euphol was able to promote reduction in proliferation as well as cell motility inhibition. No effect was found on cell cycle distribution, invasion and colony formation (anchorage-independent growth). Interestingly, euphol-treated glioma cells does not induce apoptosis; however, the expression of the autophagy-associated protein LC3-II was demonstrated a markedly increase and cells treated with bafilomycin A1 and euphol showed an increase cytotoxicity. In addition, proteome arrays revealed that euphol promotes a balance between pro-apoptotic and apoptotic protein modulation, and differently alters the state of several components of the cellular stress pathway in glioma cell lines. Euphol also presented antitumoral and antiangiogenic activity in vivo, as assessed by Chicken Chorioallantoic Membrane (CAM) assay. Finally, synergistic interactions were observed for euphol and TMZ in most glioma cell lines. Conclusion: Euphol exerted a cytotoxic activity against tumor cell lines. Taken together, these findings suggest euphol, either as a single agent or in combination with chemotherapy, as an antineoplastic compound interesting for GBM treatment.

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Título: CASE REPORT OF RARE MANIFESTATION OF CENTRAL NERVOUS SYSTEM TUMORS ASSOCIATED WITH GENETIC MUTATION

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Resumo: Case report: Patient presented progressive visual loss since 5 years old and learning difficulties that were investigated several times, but only with 11 years old were did images and seen two expansive formations, one if cystic aspect in the temporo-parietal region at left and a other predominantly solid one next to the right cerebral peduncle. The temporal lesion was partially resected and analyzed in another service, with a diagnosis of ganglioglioma grade I WHO. In the initial evaluation in the hospital, it was observed that the patient presented syndromic facies, being asked for genetic evaluation, and repeated imaging tests. Due to the presence of leptomeningeal dissemination, it was decided to perform a new biopsy of the lesions that, in the analysis, confirmed a diagnosis of ganglioglioma in temporal lesion, but the lesion in optic chiasm was diagnosed as pilocytic astrocytoma. In view of the results, a BRAF V600E gene mutation study was performed, with a positive result. In a multidisciplinary meeting, chemotherapy with carboplatin and vincristine and immunotherapy with BRAF inhibitor, if possible, were chosen. Discussion: Low-grade gliomas (LGGs) are a heterogeneous group of tumors common in childhood, which generally have slow growth and the signs and symptoms are generally secondary to the location and direct compression of neural structures. The spread of these tumors in the neuraxis is rare, occurring in approximately 5% of the cases. Although LGGs are histologically and genetically different, all patients with this diagnosis receive similar treatment. However, in recent studies it has been observed that approximately 45% of BRAF V600E positive tumors progress after total resection and that continuous progression is associated with late deaths. Patients with this mutation generally respond poorly to conventional treatment and show good response with target therapy. Although the long-term effects of BRAF inhibitor drugs are not yet known, they can induce rapid response and prevent neurological sequels and disease progression when the tumor responds poorly to classical treatment. Final considerations: Given the association of two concomitant tumors and presence of leptomeningeal dissemination, we believe that the patient has a genetic syndrome to clarify and he will benefit from the use of BRAF inhibitors.

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Título: CEREBRAL TUMOR AS CAUSE OF ACUTE MENTAL CONFUSION IN ELDERY PEOPLE

Autores: AMAURI PEREIRA DA SILVA FILHO; Diego Henriques de Melo Lula; Luana Talita Bezerra Antunes; Rayra Almeida Araújo; Gabrielle Avelino Diniz Gonzaga; Ananda Sobral Soares do Nascimento; Andrew Bonifácio Ferreira; Gabrielly Lima Medeiros; Vinicius Herbet Sales

Resumo: CASE PRESENTATION: Patient, 62 years old, male, Mathematics titular professor at local University, searched the hospital with sudden and episodic complaints of mental confusion and disorientation. Exposed yet symptoms with Linguistics as regards the articulation of repetitive sentences and difficulty to interpret words, texts, and mathematical calculus. Family members reported that he evolved with worsening of mental frames and started with headaches and incoercible vomits. Image examination was requested. The Magnetic Resonance Imaging (MRI) revealed a voluminous lesion extra-axial in the left-brain hemisphere with presence of dural tail, middle line deviation and discrete perilesional edema, suggestive of Meningioma. Patient was referred for surgery, where he held tumor resection, whose biopsy confirmed the diagnosis of Meningioma. Postoperatively, he evolved with improvement of mental confusion, however, developed right motor deficit. DISCUSSION: The main clinical features of patients with SNC tumors are headache, convulsions, focal neurologic deficits and alterations of cognition or personality that are unspecific. These signs and symptoms can be present in several metabolic, psychiatric or neurological diseases, having its clinical presentation low specificity to stablish the cerebral neoplasia diagnosis. Herewith, despite the focal signs may define, in some cases, the topographic localization of the lesion, it has not accuracy to define the specific type of the tumor. Tumors with slow grow, such as meningiomas and low-level gliomas generally present a great volume when diagnosed, due to the cerebral tissue accommodation inside the skull in a determined time lapse. Fast grow tumors and whose develop cerebral edema, however, can develop clinical findings even with small tumoral volume. Behavior, memory or level of consciousness alterations are present in 10-20% of the patients, due to a commitment of cerebral cortex (mainly the frontal lobe) or to intracranial hypertension. CONCLUSION: In virtue of the global encephalic mass reduction, elderly patients may mask the diagnosis, once that the symptoms may delay more to appear. It is important to be attempt to the condition of acute mental confusion, which can be the most precocious finding of a cerebral tumor. Therefore, every patient, with acute mental confusion, must be evaluated by an imaging exam, making, by the way, the differential diagnosis.

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Título: CHOROID PLEXUS CARCINOMA IN AN ADULT WITH TP53 BRAZILIAN MUTATION.

Autores: SAHLUA MIGUEL VOLC; Carlos Afonso Clara; Alisson B. Borges; Edenir Inez Palmero; Henrique Campos Galvão;

Resumo: Presentation: We describe a 28 years-old man who presented with new onset seizures. MRI depicted a cerebral cystic mass in left hemisphere. Complete resection was performed. Pathology examination revealed a Choroid plexus carcinoma. After resection, he was successfully treated with Stupp protocol (Temozolamide and radiotherapy) and is free of events after two years of treatment’s ending. There was no cancer family history, nevertheless, we referenced the patient to Oncogenetic department. The Arg337His mutation in TP53 gene was found in our patient, her mother and two of his three brothers. Discussion: Choroid plexus is a complex structure composed of epithelium, stroma and vascular tissue, that occupies either the lateral, third and fourth cerebral ventricles, producing cerebrospinal fluid. Choroid plexus tumors (CPT) range from benign to malignant lesions. Benign lesions are called choroid plexus papillomas (CPP), which are rare indolent neoplasms, with an annual incidence of 0,3 per 1.000.000 inhabitants. They are five times more frequent than their malignant counterpart, choroid plexus carcinoma (CPC). Their phenotypic diversity suggests that these tumors are best described as a spectrum rather than distinct lesions. Either benign and malignant choroid plexus tumors correspond to less than 1% of all intracranial tumors, comprising 10-20% of them in the first year of life. The majority occurs in childhood, and the median age at diagnosis is 3,5 years. Thus, these tumors are considered a pediatric pathology. Although, almost all choroid plexus tumors are sporadic, there has been significant efforts to examine associations with specific genetic mutations, mainly Li Fraumeni Syndrome (LFS). CPC has been recognized as one of the core tumors for the so called Brazilian mutation in TP53 (Arg337His), which we have found in our case. Conclusion: Despite of being a pediatric condition, choroid plexus carcinoma can occur in adult life. As a core tumor for LFS, this condition must be investigated in patients with CPC. Cancer prevention is an important strategy in clinical practice for this type of tumor. In Brazil, due to high prevalence of TP53 Arg337His mutation, it must be emphasized.

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Título: COMPARING SUPERSELECTIVE INTRA-ARTERIAL CEREBRAL INFUSION BEVACIZUMAB AFTER BLOOD-BRAIN BARRIER DISRUPTION WITH THE OTHERS THERAPEUTIC WAYS FOR RECURRENT GLIOBLASTOMA: A SYSTEMATIC REVIEW.

Autores: RENATO TAVARES TOSELLO; Marcos Perocco; Benedito Jamilson Araujo Pereira; Igor Stroher; Marcos Vinicius Calfat Maldaun; Ronie Leo Piske;

Resumo: Introduction: The use of superselective intra-arterial cerebral infusion bevacizumab after blood-brain barrier disruption in the dramatic scenario of recurrent glioblastoma. Objective: To analyse the safety and efficacy of superselective intra-arterial cerebral infusion of bevacizumab after blood-brain barrier disruption against the others therapeutic means. Methods: Clinical trials using intra-venous chemotherapy (nitrosoureas, temozolamide and bevacizumab), targeted therapeutics, combinational approaches, novel concepts including immunotherapy and superselective intra-arterial cerebral infusion bevacizumab after blood-brain barrier disruption in patients with recurrent glioblastoma are reviewed until January 2018. We included only clinical trials (randomized and non-randomized) that used RANO criteria in this analysis for recurrent glioblastoma. Results: The standard care treatment for glioblastoma (surgery + radiotherapy + temozolamide) showed a rate of 9,8% overall survival in 5 years. However, we know that most of the patients have recurrence after 6-9 months after primary treatment. Recurrent glioblastoma have a dramatic scenario, without well-defined protocol treatment. The best results we could find on all studies analyzed are that the median efficacy results for progression-free survival were 6 months and the overall survival were 4,2 vs 1,5 months and 9,1 vs 8,6 (lomustine plus bevacizumab vs lomustine alone); 10 vs 6 and 11,6 vs 9,3 (rindopectimut plus bevacizumab vs KLH plus bevacizumab), respectively. Superselective intra-arterial cerebral infusion of bevacizumab after blood-brain barrier disruption has shown promising results, with a median for progression-free survival of 6 months, and 3,8 months with a single dose and a median overall survival of 11,8 months, without significant collateral or adverse effects, such as intracranial hemorrhage or malignant hypertension, which has previously been associated with IV BV, and others complications related with the procedure. Conclusion: The superselective intra-arterial cerebral infusion bevacizumab after blood-brain barrier disruption is an easy and safe procedure, with well tolerate minimal side effects, but needing more randomized trials phase II/III to prove your superiority over other ways treatment.

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**Título:** COMPARISON OF INCIDENCE RATES OF THE CENTRAL NERVOUS SYSTEM NEOPLASM IN ADULTS AND ITS RELATION WITH THE HEALTH EXPENSES IN LATIN AMERICA AND NORTH AMERICA COUNTRIES: AN ECOLOGICAL EPIDEMIOLOGICAL STUDY

**Autores:** MONICA D’ALMA COSTA SANTOS; DANIELI AZEVEDO DA SILVA; JESSICA MEDEIROS CABRAL DE SIQUEIRA; MARCELO SOARES SANTOS FERREIRA DA PALMA; RODRIGO FERRARI FERNANDES NAUFAL;

**Resumo:** INTRODUCTION: The Central Nervous System (CNS) neoplasm, despite the low rates, are responsible for the high morbimortality in the whole world and present variable distribution in different countries. OBJECTIVE: In order to compare the incidence rates of these neoplasm and the health expenses relation between Latin America (LA) countries and North America (NA), it were used IARC available data and the Global Health expenses data base from OMS. METHOD: From these, the countries in both data base were selected and they were allocated in a representative group of Latin America that comprehends Argentina, Brazil, Chile, Colômbia, Costa Rica, Cuba, El Salvador, Equador, French Guiana, Jamaica, Mexico, Peru and Uruguai. And the North America, Canada and United States of America. In the BioStat, it was made the Linear correlation test from Pearson between incidence rate standardized by age (ASR), by gender and the Health expenses of these countries and the ANOVA test to compare the average incidence (100.000 people-year) in LA and NA nations, according to gender and age distribution (20 to 85 years). RESULTS: At the Pearson linear correlation, for the male sex, \( r = 0.4492 \) and \( p = 0.0929 \) and for the female sex \( r = 0.4953 \) and \( p = 0.0604 \). For the ANOVA test, in age comparison, we verified \( p = 0.044 \) for men and \( p = 0.0527 \) for women. Despite the fact that there are higher incidence of CNS cancer and the imparity regarding to health expenses, with a per capita average of $682,308 in LA and $7347,05 in NA, these present weak correlation with the new cases number of CNS cancer. The verified \( H1 \) in ANOVA satisfied the hypotheses that the higher the health expenses, higher these neoplasm incidence, and it showed to be true and statistically significant in the male gender, but it was rejected by the female gender. CONCLUSION: Still, it is necessary that other studies come up to relate the health investment impact to the detection of new cases and studies about socioeconomic factors, due to the fact that countries that invest more in health present better social index. REFERENCE: J Ferlay, F Bray, E Steliarova-Foucher, D Forman. Cancer Incidence in Five Continents, CI5plus. IARC CancerBase N.9. Lyon: International Agency for Research on Cancer; 2014. Available from: http://ci5.iarc.fr, accessed 06/11/17.

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Título: CORRELATION BETWEEN MOLECULAR FEATURES AND GENETIC SUBTYPES OF GLIOBLASTOMA: CRITICAL ANALYSIS IN 109 CASES

Autores: THAIS FERNANDA DE ALMEIDA GALATRO; Paula Sola; Isabele Fattori Moretti; Flavio K Miura; Sueli M Oba-Shinjo; Suely KN Marie; Antonio M Lerario;

Resumo: Glioblastoma, the most common and lethal brain tumor, is also one of the most defying forms of malignancies in terms of treatment. Integrated genomic analysis has searched deeper into the molecular architecture of GBM, revealing a new sub-classification and promising precision in the care for patients with specific alterations. Here, we present the classification of a Brazilian glioblastoma cohort into its main molecular subtypes. Using a high-throughput DNA sequencing procedure, we have classified this cohort into proneural, classical and mesenchymal sub-types. Next, we tested the possible use of the overexpression of the EGFR and CHI3L1 genes, detected through immunohistochemistry, for the identification of the classical and mesenchymal subtypes, respectively. Our results demonstrate that genetic identification of the glioblastoma subtypes is not possible using single targeted mutations alone, particularly in the case of the Mesenchymal subtype. We also show that it is not possible to single out the mesenchymal cases through CHI3L1 expression. Our data indicate that the Mesenchymal subtype, the most malignant of the glioblastomas, needs further and more thorough research to be ensure adequate identification.

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Título: CYTOTOXIC ACTIVITY OF A SEMI-SYNTHETIC INGENOL DERIVED FROM EUPHORBIA TIRUCALLI ON HUMAN GLIOMA CELL LINES

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Resumo: Introduction: The attempt to improve the antitumor therapy with new antineoplastic agents from natural sources have revealed efficacy and offers a large field for scientific research. Euphorbia tirucalli is used in traditional medicine in the northeast region of Brazil as antimicrobial, antiparasitic, anticancer and other disease. However, little is known about its anticancer proprieties. Aim: The present study aimed to investigate the cytotoxic activity of ingenol C, a semi-synthetic compound from Euphorbia tirucalli, on human glioma cancer cell lines. Results and Discussion: Ingenol C exhibited dose-time-dependent cytotoxic effects on glioma cell lines (Adult and pediatric cancer cells) and effectively reduced colonies formation on GAMG cells. However, the cell migration evaluated by wound-healing was not attenuated. Flow-cytometry further revealed U373 and GAMG cells treated it that compound to be arrested in S phase and does not induces apoptosis. Moreover, this drug treatment led to LC3B-II accumulation, indicative of autophagy. More importantly, cells treated with bafilomycin A1, a specific inhibitor of vacuolar type H (+)-ATPase that prevents autophagy at a late stage, showed an increase in the ingenol C cytotoxicity. Validated western blot analysis established ingenolC-ability to target a broad range of signaling effectors related to survival and cell cycle regulation, including the upregulation of anti-apoptotic protein p21CIP/WAF1 in both GAMG and U373 cells. In comparison with TMZ, ingenol C showed a median of 135 fold increase in efficacy, in the glioma cell lines. However, we found that when combined, Ingenol C and TMZ treatments, the effect seems to be antagonistic (combination index >1) on the most glioma cells lines investigated. Conclusions: These results suggest that ingenol C is an effective semi-synthetic compound and induces autophagy-associated cell death in human glioma cancer cells.

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Título: CYTOTOXIC POTENTIAL OF BRAZILIAN CERRADO PLANTS EXTRACT CRUDE ON HUMAN GLIOMA CELL LINES

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Resumo: Introduction: Glioblastomas are the most common and aggressive primary brain tumors. The use of new antineoplastic agents of natural sources offers a wide field for scientific research. Studies have shown that Brazilian cerrado plants have been broadly used in popular medicine as analgesic, anti-inflammatory and anticancer agents. However, little is known about their anticancer properties in brain tumors. Objective: To investigate the antitumor effect of thirteen Brazilian cerrado plants extracts on glioma cell lines. Results and discussion: The Brazilian cerrado plants extracts exhibited dose-dependent cytotoxic effects in most of the commercial glioma cell lines (GAMG, U373, SF188 and RES259) and primary glioma cell line (HCB151) derived from glioblastoma surgical biopsies. Amongst the thirteen crude extracts tested, three extracts (17, 18 and 19) from melastomataceae family displayed the best activity among glioma cell lines, with an IC50 mean ranging from 25 to 35 µg/mL. Additionally, the partitions of the crude extract 19 were tested, and the C partition (chloroform) showed a cytotoxic activity higher against the glioma cell lines, when compared to the other evaluated partitions, with the average IC50 value of tumor cell lines of 19.79 µg/mL. Moreover, the extracts 17, 18 and 19 treatment suggested DNA damage induction evidenced by increase levels of H2AX activity in glioma cells (GAMG and SF188) more sensitive. The results also showed that the extract 19 and its partitions have not been able to promote migration and invasion inhibition on glioma cell lines. We also compared the antitumor efficacy of these phytotherapeutic with standard glioblastoma therapy (temozolomide-TMZ) and melastomataceae extracts showed a median of 2.3 fold higher efficacy in the glioma cell lines analyzed, with a range of 0.9 – 5.3 fold. Conclusions: The extracts from the melastomataceae demonstrated potent cytotoxic activity against glioma cell lines. Taken together, our findings may provide insight into the tailoring designing of the natural compounds based therapies for cancer patients. Financial Support: FINEP (MCTI/FINEP/MS/SCTIE/DECIT-01/2013-FPXII-BIOPLAT), FAPEMIG, FAPESP and Barretos Cancer Hospital.

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Título: DISCOVERING THE INFLUENCE OF 15-LIPOXYGENASE AND ITS METABOLITES IN GLIOBLASTOMA GROWTH AND MIGRATION/INVASION

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Resumo: Background: The relationship between extremely aggressive cancers, like glioblastoma (GBM), and fatty acid metabolism could be the key to elucidate more effective therapeutic targets. 15-Lipoxygenase-1 (15-LOX-1), a linolenic acid (LA) and arachidonic acid (AA) metabolizing enzyme, induces both pro- and anti-tumorigenic effects in different cancer types. Its role in glioma activity has not yet been clearly described. Aim: To identify and describe the influence of 15-LOX and its metabolites on glioblastoma cell activity. Methods: Human patient samples of astrocytomas (WHO Grades II, III, IV) were examined using HPLC-MS/MS to identify the endogenous production of 15-LOX metabolites. In vitro culture of different GBM cell lines, treated exogenously with 15-LOX metabolites (13-HODE and 9-HODE) and two 15-LOX inhibitors were also examined. Dose response and viability curves, conventional and quantitative RT-PCR’s, flow cytometry, and wound healing/ transwell assays were performed to identify their influence on GBM growth, migration and, potentially, invasion. Results: The 15-LOX pathway is present and active in GBM cell lines. Higher quantities of 13-Hydroxyoctadecadenoic Acid (13-HODE) were found in patient samples and in five GBM cell lines compared to other lipids analyzed. Both 13-HODE and 9-HODE treatments increased cell count in the tumorigenic cell line U87MG. 15-LOX Inhibition using luteolin (15-LOX-1) and NDGA (12-/15-LOX) generally decreased migration, and increased cell cycle arrest in G2/M phase. Conclusion: 15-LOX and its LA-derived metabolites exercise a certain pro-tumorigenic influence on GBM cells in vitro. Elevated levels of 13-HODE found in the patients/ cell lines call attention to the possible relationship between linoleic acid metabolism and GBM. Further studies are needed to clarify if this relationship positively correlates with malignancy.

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Título: EPENDIMOMA MIXOPAPILAR SACRAL, RELATO DE CASO E REVISÃO DE LITERATURA

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Título: EPIDEMIOLOGIC CHARACTERIZATION OF THE PROFILE FROM MAIN CENTRAL NERVOUS SYSTEM TUMORS AT THE PEDIATRIC POPULATION

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Resumo: INTRODUCTION: the central nervous system (CNS) tumors are the second class of the most prevalent tumors at the childhood, losing only to the hematological lineage tumors, being then an important cause of morbimortality inside of the pediatrics area. The CNS tumors can clinically express themselves by many ways, depending on the its site and the age of the patient. Concerning about these clinical manifestations, it can be noted: intracranial hypertension, focal neurologic deficit, convulsions, nausea and vomits, compressive symptoms, ataxia, headache and cranial nerves palsy, to illustrate some of them. OBJECTIVES: characterize the profile of central nervous system tumors according with its site, age-group and histologic type at the pediatric population at a reference hospital in Neurosurgery. METHODS: it treats of a retrospective and descriptive study, with quantitative approach of the data from 25 patients with age lower than 16 years old, admitted in a reference hospital with the diagnosis of cerebral tumor, in the period of January 2016 to December 2017. The data were collected from a standard form and organized in a spreadsheet of the Microsoft Office Excell 2013®. RESULTS: the female population prevailed and represented 56% of the sample (n = 14). In relation to the period, there was more cases in 2016 (64%). The age-group most prevalent were between 7 and 12 years (44%); followed by the age-group of 4 to 6 years (28%), from 5 months to 1 year (16%) and from 13 to 15 years (12%). The most present histologic type was the pilocytic astrocytoma, with 40% of the cases representation (n = 10). However, the ependymoma were present in 24% of the sample (n = 6). Other histologic types were craniopharyngioma (12%), cerebral metastasis (8%), papilloma of choroid plexus of lateral ventriculus (4%), medulloblastoma (4%) and PNET (4%). About the tumors topography, prevailed the infratentorial localization (60%), while 40% were supratentorial. All the patients were surgically treated. CONCLUSION: the data analysis allows the identification in the studied sample of the significative incidence of infratentorial tumors, respecting the literature, which pointed that the posterior fossa tumors are most prevalent. The study of the CNS neoplasia in children have a great magnitude and its precocious diagnosis is needed to reduce the morbity and mortality of the kids affected by this disease.

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INTRODUCTION: Sellar masses typically present due to neurological symptoms, such as bitemporal hemianopsia, headache; such as an incidental radiological finding or hormonal disorders, such as Cushing’s Syndrome, Acromegaly, among others. These lesions may be characterized histologically as: pituitary adenomas, craniopharyngioma, meningioma, rathke cyst, arachnoid cyst. The etiologic classification of the sellar masses, through histopathology, is extremely important for the treatment and clinical follow-up of the patient. OBJECTIVES: To characterize the profile of sellar masses according to gender, age group and histological type in a population attended at a referral hospital in Neurosurgery. METHODS: This is a retrospective, descriptive study with a quantitative data approach of 24 patients aged 6 to 68 years admitted to a referral hospital with diagnosis of pituitary tumor from January 2010 to December of 2017. Data were collected from a standard form and organized into a worksheet of Microsoft Excell 2013. RESULTS: Females were the predominant gender (n = 18). The most prevalent age group was between 20 and 40 years of age (n = 9), followed by the age group over 40 years (n = 8) and below 20 years (n = 7). Pituitary adenomas were the most frequent tumors (n = 18), of which: clinically non-functioning pituitary adenomas were more prevalent (n = 8), followed by prolactinoma (n = 6), somatotropinoma (n = 2), and corticotropinoma (n = 1). In addition to pituitary adenomas, craniopharyngioma was the second most frequent histological type (n = 5), followed by meningioma (n = 1) and hemangioma (n = 1). CONCLUSION: The above study corroborates with data from previous population studies, showing that pituitary adenomas are the main cause of sellar masses. However in the present study, clinically non-functioning pituitary adenomas were the most frequent histological type. Thus, during the etiological investigation of the sellar masses, pituitary tumors should be a priority in the differential diagnosis, accompanied by hormonal evaluation for possible comorbid endocrinopathies.
Resumo: INTRODUCTION: The spine is the most common site of bone cancer metastasis. These are localized in the thoracic spine in the 70% of the cases, characterizing 2.5% the probability of an oncologic patient to develop at least one episode of medullary and/or equine compression in the 5 years preceding his death. OBJECTIVES: To determine the epidemiological profile of patients with vertebral metastasis in a tertiary hospital. METHODS: This is a retrospective and descriptive study with a quantitative approach of data from 34 medical records of hospitalized patients diagnosed with vertebral metastasis, from January 2013 to January 2018. Data were collected from a standard form and organized in Microsoft Office Excel 2007® spreadsheet. RESULTS: There was a higher prevalence in the female gender, 52.94% of the cases (n = 18); being 47.06% from the male gender (n = 16). The age group over 60 was the most prevalent, with 67.64% (n = 23). About the topography, 64.70% (n = 22) were in the thoracic segment, 14.70% (n = 5) in the lumbosacral segment, 11.76% (n = 4) in cervical segment and 8.82% (n = 3) were multiple metastasis. The primary sites were found in the lungs, with 7 cases (20.58%); prostate, with 5 cases (14.70%); breasts; multiple myeloma, bowels and undefined site (4 cases each = 11.74%); vesicle and bladder, with 2 cases each (5.88%) and renal and pancreatic cells, with 1 case each (2.94%). According to the modified Frankel scale, 50.00% of the patients that entered the service were classified as Frankel A, having pain as the main symptom. Surgical treatment was instituted in 31 cases. The complications were: Urinary Tract Infection - UTI (35.29%); Deep Venous Thrombosis - DVT (23.52%), pneumonia (20.58%), Less important complications (8.82%); DVT + UTI (8.82%) and sepsis (29%). CONCLUSION: The histological type of cancer is a predictive factor regarding the possibility of metastasis to the spine and the development of spinal cord compression, which is a neurosurgical emergency. Diagnosis and early intervention prevents sequels and promotes a better quality of life for cancer patients.
Resumo: INTRODUCTION: Brain tumors, unlike other types of cancer, are much less frequent, however, they are important due to the high numbers of functional deficits and high mortality in relation to other neoplasms. The cerebellar angle point is a vital area for the neurological tissue. Tumors that grow in this region can cause severe brain dysfunction and even death, depending on the size and speed of growth. These tumors account for 10% of all intracranial tumors. OBJECTIVE: To establish the prevalences of cerebellar angle tumors in the general population. METHODS: Data were collected from records of patients admitted to the neurosurgery department of the reference hospital of Campina Grande, who were admitted from January 2010 to January 2018. Eleven patient charts of the neurosurgery service Hospital of Emergency and Trauma of Campina Grande, between 20 and 72 years, with average age of 46 years RESULTS: A higher prevalence was observed in males (72.72% (n = 8)) than females (27.27% (n = 3)); of all cases, 5 had the diagnosis of Schwannoma, 2 of Meningi 1 of arachnoid cyst, 1 of epidermoid cyst, 1 of neurocysticercosis and 1 of cerebral abscess. Among the main symptoms presented by the evaluated patients, hearing loss was the most prevalent, being present in 63.63% of the cases. Other symptoms, such as dizziness, presented a prevalence of 36.36%, being, therefore, the second most mentioned symptom. Facial paralysis with 9.09%, paraesthesia with 9.09%, headache with 9.09% and asymptomatic patients with 9.09%.presented a prevalence of 36.36%, being, therefore, the second most mentioned symptom. Facial paralysis with 9.09%, paraesthesia with 9.09%, headache with 909% and asymptomatic patients with 9.09%. CONCLUSION: It was observed a higher prevalence in the following situations: cerebellar point angle tumors are more frequent in males, with the highest occurrence of Schwannoma, among all tumors. The most frequent symptom was hypoacusis followed by dizziness.

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**Resumo**

Introduction: WNK2, a member of the WNK (with-no-lysine [K]) subfamily of protein kinases, had been found downregulated by its promoter hypermethylation, and has been proposed to act as a specific tumour-suppressor gene in brain tumors. Although some contradictory studies indicated WNK2 as an autophagy modulator, its role in cancer cell death is largely unknown. There is also growing evidence for additional roles of WNK kinases in vesicular traffic. 

Aim: To evaluate the role of WNK2 in autophagy and endocytosis on glioma context.

Methods: Wild-type (WT) A172 cells (WNK2 promoter-methylated), and A172 transfected either with an empty vector (EV) or with a WNK2 expression vector, were used to assess the cellular basal capacities to promote autophagy, through western blot and flow-cytometry analysis. Additionally, we evaluated the effect of WNK2 on general endocytosis trafficking routes by immunofluorescence.

Results: The re-expression of ectopic WNK2 did not interfere with autophagy-related protein light chain 3 (LC3-II) expression levels as well as did not promote mTOR signaling pathway alteration when compared with EV or WT A172 cells. However, the restoration of WNK2 resulted in a marked increase (8 to 92.4%) of Acidic Vesicular Organelles formation (AVOs). Results also suggest that WNK2 cells promotes the greater delay in uptake and internalization rate of cholera toxin B and transferrin ligands.

Conclusions: The restoration of WNK2 interferes in vesicular traffic during endocytosis pathway and increase AVOs formation. This results also suggest the role of WNK2 in growth factor receptor turnover related to cell growth and homeostasis and associates one more time, WNK2 silencing contribution in genesis of gliomas.

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Título: EXPANSIVE LESION ON OPTIC NERVE AND CENTRAL NERVOUS SYSTEM (CNS) DUE TO A LYMPHOPROLIFERATIVE METASTASIS

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Resumo: CASE PRESENTATION: Patient JLS, 60 years old, female, hypertense, diabetic, glaucoma patient, started a grade IV paresis in left inferior limb a year ago, resultant of a previous stroke. She was admitted with deviation of oral rhyme to right, dislalia, dysphagia associated to an ipsilateral hemiparesis and sudden headache of strong intensity. Skull tomography presented left intraparietal bleeding of 5,0 cm³, without middle line deviation, taking as diagnostic hypothesis a new hemorrhagic stroke. Patient started to present conjunctival edema and ocular pain to the right with limited campimetry. Skull magnetic resonance showed an expansive retroocular lesion at right with compression of the medial rectus muscle and intense contrast captation in the ipsilateral optical nerve and heterogeneous captation in parietal solid lesion with hemorrhagic transformation, suggestive of metastatic lesions. An investigative sequence pointed lymphoproliferative neoplasia as the primary site of the implantations. However, the patient evolved rapidly with worse of the clinical condition and went to death. The optical nerves lymphoproliferative infiltration with opthalmologic signs isolated, as a main or recurrent disease, occurs with low frequency. DISCUSSION: There are low prevalence of leukemic metastasis to the Central Nervous System (CNS) and, when occurs, it has as main sites the Kaposi Sarcoma, head and neck or lungs neoplasia and malign melanomas. It’s uncommon the impairment of peripheral nerves. Therefore, is important to highlight the leukemic metastasis in optical nerve as alert to the differential diagnosis between neoplastic bleedings and strokes. CONCLUSION: this case reveals to be atypical by the rare impairment of the optical nerve, evidencing the intraparenchymal bleeding of the metastatic implantation, clinically confounded with hemorrhagic stroke. Therefore, it’s pointed the needing of confront the wide diagnostic hypothesis in the clarification of clinical primary conditions to an accurate investigation of the neurologic pathologies.

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**Título:** EXPRESSION OF HSA-MIR-630 IN PEDIATRIC EPENDYMOMA SAMPLES  
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**Resumo:** Introduction: The Ependymoma (EPN) is the third most common childhood cancer, constituting approximately 10% of central nervous system neoplasms in this age group. Recently, EPNs were segregated into nine molecular subgroups, which represent genetically, epigenetically, transcriptionally and clinically distinct disease entities. Patients diagnosed with ST-EPN-RelA or PF-EPN-A exhibit a more aggressive tumor and poor outcome. MicroRNAs have been described to play a role in many biological and pathological processes such as cell proliferation, metastasis and apoptosis. The hsa-miR-630 has been related as deregulated in several types of tumors, as well as associated with radio-resistance in gliomas. However, little is known about its role in EPN. In this study, we aimed to investigate the expression profile of hsa-miR-630 in pediatric EPN samples. Methods: Tumor samples from 32 patients from Clinical Hospital of the Ribeirão Preto Medical School and Centro Infantil Boldrini, as well as three non-neoplastic brain samples and two EPN cell lines (D612EP and BXD-1425) were evaluated. The hsa-miR-630 expression was accessed by RT-qPCR and the reactions were normalized to the endogenous reference microRNA RNU6b. All statistical analyses were carried out using the software SPSS 20.0. Results: We observed lower expression of hsa-miR-630 in EPN samples classified as poor prognostic molecular subgroups (ST-EPN-RelA and PF-EPN-A) (n=19), when compared with those EPN samples with no specific molecular classification (n=11) (OR=10; 95% CI 0.97-108.8; Two-tailed Fisher’s Exact Test p=0.047; Fold-change=2.97). Although no significant difference was observed regarding the expression of hsa-miR-630 between EPN and non-neoplastic brain, hsa-miR-630 levels were 10-fold lower in tumor samples (n=32) than in non-neoplastic brain (n=3) (Fold-change=5.25; Two-tailed Fisher’s Exact Test p=0.095; OR=10). No other important association was found between the clinical or pathological parameters and miR-630. Conclusion: We found lower levels of hsa-miR-630 in pediatric EPN, which can be related with tumor poor prognosis, specifically, with the molecular subgroups RelA and Group A, whose patients show 10-year overall survival rates of 50% and 56%, respectively. Similar to the study with glioma, our data suggest that this microRNA can play a role in EPN progression. However, in vitro studies with functional assays will be performed to investigate this hypothesis.

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Título: FRONTAL LOBE TUMOR WITH PRESENTATION OF PAROXYSMAL HEMICRANIA

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Resumo: CASE PRESENTATION: Patient, male, 38 years old, without pathologic precedents, just with historic of tensional headache that was presented occasionally. Started to present typical right hemicranial pain, throbbing, of severe intensity, during some minutes, countless times a day and associated to autonomic signs and symptoms. The initial diagnostic hypothesis was of Primary Paroxysmal Hemicrania. However, when submitted to indotest, occurred partial response, being necessary investigate the diagnosis. So, it was done a skull Computerized Tomography (CT) that showed a voluminous expansive process in right frontal region, suggestive of meningioma. He was submitted to total resection, being confirmed the diagnosis of meningioma. After the surgical approaching, happened the cessation of symptomatology.

DISCUSSION: The trigeminoautonomic headaches are characterized by pain with trigeminal distribution, unilateral that occurs with cranial autonomic impairment ipsilateral and presents low prevalence in the world population (<1%). Between these are the cluster headache, paroxysmal hemicrania, short-lasting unilateral neuralgiform headache attacks (SUNCT/SUNA) and hemicrania continua. On the related patient, the diagnosis of paroxysmal hemicrania was considered due to the features of the headache, such as unilateral pain, excruciating and throbbing; duration of the attacks till 30 minutes and the presence of autonomic symptoms, like tearing, rhinorrhea, nasal congestion and ptosis. During the diagnostic evaluation of the patient described above, was done a CT to exclude the possibility of secondary paroxysmal hemicrania. From the CT, this diagnose was considered, once that this disease may have the following etiologies: brain arteriovenous malformation, middle cerebral artery infarction and occipital infarction, pituitary adenoma, frontal lobe tumor, gangliocitoma of turkish saddle, cavernous sinus meningioma, short-lasting unilateral neuralgiform headache attacks (SUNCT/SUNA) and hemicrania continua. Despite the low prevalence of paroxysmal hemicrania, the knowledge about this pathology is necessary due to the important differential diagnosis with the frontal lobe tumors, which may simulate a secondary paroxysmal hemicrania. These tumoral lesions has a good prognosis after surgical, once that generally are benign neoplasias.

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**Título:** FUNCTIONAL ROLE AND CLINICAL IMPACT OF KIT GNNK+ AND GNNK- ISOFORMS IN Glioblastoma  
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**Resumo:** Glioblastoma is the most common adult brain tumor, one of the deadliest human malignancies and this scenario has not changed significantly in the last 3 decades due to the biological properties of glioblastoma. Therefore, it is urgent to understand its molecular players in order to develop novel and targeted therapeutic strategies. KIT, a member of the receptor tyrosine kinase (RTK) family III, is involved with the tumorigenesis of some tumors and the existence of specific small molecule inhibitors for KIT made this protein a key molecular therapeutic target in cancer. Importantly, due to mRNA alternative splicing, KIT is expressed by two different functional isoforms, which are characterized by the presence (+) or absence (-) of a tetrapeptide sequence (GNNK) in the extracellular juxtamembrane region. They were shown to display distinct intracellular signaling features and also different tumorigenic transforming activities in mouse fibroblasts. Hitherto, there are no reports assessing KIT GNNK isoforms functional role in both normal and tumor brain tissues. We aim to shed light on the functional and biological roles of KIT GNNK isoforms in glioblastomas and to assess the tumorigenic role of each KIT isoform and anti-KIT therapy response. The mRNA of glioblastoma tissues was evaluated for expression of GNNK isoforms and also evaluated the KIT expression by immunohistochemistry. Additionally, cellular assays were performed (in vitro and in vivo) in glioblastoma cell lines transfected with GNNK isoforms. We observe the GNNK+ isoform predominance in tumor tissues, differences in survival between patients that express the mRNA of those who do not express, these have a better survival; in cellular assays, we noticed greater viability, potential invasion, tumor growth and angiogenesis of cells transfected with the GNNK-isoform. We did not observe distinct pharmacological role of KIT inhibitors between GNNK isoforms in vitro, but in vivo we observed significant inhibition differences. Although we didn’t find statistically significant differences between the expression of isoforms and clinicopathological information, through cellular assays, we can notice that there are differences in the KIT activation and tumorigenic role between isoforms, thus cells transfected with GNNK- have a more aggressive potential. And, relative to the KIT target therapies, we observed different inhibitors sensitivities (in vivo) according to the isoforms.  

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Título: IGG4-RELATED DISEASE PRESENTING HOW SKULL BASE TUMOR. A CASE REPORT.

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Resumo: CASE REPORT: A male patient, 38 year old presenting in emergence of a reference Hospital with pulsatile headache associated with nauseas, vomit and diplopia. Previous diagnosed with HIV infection. He presented initially Glasgow Coma Scale 15, asymmetric pupils (R>L), Marcus Gunn and right VI cranial nerve paralysis. Fulfilled Brain Magnetic Resonance that showed expansive lesion with contrast capitation in clivus and parasellar regions with size 3,3 x 2,7 x 3,4 cm. The patient was submitted to endoscopic surgery for cranial base tumor at September of 2016. The pathological analysis presented morphological aspect of lymphoplasmocitary lesion igG4 positive in plasma cells. The immunohistochemistry analysis confirmed the diagnosis of IgG4-related disease. DISCUTION: IgG4-related disease is an uncommon immunological condition and little known. The first description was characterized in 2003 when patients with autoimmune pancreatitis were noted to have extrapancreatic manifestations. Related to numerous disturbances who sharing pathological, serological and clinical characteristics particulars. This pathology can course with systemic injury and manifest as solid tumors those mimetic expansive lesions of target organs primary. Involvement of numerous organ systems has been described for IgG4-related disease, including pancreas, salivary glands, periorbital tissues, lungs, meninges and aorta. The exocrine tissue seems preferentially affected. These tumors are composed by infiltrate enriched cell lymphoplasmocitary with positivity for IGG-4 and variable fibrosis level. The clinical presentation is variable and dependent on the organ system involved. Single or multi-organ disease is possible. After the pancreaticobiliary system, the head and the neck is the next most common system involved. Tumefactive lesions in skull base necessitate a broad differential how neoplasia, vasculitides, autoimmune disease and granulomatous conditions. The IgG4-related disease be considered in the differential diagnosis. CONCLUSION: Skull base IgG4-related disease is rare presentation and may be an underrecognized condition. Cases presentation with tumefactive lesions in skull base should have as differential diagnosis the IgG4-related disease. A high index of clinical suspicion and IgG4 immunohistochemical stains can assist in diagnosing.

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Título: IMPORTÂNCIA DO SISTEMA DE CLASSIFICAÇÃO “BERGER-SANAI” PARA PREVER A EXTENSÃO DA RESSEÇÃO DE GLIOMAS INSULARES

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Resumo: INTRODUCTION: 215,000 people under 15 years old are diagnosed with cancer and 80,000 die of it every year in the world. In order of occurrence, the most common pediatric neoplasms are leukemia, lymphoma, tumors of Central Nervous System (CNS) and embryonic tumors. In Brazil, cancer represents the first cause of death per disease in the 1 to 19 years old population, and CNS tumors are nowadays the biggest challenge of pediatric oncology, because they occupy the second place in childhood cancer death. OBJECTIVE: To determine the geographic distribution of new diagnosed cases and deaths due to CNS tumors in Brazilian five regions in the population aged 1 to 19 years in twenty years. METHOD: Descriptive epidemiological study with quantitative approach. From the availability, between 1996 and 2015, absolute values of new cases were collected from the Brazilian Population-Based Cancer Registries (PBCR), according to group III of the International Classification of Cancer in Childhood, third edition (ICCC-3); and deaths per residence, from the Brazilian Mortality Information System (SIM), according to categories C70-C72, D32-D33, D42-D43 of the International Classification of Diseases, tenth revision (ICD-10). Data were extracted in the five regions of Brazil, in the age group from 1 to 19 years, and, after tabulation, submitted to analysis. Data are secondary, in public domain, so there was no need to submit the work to the Ethics Committee on Research in Human Beings (CEP). RESULTS: In the period 1996-2015, the mean number of new cases of CNS tumors per year in Brazil was 235.8, while the mean number of deaths was 511.96. Among the five Brazilian regions, the Southeast had the highest incidence rate, with 89.04 cases (37.76%), and the Northeast, the highest number of deaths per year, with 167.8 cases (32.78%). The North reached the lowest annual average of both new diagnosed cases (21.91 cases) and deaths (48.08 cases), which corresponds respectively to 9.29 and 9.39% of the national average. CONCLUSION: It can be noticed that Brazilian annual average of deaths due to CNS tumors in children and teenagers is high, mainly when compared to the new diagnosed cases per year average. Based on the results, the Southeast and Northeast deserve special attention in the monitoring of new cases and in the treatment of diagnosed patients, with the purpose of avoiding that the high incidence increases the number of deaths beyond expected – when unable to treat.

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Influence of Polyunsaturated Fatty Acids on the Chemotherapeutic Treatment of Glioblastoma

Background. In addition to surgery resection, the most used strategies to treat brain tumors such as glioblastoma are chemotherapy and radiotherapy. However, such treatments fail due to tumor’s acquired resistance mechanisms. Increased protein expression of the superfamily ABC transporters, thereby increasing an activity of multiple drug resistance proteins (MRPs). Polyunsaturated fatty acids (PUFAs) are described in the literature as modulators of the expression of such transporters. Aims. Evaluate the role of ω-3 and ω-6 fatty acids in drug resistance of human GBM cells, verifying the effects upon tumor growth and chemotherapeutic action of Vincristine (VCR), Temozolomide (TMZ) and Etoposide (ETO). Methods. Drug resistant U87MG cell lines were produced by treating cells with VCR, TMZ and ETO in doses according to the literature (0.4nM, 25μM and 100nM respectively). MRPs activity was assessed through the efflux activity assay with the fluorescent compound carboxyfluorescein diacetate. Cell growth assays with fatty acids treatment were performed with GLA (ω-6) and EPA (ω-3) on U87MG and TMZ resistant-U87MG cells (TMZ-R). Results. Cell growth decreased in TMZ-R cells compared to U87MG with TMZ and GLA combination. The combination of TMZ with 25 μM and 150 μM EPA was also effective in decreasing cell growth of resistant cells (p<0.05 and p<0.01 respectively). For non-resistant cells, EPA and TMZ/EPA are effective in decreasing cell growth after 48h at all concentrations. For VCR, U87MG growth with GLA treatments was reduced at different concentrations (100μM and 150μM) and GLA/VCR (p<0.001). Conclusions. Co-treatment with fatty acids (GLA and EPA) and TMZ reveals that resistant cell lines respond differently compared to non-resistant cells. The association between resistance phenotype and treatment’ s response raises questions about the association between MRPs, fatty acid metabolism and resistance. Since we have established our resistance model, new tests are already under way. Financial support. FAPESP.

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Introduction: Astroblastoma is a rare glial neoplasm with uncertain origin, usually located in the cerebral hemisphere of children and young adults. Although insufficient clinicopathological data to establish a WHO grade, these tumors are categorized as well differentiated or anaplastic. Diagnosis can be difficult due to common neuropathological findings with other glial neoplasms. The role of adjuvant therapy after surgical removal remains unclear. Case presentation: the authors report a case of malignant astroblastoma in a 38-year-old female with an initial diagnosis of an anaplastic left temporal meningioma treated with surgical removal and irradiation. After various early recurrences and histopathological reevaluation, the diagnosis of Astroblastoma was confirmed with immunochemistry and molecular analysis. The patient underwent reoperation and stereotaxic radiosurgery (Gamma Knife) and still in continuous post-operative surveillance. Conclusions: Astroblastoma diagnosis still a challenge and must be considered in the differential of supratentorial tumors. Although insufficient data, the best suggested treatment is total gross resection with adjuvant irradiation for tumors with aggressive features.
INVISTIGATING THE TEMOZOLOMIDE CYTOTOXIC AND GENOTOXIC POTENTIAL IN U87MG CANCER CELL LINE

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Glioblastomas multiform (GBM) refers to cancerous cells characterized by invasion and destruction of brain tissue, as well as resistance to radiation therapy and chemotherapy. The use of the antineoplastic drug temozolodamide (TMZ) as a complement to postoperative radiotherapy in patients with GBM demonstrated an increase in patient survival, due to its efficacy and low toxicity. However, resistance remains to be the greatest obstacle on GBM. The objective of this work is to investigate the genotoxic and cytotoxic potential of TMZ in human glioblastoma multiforme U87MG cell line. The U87MG cultures were maintained under standard culture conditions. Initially, the U87MG cell line was treated with serial doses of TMZ for 72 h. 24 h prior to drug treatment, the cells were incubated in a 96-well microplate, at a density of 4 x 104 cells/100 μL/well. Cytotoxicity was assessed using the sulforhodamine B (SRB) colorimetric assay. From this assay we determined IC50 (355 μM) value (drug concentration required to inhibit 50% of cell growth), as well as, IC20 (89 μM) and IC70 (830 μM). Detection of DNA damage was performed by the comet alkaline assay. For this test, the cells were exposed to doses of IC20, IC50 and IC70 of TMZ for 24 h, in addition to the untreated control. After being immersed in lysis solution, they were electrophoresed under alkaline conditions (pH> 13). They were then stained with ethidium bromide so that the nuclei of the cells carrying DNA breaks were visualized in the form of a comet under a fluorescence microscope (Olympus BX51). The intact nuclei appear round, while in the damaged cells, the free DNA migrates from the nucleus towards the anode, showing a tail of fragments. The comet classification was performed using a software (Comet Assay IV - Perceptive) coupled to the microscope. It could be observed a considerable increase of genotoxic damage with increasing dose. The most significant effect being on doses above 355 μM. However, a significant difference is not seen in the damage done to cells exposed at both 355 μM and 830 μM. The study is ongoing, but the results suggest a genotoxic potential of TMZ in the U87MG cell line.

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Case presentation: In October 2012, a 62-year-old woman was admitted with a history of progressive headache and left hemiparesis for about two months. Magnetic resonance imaging (MRI) showed a right temporo-parietal heterogeneous expansive lesion. In the surgery was made the maximum possible macroscopic exeresis. The histological examination, corroborated by immunohistochemistry, showed glioblastoma. The postoperative course was uneventful, with a motor deficit regression at one month and as adjuvant therapy, she underwent full-brain radiotherapy and chemotherapy with temozolamide. Since then, has undergone multidisciplinary outpatient follow-up, being submitted to periodic clinical and imaging exams, which do not demonstrate recurrence of the disease until the present date.

Discussion: Glioblastoma is the most common and unfortunately most aggressive tumor among primary brain tumors. Despite advances in surgical techniques and adjuvant therapies in recent years, the prognosis remains frustrating: most patients die between 12 and 18 months after diagnosis. Only about 2% of these have long survival after diagnosis and concomitant treatment, i.e. three or more years. Clinical and molecular factors that contribute to long-term survival are not yet fully understood. The literature indicates that the most associated factors are: lower age at diagnosis, good performance status, tumor location and multimodal therapy, like surgical resection, radiotherapy and adjuvant chemotherapy. It is also known that the IDH mutation provides a better prognosis in the short term, but survival beyond four years does not require this mutation. In contrast, methylation of the MGMT gene continues to have a strong prognostic value for survival beyond this period. Therefore, such findings have a substantial impact on understanding the biology and progression of glioblastoma. Final comments: Although the advances in the treatment of glioblastoma in recent years, such as the improvement of neuronavigation techniques, functional MRI and the use of substances such as 5-amino-levulinic acid, the prognosis is still poor and cases of long-term survival term are unfortunately the exception. But these cases serve as a stimulus for research in order to better understand the biological behavior of this tumor.

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**Título:** MENINGIOMA IN PREBULBAR CISTERN: CASE REPORT

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**Resumo:** CASE PRESENTATION: female patient, 56 years old, presents complaining of dizziness and subjective vertigo, as well as a discrete difficulty on the walking observed few weeks ago and at the physical exam. She has systemic arterial hypertension. At the exam, no consciousness alterations, presenting vertigo associated to fast movement of the head. Furthermore, showed a lost of muscle strength by right with presence of Babinski’s signal at the same side.

**DISCUSSION:** the incidence of meningiomas in the general population varies between 2 and 15 every 100000 people and rises with age. It has preference by the female gender in a rate of 2-3:1. The meningiomas represents 20% of all primary intracranial neoplastic tumors and 25% of all the intraspinal tumors. The majority of meningiomas are benign, having slow grow and often asymptomatic. They can arise of any place from the dura-mater, being commonest in places of dura-mater reflection or inside of the skull. Between the intracranial meningiomas, 10-15% are located in the posterior fossa, and from them, just 3-10% are petroclival, that by definition, appear in the superior two thirds of the clivus, in the petroclival junction, medial to the fifth cranial nerve. It usually affects middle-aged people and the symptoms progresses for about three years before the diagnostic and includes ataxia, blurred sight, dysphagia, dysmetria, headache, hearing loss, nausea, vomiting and papilledema. As the main acquired risk factor, it’s the previous exposition to ionizing radiation, specially that due to radiotherapy for Central Nervous System tumors or from the head and neck. As genetic factor it’s the type 2 Neurofibromatosis (NF2), in which 50% of its carriers has meningioma. During the initial investigation it’s recommendable to request hemogram and a hormonal evaluation, in which findings as anemia and hypercalcemia can indicate additional tests to multiple mieloma. The presence of atypical findings as edema disproportional to the lesion or cerebral tissue invasion may indicate high level meningioma. **FINAL COMMENTS:** in the investigation of meningioma, the clinical history must be carefully evaluated, principally to the past of ionizing radiation and due to the major incidence at the women, as well as its association to hormonal factors. The breast cancer must be investigated, once that there is a moderate risk of its carriers have meningioma, being the opposite also true.

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Título: NANOTECNOLOGIA PARA GLIOMAS DE ALTO GRAU

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Resumo: Apesar de toda a evolução tecnológica experimentada nos últimos 50 anos, os gliomas de alto grau ainda representam um desafio para a medicina moderna, permanecendo incuráveis, resultando em morte na totalidade dos casos tratados. A quimioterapia sistêmica empregando agentes alquilantes é um dos recursos utilizados para ampliar a taxa de sobrevivência dos pacientes, porém seu emprego costuma ser limitado devido efeitos tóxicos adversos, mesmo quando se empregam doses reconhecidamente terapêuticas. A nanotecnologia é capaz de configurar estruturas biológicas dotadas de elevado poder de difusão por barreiras biológicas e com grande afinidade por tecidos neoplásicos, fazendo dessas estruturas veículos particularmente úteis para direcionar com elevada especificidade substâncias ativas até o interior de neoplasias. O presente trabalho faz uma explanação acerca do racional científico do método, exemplificado por resultados pré-clínicos empregando nanopartículas lipídica sólida frente a barreira hematoencefálica íntegra e lesada, revisando os principais sistemas disponíveis atualmente no tratamento de gliomas malignos.

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Título: NEUROCYSTICERCOSIS PRESENTING HOW CYSTIC EXPANSIVE MEDULLARY LESION. A CASE REPORT

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Resumo: CASE REPORT: A female patient, 16 year-old, presented in Pediatric Service in a Reference Hospital with lumbar pain and fever. This was followed by weakness in limbs. She presented initially Glasgow coma scale 15, no cranial nerves alterations, weakness in limbs with grade 4, bilateral Babinski and sensitive level in D10. From the spinal cord compression syndrome, the patient underwent MRI of the thoracic spine and CSF study. The resonance showed an intradural and intramedullary expansive lesion of cystic appearance in topography of D7 and D8. The CSF study results in 64 cells with 14% eosinophil. The protein was 37.8 mg/dl. Oncotic cytology was negative, as well immunofluorescence test for eschistosomiasis. The test for cysticercosis was positive. Clinical treatment of Neurocysticercosis was started, with positive evolution of the clinical symptoms, and patient received asymptomatic discharge. DISCUSSION: Spinal cysticercosis is a rare form Neurocysticercosis with an incidence of 0.7 to 5.85%. Spinal Neurocysticercosis occurs in patients with intracranial Neurocysticercosis in approximately 75% of the cases. Isolated cases of spinal Neurocysticercosis either intramedullary or extramedullary are considered to be very rare. The patients usually present with paraesthesia, paraparesis and bladder incontinence. The clinical presentation however depends on location, spinal level, lesion size and presence of inflammation. The clinical treatment of intramedullary spinal Neurocysticercosis can be considered in patients with a stable neurological status and in cases diagnosed by cerebrospinal fluid assay. In patients with acute or progressive neurological state surgical excision is the choice of treatment. CONCLUSION: Spinal Neurocysticercosis should be considered in differential diagnosis of spinal mass lesion in patients residing in endemic area such as Brazil. In patients with spinal form, clinical and imaging features may be similar to intramedullary neoplastic mass lesion.

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**Temário:** SNOLA - Neuro-Oncologia

**Título:** ORAL VINORELBINE IN PROGRESSIVE UNRESECTABLE LOW-GRADE GLIOMA: EXPERIENCE OF A SINGLE INSTITUTION

**Autores:** MILENA REIS SANTOS DE OLIVEIRA; Cynthia M Silveira;

**Resumo:** Abstract Background: The management of progressive unresectable low-grade glioma (PULGG) remains controversial. Some series suggests that chemotherapy may delay or even avoid radiotherapy and/or surgery in a proportion of children. Within this context we performed initially an institutional protocol with IV vinorelbine, a semi-synthetic vinca alkaloid that shown activity against PULGG. The objective of this study is to evaluate the response as long as the tolerability of oral vinorelbine in patients with diagnosis of optic pathway glioma (OPG). Patients and methods: Since 2013, 16 patients with recurrent (n=4) and newly-diagnosed (n=12) OPG have been treat with oral vinorelbine in a dose of 90 mg/m² days 0, 8 and 22 for 18 cycles. Response criteria used a combination of magnetic resonance imaging, physical and visual evaluation. Results: Mean age 8.6 years (4.8-17.9). Three children with neurofibromatosis type 1. Eleven patients had neurosurgical intervention revealing grade I (n=9) and grade II astrocytoma (n=2). Eleven patients were assessable after 4/8 cycles of vinorelbine with 2 objective response (OR), 7 stable disease (SD) and 2 progressive disease (PD), one died after surgery and 1 alive in different protocol. After 18 cycles, seven patients were assessable to date for response with 2 OR, 5 SD. The most important toxicity was gastrointestinal observed in 12 patients- six of them withdraw treatment. None of the patients showed neurotoxicity. Conclusion: The preliminary results suggest that oral vinorelbine may show some activity in PULGG. However, gastrointestinal toxicity should be considered. Affiliations (1) IOP/GRAACC/UNIFESP, Sao Paulo, Sao Paulo, Brazil Authors Andrea Cappellano (1) Presenting Cynthia M Silveira (1) Milena RS Oliveira (1) Sergio Cavalheiro (1) Patricia Dastoli (1) Maria Teresa S Alves (1) Gregorio Pereira (1) Frederico A Silva (1) Daniela Barbosa (1) Nasjla Saba da Silva (1) Registration Confirm Categories Low-Grade Glioma

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Resumo: Objective: There have been a limited number of reports describing the outcomes of brain metastasis (BM) arising from certain primary tumours treated with stereotactic radiosurgery (SRS). Our objective was to study the outcomes of such patients treated with gammaknife (GK). Methods: A prospective registry of 1465 patients treated with SRS between 2008 and 2016 was screened to identify 98 patients. Dose was prescribed per institutional guidelines and ranged from 15 to 21 Gy depending upon the target volume and functional area. Demographics, treatment details and outcomes were evaluated, including local failure (LF) and distant brain failure (DF). Statistical analysis was performed using SAS system (version 9.4). Kaplan-Meier product limit method was used for survival analysis, univariate analysis done by log-rank test and multivariate analysis done by Cox regression model. Results: Patients were sub classified into group 1: head and neck (5), gynaecologic (21) or genitourinary (3) primary tumours; and group 2: gastro-intestinal (GI) (39), endocrine (14), and sarcoma (16). Performance scores were ECOG 0 or 1 in 84% and extracranial (EC) disease was controlled in 46%. Whole brain radiotherapy (WBRT) had been administered previously to 17% of patients and 64% had received chemotherapy prior to SRS. At a median follow up of 9 months (range 2 to 115 months), 14 patients had experienced a LF (14.3%). Thirty-nine experienced DF (40%) and 47 (48%) died. Median time to LF was 8 months (range 1 to 110 months) and median time to DF was 7 months (range 1 to 103 months). Local control (LC) with SRS was 88%, and 73%, at 1, and 2 years, respectively. EC disease status was the only factor to impact LC (p=.02)or DF free survival (p=.004). Median overall survival (OS) was 9 months (range 2 -115). One-year OS was significantly better in group 1 compared to group 2 (92% vs. 51%, p=.02). There was a trend towards improved one-year OS when EC disease was controlled (70% vs. 57%, p=0.06). No factors were significantly associated with LC, DF, or OS on multivariate analysis. Conclusion: Patients with metastases from head neck, gynaecological and genitourinary malignancies experience improved OS compared to GI, sarcoma, or endocrine tumours. SRS provides excellent control of BM from uncommon sites. EC status is an important determinant of survival and the use of WBRT and systemic therapies need to be explored in prospective manner to improve disease control.

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Resumo: Aberrant DNA methylation plays a role in the development and/or progression of gliomas. Despite significant progress, glioma classification is suboptimal. Patient-derived neurospheres (NP) and xenograft (PDX) models have been used in glioma research and have the potential to inform our understanding of cancer biology and predict drug response. In this study, we assessed the methylome of IDH wild-type glioblastomas, their derivative NPs and PDXs in order to define the epigenetic changes that occur in such models and evaluate their fidelity to the original tumors. We also evaluated epigenetic stem cell signatures. We analyzed DNA methylation data from 52 samples (12 primary and 1 recurrent tumor, 13 NPs, and 26 PDXs). All samples were profiled using Illumina EPIC array. We applied machine learning methods to classify samples into the previously published IDHwt glioma subtypes (Classic-like, Mesenchymal-like, and LGm6-GBM) based on DNA methylation. Using stem cell epigenomic signatures, we defined a stemness score for each sample. Unsupervised analysis revealed that the DNA methylation pattern is relatively concordant between primary tumor, NP, and PDXs from the same patient. In general, DNA methylation of tumors is lower and can distinguish tumors from NPs and PDXs. The molecular subtypes are represented in the NP and PDX models. In total, 4 cases showed subtype consistency among tumor, NP, and PDX; while 9 of the 13 cases changed the subtype in the NP and/or PDX compared to their matched tumor. While 2 of the 13 tumors are classified as classic-like, we found 10 of the 13 NP classified as classic-like subtype, showing a shift of non-classic to classic-like upon culture. We observed 3 cases where the primary tumor is mesenchymal-like, NP shifted to classic-like and the PDX reverted to the mesenchymal subtype suggesting a role of the microenvironment. The molecular subtyping of tumors, NPs and PDXs are consistent between primary and matched recurrent pairs. Interestingly, NP presented lower stemness score than tumor and/or PDX while, in general, PDX stemness score was higher than in tumors; again indicating the influence of microenvironment in tumor biology. In conclusion, this study advances our understanding of the epigenetic dynamic of in vitro and in vivo glioma models and support the use of NP and PDX models for the study of DNA methylation in cancer, drug discovery, and the development of personalized cancer treatments.
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Modalidade Aprovada: Pôster

Temário: SNOLA - Neuro-Oncologia

Título: PHARMACOLOGICAL INHIBITION OF MST2 AFFECTS CELL SURVIVAL OF MEDULLOBLASTOMA CELL LINES

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Resumo: Medulloblastoma (MB) is the most common type of pediatric malignant primary brain tumor. Despite the new advances, about one third of MB patients die due to recurrence and most survivors suffer from long-term side effects. The discovery of new therapeutic targets is necessary and urgent. In this search for potential targets, we found MST2 a member of MST kinases family (Mammalian Sterile Twenty Like) that belongs to the Hippo Signaling. Several studies have shown the involvement of MST2 and Hippo pathway in carcinogenesis of different tumor types. Therefore, the aim of this study was to analyze the expression of MST2 in MB samples, and investigated the effect of pharmacological inhibition of MST2 on the viability of MB cell lines. We analyzed the MST2 expression in 48 samples of MB, 4 cell lines of MB and 5 non-neoplastic human cerebellum by qRT-PCR. We analyzed the protein expression of total and phosphorylated MST2 of 4 cell lines of MB and 4 non-neoplastic cerebellum by Western Blotting. Then we performed pharmacological inhibition of MST2 in DAOY and UW473 cell lines with the drug XMU-MP-1 (selective inhibitor of MST2). For cellular viability, was performed Resazurin assay in quadruplicate samples in three independent experiments. Cells were treated with different doses of XMU-MP-1 (1, 3 and 10µM) and times (24-96h). For clonogenic survival analysis, was performed in triplicate samples in two independent experiments. The cells were treated with the same doses of XMU-MP-1 for 72 hours and the colonies were counted after staining with giemsa. Mann-Whitney test, Two-way-ANOVA and Bonferroni post-hoc was performed for statistical analysis with SPSS Statistics 20.0. MST2 is upregulated in tumors (p = 0.015) and cell lines (p = 0.032) when compared to non-neoplastic cerebellum. Total and phosphorylated MST2 protein expression is higher in cell lines compared to controls. It was observed that the viability of DAOY and UW473 cells decreased after XMU_MP-1 treatment. The strongest effect in DAOY was from 48 hours of treatment at the doses 3 and 10µM (p<0.05). For UW473, the strongest effect was from 72 hours of treatment at the dose 10µM (p<0.05). In the clonogenic assay, after 72 hours of treatment with XMU-MP-1 the cell lines, DAOY and UW473, did not form any colonies at all doses (1, 3 and 10µM). These preliminary data show that MST2 expression is higher in MB samples and MST2 kinase may be involved in pathways that are important for cell survival in MB.

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Título: Pilocytic astrocytoma in atypical location: Case report

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Resumo: Case presentation: Patient, male, 21 years old, previously healthy, complaining of occasional headache and numbness in the right side of the body started 3 years ago, with progressive worsening, more noticeable in the last 4 months. Physical examination showed fascibracichural hemiparesis on the right (strength grade 4), and hemiparetic gait. In the diagnostic investigation, Magnetic Nuclear Resonance (MRI) of the skull revealed an extensive supratentorial lesion in the left hemisphere, intra-cystic, with a solid cystic aspect extending from the knee of the internal capsule to the posterior subinsular region, its compact part being located in the deeper and with irregular contrast pickup. Neuroradiological aspect suggesting high grade glioma. He was then admitted to the neurosurgery department and submitted to microsurgery for injury. A revised anatomopathological result was found to be pilocytic astrocytoma grade I of the WHO. He is currently undergoing outpatient follow-up. Discussion: Pilocytic astrocytoma is a benign glial tumor, common in children, most commonly located in the posterior fossa (cerebellum) and being infrequent in the supratentorial compartment, but when it usually occurs it appears in the optic, thalamus and hypothalamus pathways. Its clinical manifestation is variable and correlates with its topography. Macroscopically they are circumscribed, have a good cleavage plane, and may be cystic, solid or mixed, and well vascularized. Microscopically, they derive from the piloïd astrocyte, present Rosenthal eosinophilic fibers and intracellular eosinophilic inclusions. Surgical therapy is usually mandatory in these cases, and when completely resected we can consider healing. Usually, it is not considered an eligible lesion for adjuvant treatment with radium or chemotherapy. Rarely does malignant transformation occur in about 3% of patients. Final comments: This is an uncommon case that reports pilocytic astrocytoma with atypical neuroradiological location and behavior. Thus, the importance of clinical, radiological and pathological diagnosis in the treatment and follow-up.

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Título: PINEAL ANLAGE TUMOR IN A 7 MONTH-OLD BOY.

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Resumo: CLINICAL PRESENTATION: 7 month-old boy presented with sudden increase of cephalic perimeter, vomiting and loss of developmental milestones. Seizures and sensory deficits were absent. Neurologic examination revealed setting-sun eye, irritability and bradycardia. Magnetic resonance imaging showed a solid cystic expansive lesion centered on the midbrain with marked hydrocephalus. Near total resection was performed. Pathologic examination revealed a high-grade embryonic neoplasm, characterized by the proliferation of primitive neuroectodermic elements, consisting of small, round cells with hyperchromatic nuclei resembling retinal pigment epithelium and areas of skeletal muscle differentiation as well as areas of immature cartilaginous tissue. Based on these pathological characteristics diagnosis of pineal anlage tumor (PAT) was made. He underwent chemotherapy with methotrexate, vincristin, cisplatin, cyclophosphamide and etoposide. DISCUSSION: In embryology, anlage is the primordium and is the initial clustering of embryonic cells that serves as a foundation from which a body part or an organ develops. The term anlage has a German origin and literally refers to the act of lying on. PAT was first described 20 years and have the characteristics of a pineoblastoma. It presents neuroepithelial and ectomesenchimal differentiation, without endodermal tissue differentiation. The differential diagnosis must take into account malignant teratoma, germ cell tumor with rhabdomyoblastic component, atypical teratoid rhabdoid tumors, melanotic neuroectodermal tumors of infancy and primitive neuroectodermal tumor with mixed or metaplastic elements. FINAL COMMENTS: PAT is an extremely rare type of pineal tumor that has only recently been mentioned in the WHO classification system. After reviewing the literature the authors now present the seventh case of a patient with PAT. Similar to the other cases, this patient presented with hydrocephalus and intracranial hypertension. Although the patient has done well for over a year he now developed disease progression.

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Temário: SNOLA - Neuro-Oncologia

Título: PRIMARY LYMPHOMA OF POSTERIOR FOSSA IN ELDERY AND IT’S DIFFERENTIAL DIAGNOSIS

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Resumo: CASE PRESENTATION: Patient, male, 72 years old, hypertense and diabetic, looked for medical assistance due to sudden walk ataxia, dysmetria, conjugated deviation of seeing, dizziness and vertigos incapacitating. At neurological exam: without alterations of muscular strength, sensibility preserved and presence of horizontal nystagmus. Without other complaints or comorbidities. It was solicited Computerized Tomography (CT) of skull that showed hypotenuating area cortico/subcortical localized in the right cerebellar hemisphere. Magnetic Resonance Image (MRI) illustrated expansive solid lesion of lobulated contours, with extra-axial features, herein at the inferior aspect of right cerebellar hemisphere, occurring edema of the encephalic parenchyma adjacent. Immunohistochemistry indicated primary Central Nervous System (CNS) Lymphoma. DISCUSSION: The causes of cerebellar ataxia are countless, among which detaches the infectious, metabolic, vascular and neoplastic. The primary tumors of posterior fossa are generally more common in kids, being the metastasis, mainly from lung carcinoma or mama carcinoma, more common in adults (50%). Between the primaries, the low level astrocytomas can present with walk ataxia. The hemangioblastomas can cause ataxia both by hemorrhage and by cerebellar compression. Despite it’s strong relation with neurofibromatosis type II, the Schwannomas are great responsible for cerebellar ataxias too. Primary Central Nervous System Lymphomas (PCNSL) represent about 4% of new tumors diagnosed, that can cover either the neuroaxis, as eyes, without, however, let clues of systemic onset. The risk factor most important to the Central Nervous System Lymphomas is the immunodeficiency, with detach to AIDS or systemic illness as Rheumatoid Arthritis (RA). Radiologic findings compatible with PCNSL are peritumoral edema and unique lesion in immunocompetent patients (50-70%). The presence of hemorrhage, calcification or necrosis increases the suspect of PCNSL in immunosuppressed patients. Despite its rarity (<1%), this must be remembered, mainly by its aggressiveness and fast fatality. FINAL COMMENTS: the PCNSL is strongly associated to immunosuppressed patients. In the case, the immunodeficiency of the patient is due to the age. So, the PCNSL makes itself present in the differential diagnosis of the lesions of posterior fossa and of cerebellar ataxia.

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Case report: A 53-year-old female patient attended an ambulatorial neurosurgery clinic with history of onset progressive headache for about one year, associated with minor visual disturbance in the left eye. Physical examination did not show motor, sensory or autonomic deficits. Magnetic resonance imaging (MRI) showed an expansive lesion with a paraselar extension, especially on the left, predominantly isointense in T1 and hyperintense in T2, with homogeneous enhancement following contrast administration. Pituitary hormonal tests did not show any abnormalities. The patient underwent endoscopic endonasal transsphenoidal surgery and a complete resection of the lesion was performed. Postoperative neurological examination remained unchanged. The histological diagnosis, complemented by immunohistochemistry, proved to be a pituitary neuroendocrine tumor. Subsequently, fractioned adjuvant radiotherapy was implemented as postoperative treatment. Control MRI did not demonstrate recurrence of the lesion after two years of follow-up. Discussion: Neuroendocrine tumors originate from the diffuse neuroendocrine system and can appear in almost all organs of the body, being most commonly found in the gastrointestinal and respiratory system. The selar region is an extremely rare site for the onset of such injury. Computed Tomography and MRI findings for neuroendocrine tumors in this region are non-specific since they are similar to other common pathologies such as macroadenoma, metastasis, or meningiomas. The histopathological diagnosis is based on morphological aspects, complemented by immunohistochemical study. A multimodal approach is required for treatment. The literature mentions that endoscopic endonasal transsphenoidal surgery, followed by fractioned radiotherapy and chemotherapy represent effective and safe methods. Therefore, the objective of this case report is to expand the differential diagnoses for expansive lesions of the selar region, as well as the definition of surgical goals and adjuvant treatment strategies. Final comments: Neuroendocrine pituitary tumors, although they are rare pathologies, should be included in the differential diagnosis of lesions the selar region. For the success of the treatment, the multimodal approach is necessary.

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Título: REDUCED HYDROXYMETHYLATION CHARACTERIZES MEDULLOBLASTOMA WHILE TET AND IDH GENES ARE DIFFERENTIALLY EXPRESSED WITHIN MOLECULAR SUBGROUPS

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Resumo: Introduction: Medulloblastoma (MB) is an embryonic tumour that originates from genetic deregulation of cerebellar developmental pathways and it is classified in 4 molecular subgroups: SHH, WNT, group 3 and group 4. Hydroxymethylation levels showed a dynamic during cerebellar development, although studies of its contribution to MB development are scarce. Aims: To investigate hydroxymethylation levels in MB samples; to evaluate mutations at exon 4 of the IDH1 and IDH2 genes; and to study the expression levels of the TET and IDH genes in MB sample. Methods: 5hmC levels were quantified by immunohistochemistry (IHQ) and dot-blot; mutation of IDHs genes were studied by sequencing; and gene expression was evaluated by qPCR. Results: global hydroxymethylation is decreased in MB, and low 5hmC is associated with presence of metastasis. To explain 5hmC levels found in MB, we studied expression patterns of TETs genes and expression and mutations of IDHs genes. TET1 expression levels were decreased in the WNT subgroup, and SHH subgroup showed a low TET3 expression level. Decrease of TET3 expression was associated with presence of events (relapse and death). We observed high expression of IDH2 in MB group 3 samples; however mutations in exon 4 of IDH1 and IDH2 were not found. Conclusion: We concluded that global hydroxymethylation levels are decrease in MB, and TET1, TET3 and IDH1 genes showed specific expression levels in MB molecular subgroups. It suggests that the reduction of this epigenetic event may be important to MB development and/or maintenance; and a role for TETs and IDHs genes in the control of developmental pathways specifically activated in the MB subgroups.

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Título: ROLE OF MELK, STMN1, FOXM1 AND FANCC IN HUMAN ASTROCYTOMAS

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Resumo: Glioblastoma (GBM) is the most common and aggressive malignant brain tumor in adults. Our group performed an analysis of differentially expressed genes between GBM and pilocytic astrocytoma (grade I). One of the genes with increased expression in GBMs compared to grade I tumors was MELK. MELK (Leucine Zinc Embryonic Kinase), protein that plays an important role in various cellular processes, such as proliferation, cell cycle, apoptosis and oncogenesis. An analysis of silenced GBM cells for MELK (siRNA) was performed to identify possible genes associated with the MELK pathway. One of the genes identified was STMN1. The levels of MELK and STMN1 expression in astrocytomas of different grades of malignancy and correlated in GBMs. STMN1 encodes stathmin 1, protein that plays a critical role in mitosis by regulating microtubule dynamics during the progression of the cell cycle, migration and differentiation, through the phosphorylation of four serines. Among several proteins that phosphorylate STMN1, is FANCC (Fanconi C complementation group), which phosphorylates at Ser16 and Ser38. Thus, FANCC participates in the regulation of cell division and is involved in a signaling network that ensures the safeguarding of chromosomes. FOXM1, is indicated as a regulator in the expression of several genes for a cell cycle progression, including STMN1. This correlation was also the target of our study. The goal of this study was to analyze the expression levels of MELK, STMN1, FANCC and FOXM1 in our GBM cohort (100 cases). In addition, these data were validated in silico in larger GBM cohorts of The Cancer Genome Atlas, TCGA (165 cases). MELK and STMN1 expressions are positively correlated in our GBM series ($r = 0.678$ and $p < 0.0001$ - Spearman-rho test). MELK and FANCC expression levels also correlated ($r = 0.340$ and $p = 0.0006$). The correlations of MELK and STMN1 and MELK and FANCC were corroborated in TCGA database ($r=0.213$ and $p<0.0059$, $r=0.689$ and $p<0.0001$, respectively). FOXM1 presented a positive correlation in the gene expression with STMN1 ($r= 0.5665$ and $p< 0.0001$) and MELK ($r= 0.4623$ and $p< 0.0001$) in our series and such correlation was validated in silico with data from the TCGA ($r=0.23$ and $p=0.0029$, $r = 0.76$ and $p = 0.0001$, respectively). In summary, our results from four gene analyses, STMN1, MELK, FOXM1 and FANCC indicate that all may participate in a signaling pathway related to cytoskeletal remodeling involved in cell cycle and cell migration.

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Título: SPINAL GIANT TUMOR CELL TREATED WITH DENOSUMAB.

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Resumo: Case presentation: We describe a 17 years-old boy with an infiltrative painful mass in C2 that destroyed the vertebral body, compressing the medulla. The recommended treatment is excision with wide margin, however, in cervical spine and sacrum it is often not possible. We have performed a biopsy and an arthrodesis. Complete resection was not achieved, because it would involve a significant morbidity. Our therapeutic option was denosumab, a humanized monoclonal antibody that links to RANK-L receptor and deactivates giant cells, reversing osteolytic process. The result was successful, with an important shrink in tumor’s volume and total regression of symptoms. Discussion: Giant cell tumor (GCT) is a mesenchymal neoplasm considered one of the giant cell-rich lesions of bone. They are locally aggressive benign neoplasias, corresponding to less than 5% of all primary bone tumors. Pathology demonstrates giant multinucleated cells, whereas the mononuclear stromal cells are the neoplastic ones. Radiographically, GCTs are osteolytic masses with significant cortical destruction and no sclerotic borders, the so called “soap bubble” pattern. Fluid levels may be seen, revealing coexisting aneurysmal bone cysts. The main locations are the metaphyseal and epiphyseal regions of long bones. Spinal location accounts for 2-15% of all GCTs. The sacral region is the most common affected area in spine, and the incidence is higher in young adult patients. Although GCT is considered a benign tumor, lung metastasis can occur in few cases. When the primary site is the spine, studies suggest a higher rate of metastasis, around 14%. Sarcomatous change appears in less than 2% of GCT in primary tumors or after radiation therapy. Conclusion: Our case emphasizes that a clinical approach with denosumab could be more interesting than a radical surgical procedure in spine’s GCTs.

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Título: STUDY OF EPIDEMIOLOGIC CHARACTERIZATION OF PRIMARY TUMORS OF CENTRAL NERVOUS SYSTEM IN THE ADULTHOOD

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Resumo: INTRODUCTION: the primary central nervous system (CNS) tumors covers a diverse group of neoplasias originated at the glial cells that produces symptoms and clinical manifestations depending of the site which they affect and the mass effect they produce. Depending on the histologic type, the survival time of the patients have a wide scale of variation, making necessary to know which types of primary tumors are most found, respecting its prevalence in each age-group, observing and confronting data with various services, being important, to begin an epidemiologic profile of these patients, the reality of the service that is in study. OBJECTIVES: to determine the incidence of the primary CNS tumors in the adulthood, according to the gender and the etiologic classification. METHODS: this is a retrospective and descriptive study, with quantitative approach of the data from 86 medical records of patients admitted for primary CNS tumors, between 18 and 80 years old, in the period of January 2010 to March 2016. The data were collected from a standard form and organized in a spreadsheet of the Microsoft Office Excel® 2010. RESULTS: the male gender was the most prevalent with 53,49% (n = 46) of the patients, the women represented 46,51% (n = 40) of the admitted patients. About the histologic type, the Glioblastoma was the most prevalent with 29,07% (n = 25), followed by low-level Astrocytomas 15,12% (n = 13), Meningiomas 12,79% (n = 11), the Macroadenomas 6,98% (n = 6), Oligodendrogliomas 5,81% (n = 5), Microadenomas and the Schwannomas, with 4,65% (n = 4) each; followed by the Craniopharyngiomas and Hemangioblastomas with 3,49% (n = 3) each, the Papillomas of choroid plexus, dermoid/epidermoid Cysts, pineal Tumors and Ependymomas, representing 2,33% (n = 2) each; and the central Neurinoma and olfactory Neurinoma, with 1,16% (n = 1) each. CONCLUSION: it was observed that, in relation to the gender, the men presents a higher prevalence of primary CNS tumors, being the main histologic type the Glioblastoma, followed of the low-level Astrocytoma and the Meningioma. So, the prevalence rate acquired matches with the current data of the literature. Besides, contributes as an associative measure to diagnostic, correlating the age-group with the most prevalent histologic type of tumor to the group related.

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Título: SUBEPENDYMAL GIANT CELL ASTROCYTOMA ASSOCIATED WITH CEREBRAL ANEURYSM

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Resumo: Tuberous Sclerosis is an autosomal dominant neurocutaneous syndrome characterized by multiple organs hamartomas envolvent. Brain, skin, eye, kidney and heart can be affected. Brain lesions include cortical tubers and subependymal nodules. A 2 years and 7 months old boy presented with epileptic seizures. On examination interaction was poor and no focal deficits was observed. Cranial magnetic ressonance (MR) FLAIR imaging revealed multiple hyperintense lesions located in bicortical and subcortical areas, linear images located on the white matter extending toward to the ventricules. Bilateral subependymal nodules measuring 2 to 4 milimeters. Nodular heterogeneous lesion located on the left lateral ventricle wall extending next to Forame of Monro measuring 14 x 10 mm, suggestive of Giant Cell Astrocytoma. Angio MR demonstrated a fusiform aneurysm located on left A1. Intracranial aneurysms and Tuberous Sclerosis association are rare, few cases are reported in the literature, but not well stablished. Carefully imaging investigation may prevent further complications.

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INTRODUCTION: Gliomas are the most common primary malignant brain tumors in adults (81%) and they are able to appear in any site of the central nervous system. Any tumor that arises from the glial tissue is called a glioma and they could be such as: Astrocytoma (ASTR), Ependymoma, Brain Stem Glioma, Mixed Glioma, Oligodendroglioma, Optic Pathway Gliomas. ASTR is the most common occurring histologic type, appearing in both sex and any ages. They vary among IV forms, being Glioblastoma Multiforme (High-grade ASTR) 50% of all gliomas.

OBJECTIVE: To describe the number of deaths per year for ASTR in 0-19 years old population at the Latin American countries. METHODS: Descriptive epidemiological study with a quantitative approach. The data were collected from the International Agency for Research on Cancer of the World Health Organization. In lack of further information, the countries studied were Argentina, Brazil, Chile, Colombia, Costa Rica, Cuba, Ecuador, Honduras, Jamaica, Mexico, Peru, Porto Rico and Uruguay. The number of deaths by year in each country was calculated and then tabulated. Its values were analyzed with the use of graphics tools. The data are secondary, public domain and do not present risk to the population studied. RESULTS: The detailed study of the available information showed that Argentina has a ASTR Death per Year rate that reaches 121/year, this value matches 28% of all Deaths by Astrocytomas per year (432 total). The others values founded were 51/year for Brazil (12% of all deaths/year), 25/year for Chile (6% of all deaths/year), 32/year for Colombia (7% of all deaths/year), 14/year for Costa Rica (3% of all deaths/year), 33/year for Cuba (8% of all deaths/year), 44/year for Ecuador (10% of all deaths/year), 7/year for Honduras (2% of all deaths/year), 1/year for Jamaica (0,2% of all deaths/year), 6/year for Mexico (1.3% of all deaths/year), 35/year for Peru (8% of all deaths/year), 41/year for Porto Rico (9% of all deaths/year) and 22/year for Uruguay (5% of all deaths/year). CONCLUSION: Considering the bad prognosis of this disease and the huge prevalence of glioblastoma, it is not a surprise that we have a huge number of deaths. Once our essay studied only a population with 19 years old and some countries can have underestimated data, it shows that the total number of deaths is even bigger and we need to pay attention to start brainstorming a better way to manage the health care assistance for these patients.

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Título: TUMORAL FORM OF NEUROCYSTICERCOSIS. UNCOMMON PRESENTATION OF AN ENDEMIC DISEASE.

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Resumo: CASE REPORT: A 38-year-old male patient was admitted in emergency with headache, nausea and vomiting in July 2017. The history began in May 2017 with progressive left orbital headache. The patient presented worsening of the headache that passed the intense intensity and was associated with right weakness and mental confusion. In the initial evaluation, Glasgow Coma Scale 13 (OR4 VR3 MR6), mental confusion, semantic language alteration, isochoric pupils, right complete hemiparesis grade 4, and paretic gait. Skull resonance image showed an expansive lesion with peripheral contrast uptake and central cystic area. It had an area of peripheral edema of vasogenic characteristic. Patient underwent craniotomy and treatment of intracranial expansive injury via microsurgery in July 2017 by assistant neurosurgeons. The intraoperative appearance after brain exposure resembled tissue of non-neurological origin and with intra-axial invasion. Block resection of the lesion was performed and material was sent for histopathological evaluation. This result showed Neurocysticercosis and patient evolved well in the postoperative period, with improved language and motor deficit. DISCUSSION: Neurocysticercosis is the infection of the nervous system the larval form of Taenia solium. It is a pleomorphic disease, which assumes various forms of presentation and clinical depending on the number, location, size, evolutionary phase and type of cysticercus and individual immune reaction of the host. At tumoral form of the disease, corresponding to 22-67% hypertensive forms, the cysticercus occupies in the brain parenchyma, exerting a mass and causing clinical manifestations of Intracranial hypertension. In cases where the diagnostic procedures are not sufficient to differentiate Neurocysticercosis from a neoplasm, surgical exploration is indicated of the lesion. In addition, the hypertensive form of CN, in most cases, requires surgical treatment, in the form of descompressive craniotomy, microsurgical approach of the lesion or procedure stereotaxic. CONCLUSION: CN is generally characterized by multiple lesions. however, when a single lesion is present, it can easily be confused with a neoplasm primary disease. The differential diagnosis in the tomography of brain cystic lesion includes other parasitic lesions of the CNS (echinococcosis, for example), primary and metastatic neoplasms, tuberculomas, fungal infections and benign cystic lesions.

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**Título:** TWO INDEPENDENT MENINGEOMAS WITH DIFFERENT GRADES IN A SAME PATIENT: CASE REPORT

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**Resumo:** CASE REPORT: 52 years, female, previously health, brought to the emergency department after falling in the bathroom with head trauma. CT scans showed two independent extra-axial lesions in different cerebral hemispheres (left frontal and right scythe), compatible with meningiomas. Surgical resection of the lesions was performed without complications. The lesions were anatomopathologically compatible with meningothelial meningioma grade I (lesion of sickle) and clear cells meningioma grade II of WHO. Patient is followed up in our service, with imaging tests showing no evidence of relapses or tumor remnants. DISCUSSION: Meningiomas represent 13 to 26% of all intracranial tumors, most benign, most common in the female population. Its most well-established risk factors are exposure to ionizing radiation and deletion of the NF2 gene. Surgical resection is the treatment of choice for most lesions. In 1 to 9% of cases of meningiomas, it presents with more than one lesion without correlation with the NF2 mutation, there being 2 hypotheses: CSF propagation of a tumoral lineage or independent development of the lesions. The WHO 2016 classification for brain tumors recognizes 15 types of meningiomas, divided into 3 degrees, the Meningothelial Meningiomenoma being the most common type in the general population. They are located as follows: convexity (35%), parasagittal (20%), sphenoid wing (20%), intraventricular (5%), saddle tubercle (3%), infratentorial (13%) and others (4%). Regarding the invasive aspect of the lesion, grade I lesions are considered benign, with total resection being a curative treatment. Grade II lesions present a significant recurrence rate and up to 1/3 of the patients require reoperations within 5 years. Our patient had two lesions of different degrees, one lesion grade I, compatible with a meningothelial meningioma, and another grade II, compatible with clear cell meningioma, leading to the hypothesis of independent origins. We found in the literature 2 reports of similar cases, also involving 2 different lesions in patients without stigmas for type 2 neurofibromatosis. FINAL COMMENTS: We report a rare case of lesions independent of histopathological findings, including degrees, different in the same patient, without stigmata for neurofibromatosis type 2. We must be aware of possible evolution to malignant lesion.

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Resumo: Introduction: Voice and swallowing are very important for people’s good QOL. Voice, linked directly to oral communication, brings people together; places them in the world and enables them to express their desires and feelings, interfering straight in relationships. Swallowing, in turn, is linked to food, another facet that can significantly affect QOL. Difficulties in feeding, sometimes associated with the risk or occurrence of laryngotracheal aspiration of saliva and/or food, may even contraindicate oral feeding; in these cases, we observed that the impact on their QOL is sometimes devastating, increasing patient’s and relatives stress.

Objective: to analyze voice and swallowing quality of life in cancer patients with medulloblastoma. Method: after the clinical intervention (surgery, chemo and/or radiotherapy), patients were submitted to two quality of life questionnaires, one of which was related to voice (V-RQOL) and another to swallowing (SWAL QOL) Results: regarding V-RQOL, we observed that the overall mean of the total score showed good voice QOL for this sample, as well as for the physical and socio-emotional domains. In relation to swallowing, the mean of patients’ total score was high, demonstrating good quality of life related to swallowing; three domains presented lower scores: desire to feed, duration of feeding and communication. Conclusions: patients with medulloblastoma after clinical intervention presented good quality of life related to voice. Regarding the quality of life in swallowing, they presented good indexes, although they were found lower scores for the domains desire to feed, duration of feeding and communication.

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Introduction: Around 50% of children affected by a central nervous system (CNS) tumor are up to five years of age; however, about 15% of them present the tumor with less than two years old. Of the neoplasms of CNS in childhood, about 30% are diagnosed as medulloblastoma, tumors classified as primitive neuroectodermal (PNETs) with an infratentorial location in the region of fourth ventricle and originated in 85% of cases from cerebellar vermis. Medulloblastoma is the most malignant frequent brain tumor in childhood and its incidence peak occurs between five and seven years. The treatment is usually surgical, followed by chemotherapy and craniospinal radiotherapy. In most of localities, medulloblastoma predominates in boys, with a more evident index in Europe and Oceania. Chemotherapy can present somatic effects caused by cytotoxic drugs as they reach not only malignant tumor, but also healthy tissues and organs; however, it increases survival and contributes to reduction of the amount of radiotherapy. In case of medulloblastomas, craniospinal radiotherapy is usually indicated. Changes in vocal fundamental frequency are commonly clinically observed in the follow-up of these patients. Objective: To analyze acoustically voices of 16 oncological patients with medulloblastoma. Method: We carried out a prospective study of 16 cancer patients with medulloblastoma/PNET, being 10 males and 6 females from the Central Nervous System Tumor Outpatient Clinic of a cancer hospital. This study was approved by institution Ethics Committee. Patients and/or caregivers were invited to participate and, after acceptance, signed the Informed Consent Term and/or Assent Term. Patients were submitted to speech-language pathology questions related to voice. Then, their voices were recorded on a computer (vowel /ε/ and week days), using Multi Dimensional Voice Program (MDVP) software to measure the fundamental frequency (f0), Jitter, Shimmer, Harmonic Noise to Harmonic Ratio (NHR) and Amplitude Perturbation Quotient (APQ). Results: In prepubertal phase, boys had a mean of f0 lower than expected and in the post-puberty, f0 was slightly higher than expected; in the female group, the means of f0 pre and post-puberty remained within the expected frequency range; all other acoustic indicators were present, with values higher than expected. Conclusions: It was observed a change in f0 of male patients and other acoustic indicators also presented alterations above the normal indexes.
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Temário: SNOLA - Neuropatologia

Título: ASTROBLASTOMAS IN CHILDREN – RADIOLOGIC, ANATOMIC AND PATHOLOGIC FEATURES: A CASE REPORT

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Resumo: Astroblastomas are rare neuroepithelial tumors of unknown origin, which occur in as many as 0.45 to 2.8% of all glial neoplasms. They affect primarily young adults and children, and are not widely described in literature, especially in the pediatric field. As for their radiographic features, astroblastomas are large, peripheral, solid, and with cystic mass, which can be mistaken for other glioma. This clinical report dwells on the case of a six year old patient, female, previously healthy, whose clinical picture started with sudden lip spasms and stuttering and later evolved to mild headache. The patient underwent a magnetic resonance imaging on the head and a diagnosis of a pilocytic astrocytoma was suggested. After a complete excision of the lesion, the patient recovered completely from all symptoms, with no neurological damage. The analysis of the anatomical and pathologic features of the tumor proved it to be astroblastoma. Due to the tumor being low-grade and rare, there are divergences in current literature; however, most studies recommend clinical follow-up and, in case of recurrence, a new surgical approach followed by radiotherapy sessions. The patient is currently asymptomatic, with no radiological or clinical incidence of the disease. This study is therefore relevant to showcase the importance of anatomical and pathological analysis of tumors in the central nervous system with the objective of determining precise histology of the tumor.

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Resumo: Cerebral amoebiasis is a very rare and extremely lethal infectious disease caused by the protozoan of the genus Acanthamoeba. The parasite can be found in several places such as soil, dust and natural water. The infection can start in the large intestine, skin or by inhalation of the parasite in contaminated water, and it spreads to the CNS in the majority of the times via the hematogenic route or the nasal airways, where it arrives and crosses the blood-brain barrier. CNS involvement is more problematic in immunosuppressed patients, such as HIV-positive. The most frequent symptoms are mental confusion, headache, nausea, vomiting, fever, lethargy and focal neurological deficits. Imaging diagnosis is often not conclusive, due to the similarity of lesions with CNS tumors. Currently, there are no effective treatments, however, the better alternatives are based on surgery and the use of antiparasitic, and even in this scenario, only 10% of the patients survive. The present study reports a case of a 52 years old female patient who was referred to the Hospital de Cancer de Barretos with suspected glioblastoma. She presented apathy, disorientation and frontal syndrome. MR examination showed an expansive lesion affecting the knee of the corpus callosum and extending to the deep frontal white matter bilaterally with exuberant perilesional vasogenic edema. These findings are suggestive of high grade glioma. Biochemical tests showed normal blood counts, with no evidence of immunosuppression. During the surgical procedure, it was found to be an inflammatory infectious process of brain tissue, and subsequent empiric treatment with antibiotic and antifungal agents was initiated. Anatomopathological examination evidenced the absence of neoplastic cells, the presence of an abscess inflammatory process and the presence of morphologically cells compatible with amoebic parasites. The immunohistochemical analysis of CD68 (macrophage marker) showed the presence of CD68 positive macrophages in the inflammatory process, as well as CD68 negative amoeboid cells, reinforcing the suspicion of cerebral amoebiasis. The patient died three weeks after developing sub-sylvian herniation and decerebration due to cerebral edema. In conclusion, we report a rare, atypical and lethal case of cerebral amoebiasis, with an initial suspicion of brain tumor, highlighting the absence of signs of immunosuppression, frequently associated with other reports of cerebral amoebiasis.

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**Título:** CHOROID PLEXUS CARCINOMA WITH OSTEO SARCOMATOID METAPLASIA: CASE REPORT AND LITERATURE REVIEW

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**Resumo:** Case presentation: Male, 4 years old, intermittent headache and vomiting 2 months ago and progressed with right lower limb claudication. Important personal background: 2 maternal aunts with cancer in the CNS and maternal grandmother with breast cancer. Image study: expansive lesion rounded in the cerebral hemisphere on the left, measuring about 8cm x 8.2cm x 6.5cm, showing heterogeneous signal in all sequences, with evidence of cystic areas, calcifications, hemorrhagic outbreaks, and a calibrous vessel in its interior. It presents pronounced heterogeneous enhancement after contrast. Lesion with extensive peripheral edema and considerable mass effect causing contralateral deviation of midline structures by about 1.5cm. He underwent partial resection, followed by adjuvant chemotherapy and radiotherapy. Biopsy with morphological and immunophenotype compatible with choroid plexus carcinoma (CPC), presenting areas of osteosarcomatoid metaplasia. In palliative care, one year later, he presented with holocranial headache and vomiting, tremors and seizures, evolving with aphasia, paraparesis and death. Discussion: Choroid plexus tumors are neuroepithelial neoplasias, intraventricular, rare and correspond to less than 1% of all intracranial tumors. CPC are tumors of unfavorable behavior, grade III - WHO, typically manifest in the first decade of life and correspond to 8.1% of all tumors of the choroid plexus. The etiology has been related to infection by the SV40, syndromes linked to the X chromosome and in association with Li Fraumeni Syndrome. Bone and cartilage are uncommon histopathological findings in neuroepithelial neoplasms. Several mechanisms have been proposed to explain the development of these mesenchymal elements in gliomas such as metaplasia, heteroplasia, the teratomatous nature of these neoplasms, the mesenchymal neuroepithelial nature and mineralization and ossification as the final stage of mucoid dehydration. Metaplasia in the present case should be considered because of the pluripotential properties of the mesenchymal constituents and their ability to transform into other cell types under appropriate stimuli. Final Considerations: This is a rare case of CPC presenting joint osteosarcoma-like sarcomatous differentiation, probably of metaplastic origin, with little response to adjuvant treatment, in a child with an important family history, emphasizing the importance of diagnosis and consequent family assessment.

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Título: CRYPTOCCOMA MIMICKING A BRAIN TUMOR IN AN IMMUNOCOMPETENT PATIENT – AN EXTREMELY RARE PRESENTATION

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Resumo: CASE PRESENTATION: A 54-years-old female patient presented to neurosurgical emergency department with a quick and progressive history of confusion and completely dependency for basic activities. On her neuroimaging, a left occipital lesion was visualized and neurosurgical procedure was proposed. During histopathological evaluation an undoubtful diagnosis of cryptococcoma was performed. She received clinical support with antifungal but despite the optimal treatment, she evolved to death. DISCUSSION: Central nervous system (CNS) infectious diseases have a great prevalence in developing countries and their proper diagnosis and treatment are very important for public health planning. Cryptococcus neoformans is a fungus that may cause several CNS manifestations mainly in immunocompromised patients. Cryptococcal meningitis is the most common type of commitment. Mass lesions are very uncommon, they are described as cryptococcomas and their prevalence is even smaller in immunocompetent patients. The aim is to report an extremely rare case of a cryptococcoma causing mass effect and mimicking a brain tumor in an immunocompetent patient. Clinical, surgical and radiological data of a female patient with a rare presentation of cryptococcoma mimicking brain tumor was described. COMMENTS: Cryptococcosis infections have several forms of presentations and, in immunocompetent patients, their manifestation could be even more different. Cryptococcoma is an extremely rare presentation in which proper surgical and clinical treatment should be performed as soon as possible but even so evolve with a high mortality.

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Título: LOSS OF SPINT2 IS FREQUENT IN GLIOMAS, LEADING TO INCREASES GLIOMA CELL GROWTH AND INVASION, VIA A MMP2 ACTIVITY

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Resumo: The invasion capacity capability of gliomas is the most important feature of tumor aggressivenessmalignant characteristics of most concern. Among others, serine proteases and metalloproteases play a key role on this migration and invasion mechanismsfeature. SPINT2 is a serine protease inhibitor that was demonstrated to be underexpressed in a variety of cancers. Hypermethylation of SPINT2 promoter was demonstrated to be a common mechanism for this downregulation. Herein, we intend to determine the clinical relevance of SPINT2 expression/hypermethylation in pediatric and adult high-grade gliomas (HGG), as well as to elucidate the functional role of this protease inhibitor. A cohort series of 371 adult and 77 pediatric primary HGG samples was used to characterize protein expression (immunohistochemistry) and methylation status (methylation-specific PCR) of SPINT2. A variety of in vitro assays were performed to determine the role SPINT2 on pediatric and adult glioma cells viability and invasion and its impact on metalloproteases activity was also evaluated. We observed that SPINT2 protein is frequently absent in adult HGG (85%) and in all (100%) pediatric cases. The SPINT2 promoter was found to be hypermethylated in both adults and pediatric gliomas, in around 50% of the patients. Moreover, SPINT2 underexpression and its promoter methylation seems to be associated with glioma development and aggressiveness markers, as IDH1, PDGFRA and VEGFR (in adult age) and PI3K (pediatric age) alterations. Functional assays demonstrated a suppressor activity of SPINT2 in the control of glioma cells proliferation and viability, as well as in the migration and invasion glioma cells capacity. MMP2 expression and activity seems to be a target of SPINT2, since upon upregulation of SPINT2 both are decreased. We concluded that low expression of SPINT2 and gene hypermethylation are common events in both pediatric and adult HGG, being associated with higher tumor aggressiveness.

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Título: MAFFEI ANATOMIC NEUROPATHOLOGY ATLAS: MULTIDIMENSIONAL COMPUTERIZED ADAPTIVE TESTING AND LEARNING PROGRESSION FRAMEWORK

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Resumo: For the Pathology teaching and learning, images of morphologic alterations both macroscopic and microscopic are fundamental. Morphological recognition, through naked eyes and microscopic device, are important steps in Autopsy and Chirurgic Pathology practice. Autopsy, gold pattern in clinical quality control, unfortunately reduced in the last decades, make the PATHOLOGY ATLAS a fundamental didactic resource, that provide not only images compilation but tests and performance evaluations in a virtual environment. Although the WEB offers numerous atlases of pathology, the proposal of study and evaluation through the use of digitized images combined with Computerized Adaptive Tests (CAT), is what makes this proposal unique. Objectives: Development of an atlas of neuropathology, online, containing macro and microscopic images, obtained from autopsies, covering the topics of Pathology with a system of evaluation through CAT. A CAT is a computer-administered test in that, after the first item, the presentation of items is determined by a person’s response to previous ones, adapting to the respondent knowledge / skill. Material/Method: Seven hundred and fifty images of Neuropathology, digitalized, available online, obtained by Prof. Dr. Walter Edgard Maffei, one of the pioneers of Neuropathology in Brazil, who inspired several generations of physicians to embrace Pathology as a speciality. The photographic images, on 10 cm x 8 cm glass slides, were obtained from emblematic cases of autopsies performed at the Franco da Rocha Psychiatric Hospital. The images will be presented integrated to the CAT tests covering the topics of Neuropathology. CAT results are obtained with the application of item bank, using the Item Response Theory (IRT) - set of questions available / usable in the test. Algorithms determine the items presented initially and sequentially, depending on the correct or incorrect response. The IRT makes a psychometric approach emphasizing that the response to a given item is influenced by the qualities of the individual and the item. Web based educational systems with integrated computer based testing are the easiest way of performance evaluation, so they are increasingly adopted by universities.

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Título: METASTIC GLIOBLASTOMA: CASE REPORT AND REVIEW OF LITERATURE

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Resumo: Case report: Male, 9 years old, presented with loss of consciousness, increased blood pressure, ophthalmoplegia and cranial hypertension. Magnetic resonance imaging revealed expansive lesion with midline deviation, mass effect and irregular contrast enhancement, located in the frontal temporal parietal region. The biopsy showed a hypercellular lesion, with extension to the meninges, represented by cells with important aiptias and pleomorphism, interspersed by foci of tumor necrosis with peripheral palidation and rare blood vessels with endothelial proliferation. Immunohistochemistry demonstrated strong and diffuse positivity for GFAP, S-100, vimentin and CD-99 protein. EMA, cytokeratin, muscle and neural markers were all negative, favoring the diagnosis of glioblastoma, WHO grade IV. Radiotherapy and chemotherapy were performed and after 5 months of treatment, they presented right cervical lymphadenopathy. Lymph node biopsy was performed with morphological and immunohistochemical findings similar to those of brain biopsy. In both samples, the INI 1 was tested for the exclusion of the Teraboid Rhadoide tumor. During the evolution, two months after the diagnosis of lymph node metastases, the patient presented pain in the lumbar region, whose magnetic resonance identified multiple bone lesions in the vertebral column and posterior mediastinal mass. Radiotherapy was performed followed by improvement of symptoms, but pain returned after discontinuation of treatment. After 30 days, metastasis to the mouth and lower gingiva appeared, accompanied by respiratory distress, indicating trachestomy with rapid progression to respiratory failure and death. Discussion: Multiform Glioblastoma is highly malignant and has a tendency to spread intracranially. Extracranial or spinal metastases of high-grade gliomas are rare. Among the mechanisms proposed for the occurrence of metastases, multiple surgical interventions are a major predisposition. Ventricular drain, interstitial brachytherapy, stereotactic biopsy, and Batson’splexus propagation may also contribute to dissemination. Final Considerations: although rare, extra-cranial brain metastases should be investigated in patients with high-grade tumors, particularly if complicated with extracerebral manifestations. Unfortunately, there are few studies for a better understanding of this unfavorable outcome.

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Resumo: Pituitary adenomas have long been classified by combining hormone content, histopathological, immunohistochemical and ultrastructural features of the tumor cells. WHO (World Health Organization) 2017 classification has adopted a pituitary adenohypophyseal cell lineage designation and utilizes immunohistochemistry as the main ancillary tool for diagnosis. As consequence, a routine ultrastructural examination is not needed for the correct classification of the vast majority of pituitary adenomas. A retrospective analysis of a series of 42 pituitary adenomas that underwent surgical treatment at the Sarah Network of Rehabilitation Hospitals was performed to adapt histopathological exams to WHO 2017 classification. In addition, as our service does not have transcription factors, but we have ultrastructural analysis, this work also aims to highlight the importance of electron microscopy as a tool to validate the hormonal profile of pituitary adenomas. The patient group included 20 females and 22 males (range 25-68 years). Thirty-six were macroadenomas, 2 microadenomas and in 4 there were no clinical data. Four macroadenomas showed invasion of the cavernous sinus. Twenty-one adenomas were clinically nonfunctioning, 13 GH, 3 ACTH and 3 PRL secreting adenomas. There was no clinical data in 2 patients. Based on the immunohistochemical profile we found the following results: 7 showed no hormonal immunomarkers, 14 were monohormonal, 17 showed 2 hormonal immunomarkers and 4 were plurihormonal. The monohormonal ones were: 4 gonadotroph (LH or FSH positivity), 4 somatotroph, 4 lactotroph and 2 corticotroph adenomas. Ki-67 labeling index ranged from 0.1 to 9.3%. Diffuse p53 protein immunoreactivity was seen in 10 cases. Based on the ultrastructural study: 2 GH, 1 PRL and 1 ACTH adenomas were densely granulated. Six, 3 and 2 were GH, PRL and ACTH sparsely granulated adenomas, respectively. Ten adenomas showed oncocytic changes. Tumor recurrence was observed in 4 cases after a mean time of 18 months (range 9-24 months). Mean follow-up was 36.5 months (range 6-67 months). The classification according to WHO 2017 criteria is necessary because it allows to add substantial information for prognosis and therapeutic choice (drug, surgical and radiotherapy) of those patients with the diagnosis of pituitary adenoma. Ultrastructural study has a pivotal role in the separation of entities with overlapping immunohistochemical profiles.

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Título: THE PROSTANOID PATHWAY CONTAINS POTENTIAL PROGNOSTIC MARKERS FOR GLIOBLASTOMA

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Resumo: Background. Prostanoids derived from the activity of cyclooxygenases and their respective synthases are known to contribute to both active inflammation and immune response in the tumor microenvironment. Their role in glioblastoma has not yet been fully explored and both their synthesis and degradation require further study in order to identify their contribution to glioma biology. Methods. Using quantitative real time PCR, gas chromatography/electron impact mass spectrometry and liquid chromatography/electrospray ionization tandem mass spectrometry, we have further characterized the prostanoid pathway in glioblastoma. Results. We observed significant positive correlation between mRNA expression levels and patient survival for microsomal PGE synthase (mPGES1) and for the 15-hydroxyprostaglandin dehydrogenase (15HPGD) degradation pathway enzyme, while we observed a negative correlation for the prostaglandin reductase 1 (PTGR1) degradation pathway enzyme. We found a higher quantity of the prostanoid precursor, arachidonic acid, in grade IV tumors in comparison with grade II/III tumors. A significant difference in prostanoid concentration was found between grade II/III and grade IV tumors for TXB2, PGD2, PGE2 and PGF2α. A correlation between substrate fatty acid precursor and prostanoid product was only found for arachidonic acid and PGE2. A significant survival difference was detected for high versus low PGE2, PGE2+PGEM’ s and PGF2α in grade IV patients. Conclusions. Our findings point to the potential importance of prostanoid metabolism in the progression towards glioblastoma and provide evidence that PGE2 and PGF2α concentrations in the tumor are correlated with patient survival, as are the mRNA expression levels of certain enzymes in the prostanoid pathway. The study also highlights the importance of the enzymes 15HPGD and PTGR1 as potential prognostic biomarkers which could be used to predict survival outcome of glioblastoma patients.

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Resumo: Introdução: Ependimomas representam 5 a 8% das neoplasias em sistema nervoso central (SNC) em crianças. A radioterapia (RT) tem sido utilizada como componente do tratamento desde 1950, elevando a sobrevida global destes pacientes de 13-23% com cirurgia isolada para 45-63% com cirurgia seguida de radioterapia adjuvante. Entretanto, a principal recidiva é local. Dos pacientes que apresentam recorrência, cerca de 87% apresentam falha tumoral próxima ao leito cirúrgico irradiado. Objetivos: Avaliar o padrão de recidiva em pacientes pediátricos com diagnóstico de ependimoma submetidos à radioterapia adjuvante. Material e métodos: Estudo de coorte retrospectivo. Critérios de inclusão: pacientes com até 22 anos de idade com diagnóstico histopatológico de ependimoma submetidos a pelo menos um curso de radioterapia adjuvante no Instituto de Oncologia Pediátrica do Grupo de Apoio ao Adolescente e à Criança com Câncer (GRAACC), com intuito curativo e seguimento mínimo de 1 ano. Resultados: Foram avaliados 104 pacientes com neoplasia em SNC tratados de 2014 a 2016. Destes, 22 pacientes tinham diagnóstico de ependimoma. Foram excluídos 10 pacientes por seguimento menor do que um ano. Dos 12 pacientes avaliados, 59% eram do sexo feminino, a mediana de idade foi 6 anos (1-13 anos). A principal topografia da lesão foi fossa posterior (72%), somente 1 paciente apresentou doença em coluna ao diagnóstico. 54% dos pacientes foram submetidos à ressecção subtotal e 64% realizaram 2 cirurgias ou mais antes da radioterapia. Ependimoma grau 3 foi encontrado na maioria dos casos. 36% dos pacientes realizaram quimioterapia pré RT, um deles aos 10 meses de idade. 59,4Gy foi a dose de RT mais prescrita e todos os pacientes completaram o curso de RT proposto. A maioria dos pacientes (63%) não fez o primeiro curso de RT no GRAACC. A mediana de seguimento foi 2,6 anos (variou de 20 meses a 7 anos). 72% dos pacientes apresentaram recidiva no volume irradiado e a sobrevida livre de recidiva foi 20 meses. Apresentaram segunda recidiva 54% da população estudada e todos foram submetidos a segundo curso de radioterapia. Nenhum paciente apresentou radionecrose. 36% dos pacientes faleceram, todos relacionados à progressão da doença. Conclusão: O principal padrão de recidiva foi local e dentro do volume irradiado. Re irradiação foi bem tolerada na população estudada.

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