EM-01. POST-OPERATIVE RADIO THERAPY FOR FOURTH VENTRICLE EPENDY MO MA IN CHILDREN BELOW 3 YEARS OLD: GOOD PRELIMINARY RESULTS

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BACKGROUND: Children’s brain is continuously developing. Radiation oncologists usually refrain from radiating brain in the first 3 years. PURPOSE: To identify the feasibility of irradiating infratentorial ependymoma postoperatively in children below 3 years and to report on its effect on survival and toxicity. PATIENTS AND METHODS: Thirty seven children were diagnosed as ependymoma in children’s Cancer Hospital, Egypt (CCHE) during the period from Jan 2008 to Dec 2010. Out of these, 6 (16.2%) were below 3 years old. They were all males with a median age of 20.3 (range: 13-25) months. Two tumors were totally excised having a specific histology (G III). The other 4 were excised with residual left infiltrating the brainstem. The histopathology was G II in 2 patients and anaplastic in the other 2. Only two patients received chemotherapy prior to subtotal excision. All 6 children received intensity-modulated radiotherapy (IMRT) to decrease the dose to brainstem. RESULTS: All patients tolerated the prescribed radiation therapy dose that ranged from 5400 to 5940 cGy with a median of 5580 cGy in 42-45 days without gap (except in one patients, 4 days, for social reason). The immediate side effects were partial alopecia in 5 patients, nausea and vomiting (grade II) in 2 patients and anorexia in all patients. All 6 patients were alive for a median of 33 months (range 8-38). Four out of the 6 (66.7%) had MRI free of tumor at a range of 18-34 months. The other 2 patients showed stationary tumor size on MRI. One patient had cystic cavitation on MRI, while another one had ototoxicity that needed hearing aids. Both patients received chemotherapy postoperatively. CONCLUSIONS: Radiotherapy for pediatric infratentorial ependymoma leads to good results in children below 3 years. Though of the relatively short follow up yet, the delayed complications are limited and outweighed the survival benefit.

EM-02. ANAPLASTIC EPENDY MO MA AND DIFFUSE ASTROCYTO MA PRESENTING AS SYNCHRONOUS PRIMARY BRAIN TUMORS IN A CHILD (CASE REPORT)

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The simultaneous occurrence of multiple different primary brain tumors in children is extremely rare. The authors describe the case of a 7-years old boy with presented with a short history of intracranial hypertension. MRI imaging showed two brain masses with different MR characteristics (one in the posterior fossa and the next in the right temporal lobe). The patient underwent a gross total resection of both lesions leading to the complete resection of both tumors. The histopathological examination revealed the posterior fossa tumor to be anaplastic ependymoma and diffuse astrocytoma, respectively. The child was subsequently treated by conformal irradiation on the posterior fossa ependymoma, no specific adjuvant treatment for the completely resected diffuse astrocytoma was initiated. The boy is now on follow-up with the continuing remission. Cytogenetic analysis of ependymoma revealed clone with 47 chromosomes and translocation between chromosomes 1 and 6 - 47,XY, + der(1)(11;19), der(6)(1;6) [3/23]. Molecular cytogenetic analysis with DNA isolated from fresh tumor tissue confirmed duplication of long arm of chromosome 1 (11)(q11.1;qter) and deletion of (6)(q12qter) region. In addition, it disclosed duplication of short arm of chromosome 19. FISH with whole chromosome painting probes for chromosomes 1 and 19 disclosed translocation between these two chromosomes. Molecular genetic analysis of RB1 and NF2 genes at the level of nucleic acids based on direct sequencing and MLPA did not reveal any changes in comparison with healthy control. Analysis of TP53 gene showed substitution C>G which led to amino acid change prolin to arginin at position 72. This substitution has no influence on protein function. Cytogenetic analysis of diffuse astrocytoma was not possible because the tissue was only stored in paraffine. CONCLUSION: Two separate lesions in brain can represent a synchronous malignancy. An individual therapeutic approach should be established. The potential role of various factors in the development of multiple or synchronous primary brain tumors remains still speculative.
EM-04. NESTIN PROTEIN EXPRESSION IS AN INDEPENDENT PROGNOSTIC MARKER IN EPENDYMOMA AND DISCRIMINATES WHO II EPENDYMOMA WITH POOR OUTCOME
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Ependymomas are common brain tumors in children and adults and can arise throughout the CNS. Ependymomas are stratified into grade I-II according to the current WHO classification. Currently, many treatment protocols classify grade I and II ependymomas as low-risk tumors with patients receiving less intense or no chemotherapy after surgery and irradiation. This is in contrast to grade III (anaplastic) and IV tumors. We investigated the potential of co-regulated genes in two separate datasets (n = 75 and n = 102 ependymoma samples, respectively) revealed co-regulation of developmental and epigenetic processes. In summary, our data suggest Nestin as a useful novel marker for ependymoma risk stratification adding additional information to both old and novel risk-stratifications, with the advantage of being easily implementable in routine diagnostics.

EM-05. CERVICAL LYMPH NODE DISSEMINATION OF A RECURRENT SUPRATENTORIAL EPENDYMOMA
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A 32-month-old boy presented with a history of raised intracranial pressure since two weeks. MRI of the brain showed a right fronto lobe cystic and solid lesion (7 x 7 x 7 cm). A complete macroscopic resection of the tumor was performed. Histology revealed a clear cell ependymoma. Due to the complete resection and the young age, only a close clinical and radiological surveillance was planned. Twenty-one months later, MRI showed a relapse at the initial site and nearby in the right temporal lobe. A complete macroscopic resection of both lesions was performed. The pathological analysis confirmed the diagnosis of clear cell ependymoma. Considering the parents’ refusal for delivering radiotherapy and the absence of therapeutic target for chemotherapy, only surveillance was done. Sixteen months later, MRI showed another focal tumor recurrence within the initial site. A third complete macroscopic resection was performed and proton beam therapy was then planned. However, a painless pre-auricular mass occurred prior to start radiotherapy. The biopsy concluded to the diagnosis of a lymph node metastasis of the ependymoma. Body CT, PET scans and bone marrow biopsy revealed multiple lymph nodes, except one and the skin were normal. The primitive and metastatic areas were irradiated at the dose of 59.4 Gy. The child is in complete remission since 6 months off therapy. This is another case of a slow progressing ependymoma that could disseminate outside the CNS from primary tumor via a lymphatic route.
EM-08. LONG-TERM SURVIVAL OF SUPRATENTORIAL ECTOPIC EPENDYMOMA IN CHILD
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Ependymoma is a rare tumor developed from ependymal cells and belongs to the group of neuroglial tumors. It may be located in any part of the central nervous system, but shows a preference for the ventricular surface and approximately two-thirds of them are infratentorial. We present an unusual case of a 7-year-old boy with a supratentorial ependymoma located in the right side frontoparietal parenchyma and showing no continuity with the ventricular system. The patient presented with headache, vomiting and mild left side motor weakness. Magnetic resonance imaging showed a large sized cystic mass with highly enhancing capsule of uneven thickness located in the right side frontal and parietal parenchyma. The mass isointense on both T1 and T2 weighted images shown no relationship with the lateral ventricular system. Pathological examination revealed histological features consistent with an ependymoma. After pathological diagnosis was made, we checked whole spine MRI with emphasis on the spinal dissemination. Fortunately, there was no evidence of spinal seeding on MRI. Postoperatively, focal radiation therapy was carried out. Currently, 11 years follow-up, the patient remained neurologically intact and his school life is very active and showed no evidence of tumor recidive and no spinal dissemination. The clinical features, radiological images, pathology and surgical management of ependymoma is discussed and the relevant literature is briefly reviewed.

EM-09. OUTCOME OF CHILDREN WITH MYXOPAPILLARY EPENDYMOMA
Pratiti Randopadhayay1, Nicole Ulrich2, Liliana Goumnerova1, R. Michael Scott2, V. Michelle Silvera3, Keith L. Ligon5, Karen J. Marcus6, Nathan Robison1, Peter E. Manley1, Susan Chi1, and Mark W. Kieran1; with pain, leg weakness and sphincter disturbance. The lower thoracic and EM-09. OUTCOME OF CHILDREN WITH MYXOPAPILLARY EPENDYMOMA
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EM-10. SIX CASES OF EXTRASPINAL EPENDYMOMAS: THE AIEOP EXPERIENCE
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Primary extraspinal ependymomas are rare and usually occur in the subcutaneous or extracranial regions. Despite the rarity their treatment strategy is still controversial. In the last 15 years 6 children were treated in Italy; median age at diagnosis was 10 years, 3 were females and 3 males. All the patients had primary sacrococcygeal primaries; only one was metastatic (acetabulum and ischium). 5/6 received primary surgery with complete removal; in two cases the coccyx was infiltrated, resected completely in one case coccygectomy was performed. In one patient, the one with bone metastases, only primary diagnostic biopsy was performed. The histology according to the WHO classification was myxopapillary-grade I (3/6) and grade II (3/6). Although a delay in presentation was noted (3 years). Our limited experience suggests that: surgical removal is the favoured treatment (in case of localised disease); coccygectomy is not associated with a reduction of the recurrence rate. Despite a resistance to chemotherapy when arising in axial sites, chemotherapy (including myeloablative schedule) proved to be useful secondary treatment options in case of recurrent disease.
Evaluation of somatic mutations based on deep-sequencing revealed around 453 different mutations in total, an average of $\approx 13$ mutations per tumor, and highlighted several genes not previously implicated in ependymoma tumorigenesis. Identification of subgroup-specific mutations will help to discriminate between the two PF ependymoma entities and to identify subgroup-specific drug targets, in turn allowing for better prognostication and treatment of individual cases in future ependymoma trials.

**EM-12. REIRRADIATION FOR RECURRENT CHILDHOOD EPENDYMOMA WITH IMAGE-GUIDED INTENSITY MODULATED RADIOTHERAPY (IG-IMRT): INITIAL EXPERIENCE**

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**PURPOSE:** Pediatric primary central nervous system (CNS) tumors are seldom reirradiated due to toxicity concerns and sparse data regarding its efficacy. After St. Jude’s analysis good results on reirradiation for recurrent ependymomas, radiation therapy (RT) became a treatment option for these children. We report preliminary results of disease control and short term toxicity for patients with recurrent ependymoma treated with surgery and a second course of radiotherapy (RT2). METHODS AND MATERIALS: Between February 2010 and October 2011, 13 children from St Jude’s RT clinic were reirradiated with HIAE, RT to four of them with local recurrent disease, previously treated with surgery, chemotherapy and RT. After maximum safe resection, focal reirradiation was performed with image-guided intensity modulated radiotherapy (IG-IMRT), aiming the surgical bed and any site of persistent disease, with reduced margins. After RT2, patients were prospectively followed regarding disease control and short term toxicity. RESULTS: Time from first course of RT (RT1) and RT2 ranged from 29 to 61 months. Mean age at RT1 was 5.3 years old and 8.6 years old for RT2. RT1 and RT2 doses varied from 54 to 55.8 Gy and 50.4 to 54 Gy, respectively, with mean combined doses of 108.5 Gy. After a follow-up interval ranging from 9 to 24 months, none of the patients presented major side effects or deterioration of previous neurological symptoms. Three patients showed disease control and one eventually died from local tumor progression after 22 months of follow-up. The 3 remaining patients are still alive, 1 with stable disease and 2 with no evidence of disease, 10 to 24 months after RT2. CONCLUSIONS: CNS local reirradiation with IG-IMRT for patients with relapsed ependymoma seems to provide adequate local control without high toxicity rates. However, further follow-up is required to better evaluate long-term survival and treatment-related side effects.

**EM-13. A NOVEL LENTIVIRUS-BASED SCREEN FOR EPENDYMOMA TUMOR SUPPRESSOR GENES**

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Ependymomas include a diverse group of central nervous system (CNS) tumors that are incurable in up to 40% of cases. Previously, we developed a novel cross-species genomics approach to detect candidate oncogenes and tumor suppressor genes (TSGs) of human ependymoma subgroups, and introduced these into transcriptome-matched mouse neural stem cells (NSCs) to develop the first accurate mouse models of the disease (Johnson et al., Nature 2010). Here, we report a lentiviral-based approach that has allowed us to screen all 40 candidate TSGs of human ependymoma, and identify several new candidate drivers of ependymoma: none were previously implicated in the disease. We have compiled short pools of hairpin RNAs (shRNAs) targeting the mouse orthologs of all 40 candidate TSGs (3 per candidate; candidates are genes both deleted and under-expressed in human ependymoma) and tested their ability to promote tumorigenesis in our mouse ependymoma model. shRNAs were divided into 4 pools of 30 vectors each, 40 shRNA candidate TSGs. Transcription matched NSCs were transduced with EPHB2 (that we have validated as an ependymoma oncogene) and vector control, or EPHB2 and one of the four virus pools. Transduced NSCs were then transplanted into the forebrain subventricular zone of 30 immunocompromised mice for each pool. Tumor growth varied from pool to pool, exhibiting a significant decrease in latency, suggesting suppression of functional TSGs. Using luminescent sequencing to measure the frequency of individual shRNA integrations within genomic DNA extracted from 88 tumors, we identified several target-specific shRNAs that became enriched during tumorigenesis, indicating clonal expansion of those cells that gain a growth advantage upon TSG knock down. This approach has identified novel candidate TSGs that contribute to ependymoma development in our model. Targeting these novel TSGs, we aim to model each of the 9 ependymoma subtypes to further our efforts in disease prevention, diagnoses, and treatment.

**EM-14. DNA METHYLATION IN EPENDYMOMA**

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Epigenetic alterations, including methylation, have been shown to be an important mechanism of gene silencing in cancer. Ependymomas has been well characterized at the DNA copy number and mRNA expression levels. However little is known about DNA methylation changes. To gain a more global view of the methylation profile of ependymoma we conducted an array based analysis. Our data demonstrated tumors to segregate according to their location in the CNS, which was associated with a difference in the global level of methylation. Supratentorial and spinal tumors displayed significantly more hypermethylated genes than posterior fossa tumors, similar to the ‘CpG island methylator phenotype’ (CIMP) identified in glioma and colon carcinoma. This hypermethylated profile was associated with an increase in expression of genes encoding for proteins involved in methylating DNA, suggesting an underlying mechanism. An integrated analysis of methylation in ependymomas and mRNA expression array data allowed us to identify methylation induced expression changes. Most notably genes involved in the control of cell growth and death and the immune system were identified, including members of the JNK pathway and PPARG. In conclusion, we have generated a global view of the methylation profile of ependymoma. The data suggests epigenetic silencing of tumor suppressor genes is an important mechanism in the pathogenesis of supratentorial and spinal, but not posterior fossa ependymomas. Hypermethylation correlated with a decrease in expression of a number of tumor suppressor genes and pathways that could be playing an important role in tumor pathogenesis.

**EM-15. PI3K PATHWAY IN EPENDYMOMA**

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Ependymoma is the third most common pediatric tumor of the central nervous system. Patients with these tumors have a relatively poor prognosis. Tumors are currently treated with surgical resection followed by radiotherapy, with the extent of resection still one of the most consistent prognostic markers. Despite global molecular and genetic characterisation few candidate genes and pathways have been identified that could be used in a more targeted approach to therapy. The phosphoinositide 3-kinase (PI3K) pathway is one of the most commonly activated pathways in human cancer including glioma and medulloblastoma. PI3Ks transduce signals from growth factors and cytokines resulting if the phosphorylation and activation of downstream effectors AKT. Signalling through AKT can induce changes in cell growth and proliferation, and apoptosis. We have analysed the status of the PI3K pathway in a cohort of ependymomas using immunohistochemistry for phospho-AKT. A tissue microarray containing 172 primary ependymomas and 61 recurrences was analysed. Positive results were obtained for 124 (72%) primary ependymomas and 49 recurrences (80%). Survival analysis identified a significant link between positive staining for phospho-AKT and a poorer event free survival using univariate (p = 0.05) and multivariate analysis (p = 0.03). We sequenced exon 9 and 11 of the PIK3CA and PIK3R1 genes where activating mutations are commonly found, in 23 ependymomas. No mutations were identified. Using ependymoma SNP array data we found no copy number loss or loss of heterozygosity of the loci containing the PIK3CA gene and regulatory PTEN, Analysis of methylation array data also identified no hypermethylation of the PTEN promoter. In conclusion we have identified PIK3 pathway activation in a high percentage of ependymomas. If the pathway is proven to play a role in tumor pathogenesis it would provide a potential target for future therapies which would be effective in a large proportion of ependymomas.
EM-16. GAIN OF 1q25 PREDICTS POOR PROGRESSION-FREE SURVIVAL FOR PEDIATRIC INTRACRANIAL EPENDYMOMAS AND ENABLES PATIENT RISK STRATIFICATION: A EUROPEAN CLINICAL TRIAL COHORT ANALYSIS ON BEHALF OF CCLG, SFOP AND SIOP

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INTRODUCTION: The high incidence of recurrence and unpredictable clinical outcome for pediatric ependymoma reflect the impression of current therapeutic staging and need for novel risk stratification markers. We therefore evaluated 1q25 copy number gain across three CCLG, SFOP and SIOP trials and treated this analysis as a means to define a new genomic marker for childhood ependymoma across independent clinical trial groups. 1q25 gain predicts disease progression and can contribute to current therapeutic staging and need for novel risk stratification markers. RESULTS: Gain of 1q was initially assessed across 48 ependymomas (42 primary, 6 recurrent) using Affymetrix 500k arrays. Gain of 1q was then evaluated by interim phase FISH across 189 tumors treated on the CCLG/SIOP CNS9204 (n = 60) and BBSFOP (n = 65) adjuvant chemotherapy trials, or with primary post-operative radiotherapy (SIOP CNS9904/RT, n = 64). Results were correlated with clinical, histological and survival data. RESULTS: Gain of 1q was the most frequent imbalance in primary (7/42, 17 %) and recurrent ependymomas (2/6, 33 %). Gain of 1q25 was an independent predictor of tumor progression across the pooled trial cohort (HR 2.35, 95 % CI 1.56 - 4.16, p = 0.0002) and both CNS9204 (HR 4.03 (95 % CI 1.88 - 8.63)) and BBSFOP (HR 5.10 (95 % CI 1.22 - 20.76)) groups. The only clinical variable associated with adverse outcome was incomplete resection tumor resection. Integrating tumor resectability with 1q25 status enabled stratification of childhood ependymomas into 3 risk groups. RESULTS: Gain of 1q25 is an adverse marker in future international trials.


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BACKGROUND: Chemotherapy has limited efficacy in ependymomas. As local therapy is the most efficacious therapy in primary treatment, this analysis was set up to evaluate the local therapy and the outcome in patients with recurrent ependymomas treated in the German relapse study E-HIT-REZ-2005. METHODS: The E-HIT-REZ-2005 study is a non-randomized study treating an oral chemotherapy arm and a documentation arm (without study chemotherapy). In both arms local therapy as surgical resection and radiotherapy were administered where applicable as second-, third- or fourth-line treatment at the first or following relapses. RESULTS: Three patients received chemotherapy alone and a documentation arm (without study chemotherapy). In both arms local therapy as surgical resection and radiotherapy were administered where applicable as second-, third- or fourth-line treatment at the first or following relapses. Treatment strategies included 1) surgery as sole treatment or 2 fractions) boost to the residue still measurable after previous treatments. 3) surgery as sole treatment and 4) radiotherapy with 2 fractions) boost to the residue still measurable after previous treatments. Treatments were repeated up to 4 times. From 2003, 128 children entered the study. In 21 children (median age 4,5 years, 13 grade II, 17 infratentorial), out of 43 with residue after first surgery, second local RT as in 1) followed by a stereotactic hypofractioned (8 Gy/ 2 fractions) boost to the residue still measurable after previous treatments. From 2003, 128 children entered the study. In 21 children (median age 4,5 years, 13 grade II, 17 infratentorial), out of 43 with residue after first surgery, second local RT as in 1) followed by a stereotactic hypofractioned (8 Gy/ 2 fractions) boost to the residue still measurable after previous treatments. 6 children (15 %) are alive without progression at a median of 36 months (10-120 months) from diagnosis, 3 died of local progression at a median of 20 months, and 2 relapsed distantly 17-23 months from diagnosis. No iatrogenic death or major toxicity occurred. 4 children, irradiated with Tomotherapy, developed radiation related MRI changes regressing with steroids within 8 months. 6 months OS and PFS for the whole series were 76 % and 66 % respectively, PFS for children with and without residue at first surgery was 51 % and 75 % (P = 0.08) and local control 61 % and 86 % (P = 0.05) respectively. Hypofractionated with 2 fractions) boost was feasible and contributed to maintain local control in 18/21 children with measurable residue. An aggressive local treatment strategy, multiple surgeries and RT, is required to improve outcome in children with Ependymoma.

EM-18. HYPOFRACTIONATED RADIOTHERAPY (RT) BOOST FOR CHILDREN WITH EPENDYOMA AND A MEASURABLE RESIDUE AFTER SURGERY: RESULTS OF THE SECOND PROTOCOL OF THE ITALIAN ASSOCIATION OF PEDIATRIC HEMATOLOGY AND ONCOLOGY (AIOP)

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INTRODUCTION: Ependymomas are the third most common central nervous system (CNS) tumors in children. Surgery and radiation remains the cornerstone of management. They are relatively resistant to chemother- apy and relapse of refractory tumors following surgery and radiation are a therapeutic challenge with a five-year survival of less than 60 %. Lack of clinical models and identification of specific molecular pathways in these tumors has precluded drug testing and profiling targeted therapy. We report comprehensive drug testing on pediatric ependymoma cell lines. METHODS: Cell lines were directly established from 4 pediatric ependymoma tumors; both posterior fossa and supratentorial in origin. Each cell line was exposed to 10 different chemotherapeutic agents individually and in combination. We tested agents of Wnt, notch, and RB pathway and reagents that target DNA replication, proteosome inhibitors, EGFR/HER-2 inhibitors, DNA synthesis/ anti microtubule, TOPO-2 inhibitors and alkylating agents. Anti-tumor effect was evaluated using Cell Titer Blue (CTB) assays and dose-dependent growth inhibition over 96 hours was followed. Drug treatment for 96hrs resulted in a dose-dependent growth inhibition. RESULTS: The compounds
tested showed a differential response in ependymoma cells. The proliferation of ependymoma cells was decreased in a concentration-dependent manner with most agents. Bortezomib a proteosome inhibitor and lapatinib, a VEGFR and EGFR inhibitor, were strikingly inhibitory to ependymoma cell proliferation individually and in combination. Bortezomib’s ED50 is between 0.5 and 1 nM. Lapatanib’s ED50 is between 0.5 and 10 nM. In combination with each other there was a substantial additive effect and when either Lapatanib or Bortezomib was added to Temodar there was an additive effect. Their efficacy was independent of the original tumor location. CONCLUSION: Our study demonstrates that bortezomib and lapatinib individually and in combination inhibits growth of these tumors. These preliminary data provides better understanding of the tumor biology and therapeutic leads which need to be evaluated in prospective clinical trials.

EM-20. FEASIBILITY AND OUTCOME OF FRACTIONATED FULL COURSE REIRRADIATION USING IMRT IN CHILDREN WITH ANAPLASTIC EPENDYMO MA

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BACKGROUND: Fractionated reirradiation to full doses is seldom done because of concerns of neurotoxicity. MATERIALS AND METHODS: We retrospectively reviewed our experience with full course reirradiation in locally recurrent ependymoma. We calculated the maximum (Dmax) and mean dose (Dmean) for surviving normal structures. RESULTS: Seven children with intracranial anaplastic ependymoma underwent a 2nd course of fractionated radiotherapy (2XRT) for isolated locally recurrent ependymoma. Median age at initial fractionated radiotherapy (1XRT) was 6 years and at 2XRT was 9.7 years. All recurrences were in the high dose region of the 1XRT course. Prior to 2XRT, 6 patients had complete resection of recurrent tumor. Both 1XRT and 2XRT were delivered using intensity modulated radiotherapy (IMRT). The median time from end of 1XRT to beginning of 2XRT was 51 months (22-93 months). The median dose to the clinical target volume was 59.4 Gy for 1XRT; for the 2XRT, all patients received 54 Gy to the tumor bed with a 1 cm margin. The combined 1XRT and 2XRT median Dmax were: brainstem 77.8 Gy (7.8-113.4 Gy); optic chiasm 38 Gy (6.6-55.9 Gy); optic nerve 22.5 Gy (3.5-13.1 Gy); eyelids 11.8 Gy (3.5-49.1 Gy), lens 2.7 Gy (1.1-6.6 Gy) and spinal cord for infratentorial tumors 76.7 Gy (69.3-103.8 Gy). The combined median Dmean were: brainstem 50.9 Gy (6.5-63.5 Gy), optic chiasm 14.1 Gy (3.4-44.8 Gy), optic nerve 12.9 Gy (1.2-47.4 Gy), eye 4.2 Gy (1.2-22.8 Gy), lens 1.6 Gy (0.4-2.4 Gy) and spinal cord 12.9 Gy (5-18.2 Gy). The 2-year overall and progression-free survival was 85.7% and 71.4%. Three patients have failed at 3, 13 and 26 months after 2XRT; all had local recurrence with 1 concomitant leptomeningeal spread. With a median follow-up of 21 months after 2XRT, none of the patients had brain necrosis, myelitis or blindness. One patient had transient visualis 8 weeks after 2XRT which resolved in 6 months but completely resolved on steroids. CONCLUSION: With the use of IMRT, full-course reirradiation in locally recurrent ependymoma is feasible.

EM-21. ANAPLASTIC EPENDYMO MA. RESULTS FROM POLISH PEDIATRIC NEUROONCOLOGY GROUP

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Optimal treatment of ependymoma remains controversial. Prognostic value of histological grade is also questioned. In our historical patients with anaplastic ependymoma (AE) treated with surgery and craniospinal irradiation (CT), the tumor biology and therapeutic leads which need to be evaluated in prospective clinical trials.

EM-22. PATTERNS OF DISSEMINATION IN MYXOPAPILLARY EPENDYMO MA - OPTIMIZING CURRENT RADIATION FIELDS

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BACKGROUND: Myxopapillary ependymoma (MPE) accounts for 10-20% of pediatric intramedullary spinal cord tumors. Standard of care in children with MPE involves gross total resection with radiotherapy (RT) reserved for subtotal resection and recurrent tumors. To better understand what RT fields need to be treated in the setting of neuraxis dissemination in MPE, we investigated the patterns of dissemination in a pediatric series of MPE at our institution. Specifically, we were interested in whether craniospinal fields are needed at tumor dissemination. PATIENTS AND METHODS: Eighty patients with MPE were treated from 2000 to 2012 at the Texas Children’s Cancer Center. Median age was 13.6 years at initial diagnosis (range: 6.2-18.1 years). Tumor location was lumbar, sacral or both in all with thoracic involvement in 3 patients. Three of 8 patients had disseminated disease at initial presentation on MRI. Initial treatment was gross total resection (GTR) in 4 and subtotal resection (STR) followed by RT in 4, RT fields for the STR patients were partial spine fields including all radiographically visible tumors. RESULTS: At a median follow up of 3.2 years (range: 1-6.8 years), 3 patients progressed of which 1 died. Of 4 patients who had GTR only, 2 recurred and required RT. Of 4 patients who received STR with RT, 3 patients had stable disease while 1 relapsed. A review of the 3 recurrences revealed relapse at the initial tumor site in all patients, with 2 having disseminated disease either proximal or distal to the original site of disease. Patterns of dissemination analysis at relapse revealed the absence of intracranial dissemination. CONCLUSION: Neuraxis dissemination is a common pattern of spread in MPE. However our institutional experience suggests that the pattern of dissemination in MPE does not involve the brain which can therefore be excluded from the radiation field.

EM-23. ANALYSIS OF CHROMOSOME 1Q GAIN AS GENETIC MARKER FOR RISK STRATIFICATION OF PEDIATRIC EPENDYMO MA PATIENTS - VALIDATION AS AN ADVERSE PROGNOSTIC MARKER IN THE GERMAN MULTICENTER HIT2000 TRIAL

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In contrast to histopathological grading which varied in respect to its prognostic value between different clinical trials, extent of resection was found to be consistently associated to the clinical outcome. In retrospective series, gain of genetic material of chromosome arm 1q was identified to predict worse outcome. However, a study of 334 recently treated MPE patients showed failure rates of 15-20 % in archival material. To validate this marker, we performed a retrospective analysis of 44 children with MPE on the German Multicenter HIT2000 trial and assessed, correlated with age, localization, resection (assessed by neurosurgeon +/- MRI at 72 hrs). RESULTS: 36 out of 40 patients (11 <3yrs and 25 >3yrs of age) are alive with 3 yrs EFS and OS of 62% and 88%. Eleven of 14 pts <3yrs of age are alive, 10m-7yrs/5yrs from diagnosis. Twenty-five out of 26pts >3yrs of age are alive, 6m-8.5yrs /4yrs/m from diagnosis. All patients with supratentorial localization are alive 5m-8.5yrs /6yrs from diagnosis. Twenty-one out of 25 patients with recurrent tumors are alive from 9m-8yrs/m/3yrs/m. All 17 patients with complete tumor resection are alive with EFS of 100 %. There was favorable correlation between EFS and supratentorial tumors (p<0.025), complete resection (<0.001) and age over 3yrs (p<0.006) whereas age did not correlate with OS. CONCLUSIONS: Introduction of our protocol resulted in improved survival of children with AE. Excellent results in currently resected supratentorial AE indicate a change in the treatment strategy which we are now considering. Supported by The National Centre for Research and Development.
EM-24. TELOMERASE INHIBITION INDUCES GROWTH ARREST IN PAEDIATRIC EPENDYMOMA
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Ependymomas represent the most common paediatric brain tumour, yet effective chemotherapy regimens are lacking and 5-year survival rates remain poor at approximately 50%. Previous studies have shown that the majority of ependymomas possess telomerase, an enzyme that maintains telomere length and permits limitless growth potential. The objective of this study was to elucidate whether telomerase is an effective therapeutic target in ependymoma using the telomerase inhibitors MST-312 and Imetelstat. Paediatric ependymoma cell lines R254 and BXD-1425EPN were treated for 72 hours with MST-312 in parallel with telomerase-negative control cells. R254 ependymoma cells were also treated with Imetelstat for 17 days in parallel with mismatch control and untreated cells. Cell number, apoptosis (TUNEL), senescence (beta-galactosidase), telomerase activity (telomere repeat amplification protocol), cell cycle arrest (flow cytometry) and DNA damage (immunofluorescence (gammaH2AX)) was assessed following telomerase inhibition by either compound. MST-312 telomerase inhibition reduced proliferation by 50%, increased γH2AX associated DNA damage 2.2-fold and induced a marked increase in G2 cell populations in both R254 and BXD-1425EPN ependymoma cells but not in telomerase-deficient control cells. Imetelstat treatment of R254 ependymoma cells decreased proliferation after 6 weeks and induced growth arrest following 15 weeks of treatment while no effect was observed in mismatch control or untreated cells. The observed growth arrest was associated with an 80% increase in senescence and 35% decrease in viability. These findings suggest that telomerase inhibition may represent a potential therapeutic strategy for paediatric ependymoma.

EM-25. INCOMPLETE TUMOR RESECTION IN PATIENTS WITH PEDIATRIC EPENDYMOMA TREATED WITHIN THE HIT2000 TRIAL
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OBJECTIVE: Extent of resection is the strongest prognostic factor in intracranial pediatric ependymoma. In case of postoperative residual tumor (R+), second-look surgery is recommended whenever feasible. We analyzed the frequency and characteristics of R+ ependymoma patients with and without second surgery. METHODS: Analysis of patients with localized ependymoma aged 0-21 years with central review of pre- and postoperative MRI imagining, who were treated within the multicenter HIT2000 study (patients < 4 years of age or R+ after 2005: primary chemotherapy followed by radiotherapy; otherwise: primary radiotherapy followed by chemotherapy if WHO III) and operated before November 2010. RESULTS: 221 patients qualified for evaluation. Initial operations were performed in 70 centers. After surgery, 118 (53%) had complete tumor removal (R0). Radiological follow-up by central neuroradiological reference was available for 38% of ependymomas were located in the infratentorial region. 26 cases were argued to be WHO grade II ependymoma, 113 as anaplastic ependymoma (WHO grade III). By using multiplex ligation-dependent probe amplification (MLPA) for 5 markers located on chromosome 1q and control markers, we were able to analyse 137/138 cases (99%) and found a gain of chromosome 1q in 21 cases (15.3%). Interestingly, none of the 24 WHO grade II ependymomas had 1q gain. At a median follow-up of 3 years, patients with tumors showing 1q gain had a significantly lower 3-year overall survival (OS) (5% (± 6%)) compared to patients lacking this marker (90% (± 14%), p = 0.001). The distribution of this marker was similar when comparing patients with supra- and infratentorial tumors. Multivariable analysis demonstrated that gain of chromosome 1q was an independent risk factor for OS, and residual tumor for event-free survival, respectively. In conclusion, we validated chromosomal 1q gain to be a useful independent genetic marker for risk stratification of pediatric ependymoma patients which can be evaluated by MLPA representing a robust, reliable and cost-efficient method.

EM-26. ANTI-TUMORAL EFFECT OF THE HDACi SAHA ON PEDIATRIC GLIAL TUMORS
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Ependymoma management remains challenging as there is currently no effective adjuvant therapy besides radiotherapy due to the high chemoresistance of these tumors. Recent studies have highlighted the interest of histone deacetylase inhibitors (HDACi) in cancer treatment. We studied the effect of an HDACi, SAHA, on both primary cell cultures isolated from surgical resection of ependymomas and high grade gliomas and a pediatric glioma cell line. Anti-proliferative effect of the compound was determined using MTS assay. Induction of cell cycle changes was checked by flow cytometry prior to further protein analysis and in vivo experiments. SAHA exhibit a dose-dependant anti-proliferative effect on our various models, with IC50 of 1 μM for SF188 and around 2 μM for ependymoma cell cultures. Cell cycle analysis on SAHA treated-cells showed far greater sub-G1 population fraction although markers associated with apoptotic cell death were not displayed. We observed a high basal level of autophagy in our models, and treatment with SAHA leads to an increase in autophagic vesicles formation. To check whether autophagy could be a resistance mechanism to treatment or could participate to cell death, we inhibited autophagy using chloroquine while treating cells with SAHA. Compared to SAHA alone, this combination enhanced the anti-proliferative effect of SAHA on our in vitro models as well as its cytotoxic effect (increase in sub-G1 fraction). In a slow-growing ependymoma graft model, treatment with SAHA alone or in combination with chloroquine did not show a significant effect on tumor growth, but an increase in the sub-G1 cellular fraction was found in mice treated simultaneously with the two compounds. HDACi are potent drug candidates for glioma tumor management. Further studies are needed to assess its efficiency in vivo and determine which combination could increase its anti-tumoral effects.

EM-27. FROM MOLECULAR HETEROGENEITY TO THERAPEUTIC TARGETS IN EPENDYMOMA
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BACKGROUND: Despite recent improvements in the definition of ependymoma-specific molecular profiles by high-throughput approaches, so far such information did not promote a rational strategy for innovative therapeutic agents in patients with conventional therapy-resistant ependymoma. METHODS: We analyzed 15 ependymoma tumors, 6 ependymoma cell cultures and 5 control samples for expression and activation status of receptor kinases, their ligands, downstream intracellular kinases, as well as autophagy and cell cycle markers. RESULTS: In our various models, we observed a high basal level of autophagy in our models, and treatment with SAHA leads to an increase in autophagic vesicles formation. To check whether autophagy could be a resistance mechanism to treatment or could participate to cell death, we inhibited autophagy using chloroquine while treating cells with SAHA. Compared to SAHA alone, this combination enhanced the anti-proliferative effect of SAHA on our in vitro models as well as its cytotoxic effect (increase in sub-G1 fraction). In a slow-growing ependymoma graft model, treatment with SAHA alone or in combination with chloroquine did not show a significant effect on tumor growth, but an increase in the sub-G1 cellular fraction was found in mice treated simultaneously with the two compounds. HDACi are potent drug candidates for glioma tumor management. Further studies are needed to assess its efficiency in vivo and determine which combination could increase its anti-tumoral effects.

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EM-28. PROTON RADIOTHERAPY FOR CHILDHOOD CNS EPENDYOMA: CLINICAL OUTCOMES AND PATTERNS OF FAILURE FOR A COHORT OF 67 PATIENTS
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BACKGROUND/PURPOSE: Young age at diagnosis in combination with the proximity of critical CNS structures to target volumes for ependymoma makes an appealing modality for treatment. Clinical outcomes are needed to verify disease control and decreased toxicities. We report outcomes and patterns of failure for a cohort of 67 patients treated with involved field proton radiation. METHODS AND MATERIALS: Children with localized intracranial ependymoma treated at the Francis H. Burr Proton Facility and Harvard Cyclotron between November 2000 and February 2011 were included in this study. RESULTS: 67 patients were treated with involved field proton radiation. Median age at the time of diagnosis was 41 months (range 11 months - 20 years). 49 patients had infratentorial ependymoma and 18 had supratentorial ependymoma. 44 had a GTR while 23 had a STR. 31 patients had anaplastic histology; 36 had classic ependymoma. At a median follow-up of 36 months from the start date of radiation therapy among the 62 patients still alive, local control, progression-free survival, and overall survival at 1 and 3 years were 97%/88%, 94%/75%, and 100%/93%, respectively. STR was significantly associated with poorer local control (90%/67% vs. 100%/96%, p = 0.002) and lower progression-free survival (86%/78% vs. 98%/85%, p = 0.004). Anaplastic histology was associated with lower progression-free survival (96%/65% vs. 81%, p = 0.358). Local control was 97%/80% among patients with anaplastic histology and was 97%/92% among those with classic ependymoma, though not significant (p = 0.498). Of the 17 patients that relapsed, 6 has isolated local failures, 2 patients had synchronous failures local and distal (spine and lateral ventricle), and 9 had isolated distant failures (5 spinal, 4 elsewhere in the brain). CONCLUSIONS: Disease control with proton therapy compares favorably to the literature. Although local in-field failures did not occur, patterns of failure show that the majority of patients have failures distant from the primary site.

EM-29. PROGNOSTIC SERUM CYTOKINES IN PEDIATRIC EPENDYOMA
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BACKGROUND: Ependymoma recur in approximately 30% of children. A previous study by our group identified immunogene expression signature in primary tumor samples that was associated with a favorable prognosis. Based on these findings, we hypothesized that specific serum cytokine levels would recapitulate this good prognosis immune signature in the periphery. METHODS: Serum samples were obtained from a preliminary cohort of 21 pediatric ependymoma patients undergoing surgery and radiation at the time of radiation and at subsequent time points (3 months; 1 year). A panel of 35 cytokines was screened in these samples using a multiplexed luminex bead platform. RESULTS: An initial analysis was performed to identify expression of IL2RA, IFN, IFNG, IL10, PDGFRA, and EPHB2 were screened in a variable fraction of cases ranging from 29% to 43%. In the absence of overt mutations, the expression of known ligands and miRNA modulators (EREG, IGFB, mir-375, mir-9) suggests the existence of autocrine/paracrine loops. With the exception of the EPHB2/REBB1, recurrent co-activation events are rare. Multiple receptor kinases revealed activated expression in individual patients, including MER, TRKB, EPHA7, PDGFRA, MSFR, further supporting the described elevated molecular heterogeneity of ependymoma. In ependymoma cell cultures, response to EGFR small molecule inhibitor correlated with receptor expression level and activation status, and significantly augmented cell sensitivity to irradiation. Intracellular signaling was mediated by ERK1/2 and AKT activation, either individually or concomitantly. Concurrent activated expression of multiple molecules involved in stress response, inflammation and vascular signaling (p32alpha, CREB1, HSP27, TIE1/2, IL1A/B, LIF, mir-149) underscores the importance of these pathways, which remain poorly investigated in ependymoma. CONCLUSIONS: Despite the absence of recent genetic alterations that may have targeted treatments in ependymoma, our combined approaches identified ERBB1, Insulin- and PDGFR- pathways as candidate therapeutic targets.

EM-30. TREATMENT OF INTRACRANIAL EPENDYOMA WITH SURGERY ALONE AT DIAGNOSIS: THE CANADIAN PEDIATRIC BRAIN TUMOUR CONSORTIUM EXPERIENCE
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BACKGROUND: Gross total resection (GTR) improves survival, but deferral of radiotherapy to the developing brain in ependymoma is controversial. There is a paucity of data on such a strategy. This study reports on a group of children initially treated with GTR alone for intracranial ependymoma. We conducted a multicenter, retrospective review of children (<18 years old) diagnosed with ependymoma in 12/16 participating Canadian centers. Inclusion criteria: GTR and no adjuvant therapy. Exclusion criteria: ependymoblastoma or mixed pathology. Pathology was centrally reviewed and immunohistochemistry for EGFR was performed. RESULTS: A total of 201 patients with intracranial ependymoma were identified: 150 had posterior fossa ependymoma (PFE); 51 had supratentorial ependymoma (STE). 52 patients were treated with GTR alone upfront: 18 PFE; 14 STE. Staging was only performed in 18/32, all of which were negative for metastatic disease. 3 yr PFS and OS were 48%; and 68%; no significant difference was observed between PFE and STE (p = 0.70). Relapses occurred in 9/18 (50%) PFE and 8/14 (57.1%) STE; all but 2 relapses occurred within 2 yrs; 5/9 PFE relapses had dissemination whereas only 1/8 STE relapses had dissemination. 4 PFE and 3 STE were salvaged with resection and adjuvant therapy. Survival was inferior for patients <3 yo at diagnosis for both groups (p < 0.035). Negative EGFR stain and WHO grade 2 had a trend toward improved survival but failed to reach significance. CONCLUSIONS: Treatment of intracranial ependymoma with GTR alone is a reasonable strategy in selected patients. Relapses occur at the primary site in STE but there is 50% risk of dissemination in PFE. Successful salvage occurs in both PFE and STE. Survival is inferior for infants, identifying which ependymomas can be successfully treated in this fashion is essential. Identifying a specific molecular signature is imperative towards developing new therapies.
EM-31. ADVANCED PHOTON RADIOTHERAPY TECHNIQUES COMPARED TO PROTON TREATMENT FOR SMALL TARGETS, A DOSE PLANNING STUDY IN A RECURRENT CHILDHOOD EPENDYMOMA
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PURPOSE: Proton therapy is often considered superior to photon therapy due to favourable depth-dose characteristics, especially in radiotherapy of childhood cancers. We performed a dosimetric case study in a small target to compare advanced photon techniques, stereotactic radiotherapy (SRT) and volumetric arc therapy (VMAT) to intensity modulated proton therapy (IMPT) technique. METHODS: A treatment planning study was performed on a small recurrence of a grade III childhood ependymoma (0.8 cm in diameter) close to the brainstem. The enhancing tumour was defined as the clinical target volume (CTV). A dose of 20 Gy in 10 fractions was planned with the three techniques using setup margins of 2, 3, 4 and 5 mm on an eclipse dose planning system (Varian Medical Systems, Palo Alto, CA). RESULTS: Target coverage and dose to the brainstem were comparable for the three techniques. Mean dose to normal brain tissue for the 2mm margin was 0.78, 0.61 and 0.55 Gy for SRT, VMAT and IMPT, respectively, whereas the low dose volume receiving 5 Gy was 28, 36 and 25 cm³. Mean conformity index was observed for the 2mm margin setting in clinical practice. Image guided proton therapy is delivered using 2-3 mm margins, whereas proton therapy should be delivered with 4-5 mm margins, because of range uncertainties and the larger penumbra of protons. With these margins applied, the mean dose to the normal brain tissue was 0.78, 0.61 and 0.63 Gy for SRT(2mm), VMAT(2mm) and IMPT(4mm), respectively, whereas the low dose volume receiving 5 Gy was 28, 36 and 30.5 ccm for SRT(2mm), VMAT(2mm) and IMPT(4mm). CONCLUSION: For small targets, the dose delivered to the surrounding normal tissue could be vanishing for proton therapy compared with advanced photon therapy techniques.

EM-32. EPENDYMOMA-ANGIOGENESIS: PLATELET DERIVED GROWTH FACTOR RECEPTORS OVER-EXPRESSION HAS PROGNOSTIC SIGNIFICANCE
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Although vascular proliferation is commonly seen in ependymomas, relatively little is known about the angiogenic profile of these tumors. The platelet derived growth factor (PDGF) pathway is well established to be involved in various angiogenic factors and investigate their prognostic significance. Tissue samples were obtained from 24 patients treated at our institution with the diagnosis of ependymoma from 1991 to 2009, with IRB approval. Clinicopathological characteristics and outcome of these patients were recorded. Intensity of staining was scored semi-quantitatively in a blinded manner as either ‘moderate/high’ or ‘low’/no expression by one pathologist (JP). Percutaneous biopsy (PCI) was calculated as the ratio SMA/C3D4. The PCI was evaluated and average ± SD was 91.1% ± 12.7. PDGFR-a and b were found to be over-expressed in the ependymoma tumor cells in 29.2% of the patients and PDGFR-b was over-expressed in 50% of the patients. High expression of PDGFR-a and b in tumor cells and tumor endothelial cells correlated with PFS: 2-year PFS was 16.7 ± 15.2 for those cases that showed overexpression of PDGFR-a in the tumor vs. 74.5 ± 15.2 for those with low/no expression (p = 0.001). Additionally, 2-year PFS was 33.3 ± 17.3 for those with high expression of PDGFR-a and b in tumor cells and tumor endothelial cells correlated with PFS: 2-year PFS 14.3 ± 13.2 vs. 79.5 ± 10.7 (p < 0.001). Multivariate analysis confirmed the prognostic significance of PDGFR-a. In conclusion PDGFRs might represent a target that requires prospective validation in ependymoma.

EM-33. mTOR AND MAP KINASE SIGNALING IN CHILDHOOD EPENDYMOMA OF THE POSTERIOR FOSSA - A POTENTIAL NEW THERAPEUTIC INTERVENTION
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BACKGROUND: Little is known regarding activation of the MAP kinase and mTOR pathways in childhood ependymomas. METHODS: 21 pediatric, posterior fossa ependymomas (23.8% females; mean age = 5.35 ± 5.72 years (range: 0.45 - 17.18 years) were examined for immunohistochemical expression of phosphorylated (Ser235/236) S6 ribosomal protein, a marker of mTOR complex1 activation; cyclin D1, a member of the cyclin protein family that is involved in regulating cell cycle progression; and Erk1 and Erk2. RESULTS: Three lines of evidence provided evidence of over-expression of this pathway with daily rapamycin were described. RESULTS: Immunohistochemistry studies were as follows: pS6 showed cytoplasmic reactivity (9-20% of tumor cells) 19/21 (90%) of cases, pERK staining was diminished in 20/21 (95%) of cases. Cyclin D1 showed nuclear staining in 16/21 (76%) cases. Tumor cell line viability at 48 hours was reduced by 65-85% in the three pS6-positive tumor cell lines exposed to 15-20 ng/ml rapamycin compared to 50% reduction in viable cells in the control HEK-293T/17 cell line and 40% reduction in the two pS6-negative cell lines exposed to the same concentration of rapamycin. Two different immortalized ependymoma cell lines showed complete tumor responses to daily rapamycin (18 months) or daily rapamycin + oral etoposide (12 months). CONCLUSIONS: mTOR pathway signaling and the MAP kinase pathway may play a role in childhood ependymoma biology. Further investigation of potential biomarkers and targets of these pathways is warranted to improve therapy for children with ependymomas.

EM-34. PEDIATRIC EPENDYMOMAS HAVE INCREASED EXPRESSION OF GLIOMA-ASSOCIATED ANTIGENS (GAA): IMPLICATIONS FOR VACCINE THERAPY
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BACKGROUND: Despite surgery and radiotherapy, as many as 50% of children with ependymomas will suffer from tumor recurrences that will ultimately lead to death. New treatment modalities are urgently needed. METHODS: We investigated the protein expression of three GAs that are the targets of an existing vaccine for low- and high-grade gliomas. Immunohistochemistry was performed using antibodies specific for Epha2 (1:100), IL13Ralpha2 (1:100), and Survivin (1:250). We included 1 WHO grade I (myxopapillary), 3 WHO grade II, and 5 WHO Grade III (anaplastic) ependymomas. Paraffin-embedded tissues were deparaffinized using xylene and serial ethanol washes. Antigen retrieval was performed using citrate buffer in a pressure cooker. After blocking, primary antibodies directed at each GAA were incubated overnight at 4°C. Negative controls were established by omitting the primary antibodies. Staining was visualized by HRP-conjugated secondary antibodies and DAB chromogen. Normal brain and ependyma were used for background staining controls. RESULTS: All ependymomas stained more strongly for all three GAs than normal brain tissue or normal ependyma. Non-neoplastic tissues within and around the tumors also did not stain. Negative controls showed no staining. Most ependymomas showed diffuse staining, but in some there was patchy variability in intensity: Epha2 (2/9), IL13Ralpha2 (2/9), and Survivin (5/9). There was more variability in overall staining intensity for IL13Ralpha2 and Survivin than for Epha2 among the cases. Nuclear expression of survivin was observed in grade 2 and 3 ependymomas and 2 were IL13Ralpha2+ and 1 myxopapillary case. CONCLUSION: Pediatric ependymomas overexpress Epha2, IL13Ralpha2, and Survivin compared to normal brain. This provides the basis for the utilization of an established GAA-based glioma vaccine for pediatric ependymoma in a clinical trial setting.

EM-35. RECURRENT ANAPLASTIC EPENDYMOMA WITH FATTY MACROSCOPIC METASTASIS - TREATMENT WITH SURGERY, RADIATION AND ORAL CHEMOTHERAPY
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INTRODUCTION: Intracranial ependymoma represents approximately 8% of pediatric brain tumours. Anaplastic ependymoma (WHO Grade III)
is usually considered to have a more aggressive clinical course. Metastatic disease to locations outside the CNS has been reported, but is extremely rare. We describe a patient treated for supratentorial ependymoma with surgery and radiation, with multiple local recurrences and extracranial metastatic disease in her neck and mediastinum. **CASE REPORT:** A previously healthy girl presented at the age of 13 with new seizures. Neuro-imaging revealed a large supratentorial mass growing in the left cerebral hemisphere. The patient underwent gross total resection and received focal radiation to a dose of 59.4 Gy. One year later, she had disease recurrence on surveillance MRI at the original site. She had another gross total resection and was treated with stereotactic radiosurgery to a dose of 18 Gy. After another year she presented a recurrent nodule in the tumour bed, which was unresectable due to its proximity to the sagittal sinus. She was treated with another round of radiosurgery (18 Gy). She tolerated this well and her disease remained stable for another year. She then presented with local recurrence and cervical lymphadenopathy; biopsy proved this to be anaplastic ependymoma. She also had a mass lesion in her mediastinal area. She received a third dose of radiosurgery to the initial tumour bed, as well as radiation (35 Gy) to the neck. She was started on oral chemotherapy (temozolomide and etoposide). One year later she received 30 Gy to treat her progressive mediastinal disease, and then was changed to oral metronomic chemotherapy. She has remained on this regimen, and is doing well with stable disease and a good quality of life. **SUMMARY:** Extracranial metastatic ependymoma is rare, and treatment options poorly defined. This case reviews a multi-modality approach and oral chemotherapy options for this disease.