

lung cancer. All the patients received cranial radiation (range: 12–60 Gy). The median latency time between primary disease and RIG was 16 years (range: 9–30 years), which was not correlated with age at the time of primary disease ( $r^2=0.014$ ,  $p=0.74$ ). Radiation-induced gliomas included 8 glioblastoma and 2 grade III glioma based on histological diagnosis. After surgical removal or biopsy of the RIG, 4 patients underwent chemotherapy alone (nimustine, temozolomide (TMZ), carboplatin and etoposide), and 6 received chemotherapy (nimustine, TMZ, bevacizumab) combined with radiotherapy (range: 40–66Gy). The median progression free survival and survival time from RIG were 10.1 and 27.5 months, respectively. In summary, RIG may occur many years after successful initial treatment using radiotherapy, and the outcome of our patients with RIG supports the use of radiotherapy and/or chemotherapy after surgical resection.

#### HGG-40. EXCEPTIONAL SYNCHRONOUS OCCURRENCE OF A BRAF V600E MUTANT GLIOBLASTOMA AND A H3.3K27M MUTANT DIFFUSE INTRINSIC PONTINE GLIOMA: A CASE REPORT

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We report herein the case of a 17-year-old female who presented with intracranial hypertension and diplopia. Magnetic resonance imaging showed a large left cystic and solid temporoparietal lesion, associated with an infiltrating lesion of the brainstem, hypointense in T1 and hyperintense in FLAIR sequences, without enhancement after injection of gadolinium. Complete resection of the parietal mass and biopsy of the brainstem lesion were performed. Histopathological analysis of the parietal mass showed glioblastoma (WHO grade IV) with no IDH1/2 or H3.3/H3.1 gene mutation detected by Sanger sequencing. Immunohistochemistry found the expression of the proteins of mismatch repair system. Whole exome and RNA sequencing identified a BRAF-V600E mutation. The brainstem lesion was a diffuse midline glioma, H3K27M-mutant (grade IV) according to the 2016 WHO classification. Pan-genomic SNP arrays of the 2 tumors showed distinct genetic alterations. The parietal glioblastoma displayed complex genomic alterations whereas the brainstem glioma harbored chromosome 7q gain, chromosome 9p and 10 losses, and RB, TP53 and CDKN2A homozygous deletions. The patient was treated by concomitant radiochemotherapy (according to Stupp protocol). After 12 cycles of temozolomide, there was complete remission persistent in the parietal lobe. The brainstem tumor was stable but progressed after 3 months of temozolomide discontinuation. Treatment with mTOR inhibitors was initiated. At 21-month follow-up, the patient remains with few symptoms. No predisposition syndrome was identified in the patient or her family. Concurrent glioblastomas with distinct driver gene mutations are exceptional.

#### HGG-41. STRUCTURAL VARIANT DRIVERS IN PEDIATRIC HIGH-GRADE GLIOMA

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**BACKGROUND:** Driver single nucleotide variants (SNV) and somatic copy number aberrations (SCNA) of pediatric high-grade glioma (pHGGs), including Diffuse Midline Gliomas (DMGs) are characterized. However, structural variants (SVs) in pHGGs and the mechanisms through which they contribute to glioma formation have not been systematically analyzed genome-wide. **METHODS:** Using SvABA for SVs as well as the latest pipelines for SCNAs and SNVs we analyzed whole-genome sequencing from 174 patients. This includes 60 previously unpublished samples, 43 of which are DMGs. Signature analysis allowed us to define pHGG groups with shared SV characteristics. Significantly recurring SV breakpoints and juxtapositions were identified with algorithms we recently developed and the findings were correlated with RNAseq and H3K27ac ChIPseq. **RESULTS:** The SV characteristics in pHGG showed three groups defined by either complex,

intermediate or simple signature activities. These associated with distinct combinations of known driver oncogenes. Our statistical analysis revealed recurring SVs in the topologically associating domains of MYCN, MYC, EGFR, PDGFRA & MET. These correlated with increased mRNA expression and amplification of H3K27ac peaks. Complex recurring amplifications showed characteristics of extrachromosomal amplicons and were enriched in coding SVs splitting protein regulatory from effector domains. Integrative analysis of all SCNAs, SNVs & SVs revealed patterns of characteristic combinations between potential drivers and signatures. This included two distinct groups of H3K27M DMGs with either complex or simple signatures and different combinations of associated variants. **CONCLUSION:** Recurrent SVs associate with signatures shaped by an underlying process, which can lead to distinct mechanisms to activate the same oncogene.

#### HGG-42. CLINICAL FEATURES AND TREATMENT OUTCOME OF MALIGNANT GLIOMAS IN CHILDREN AND ADOLESCENTS

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**INTRODUCTION:** Malignant gliomas in children and adolescents are rare. They are difficult to treat and are associated with an extremely poor prognosis. **SUBJECTS AND METHODS:** The treatment and outcomes of WHO grade IV -gliomas and diffuse intrinsic pontine gliomas (DIPG) in children and adolescents (Age 4–39, median 28) treated at our institute since 2001 were retrospectively reviewed. Thirty-five cases were included in this study. Nine cases were located in their brain stem and 2 of them were diagnosed as DIPG clinically without biopsy. Three (brain stem -2, thalamus-1) cases were diffuse midline glioma H3 K27 M mutant. Remaining 30 cases were diagnosed histologically as glioblastoma. Except for 2 cases, all were irradiated. Twenty-four cases were treated with temozolomide (TMZ). Bevacizumab (BEV) was administered as an initial therapy in 10 cases (concomitant with TMZ in 9 cases) and was administered at the time of relapse in 9 cases. In summary, 19 cases were treated with BEV. **RESULTS:** Median survival time (MST) of all cases was 16.8 (4.4 -152.3) months. In total, BEV did not prolonged overall survival (OS), MST 16.02 vs 14.44, ( $p=0.498$ ). Among adolescents (age 15–39), patients treated with BEV had a trend of longer OS but did not reach statistical significance, MST 19.64 vs 10.76 ( $p=0.167$ ). An extent of associated and KPS  $\geq 70$  at discharge from hospital were beneficial factors associated with prolonged OS. **CONCLUSION:** As well as in elderly cases, multidisciplinary treatment including resection, radiation and chemotherapy including BEV improves outcomes.

#### HGG-43. CONGENITAL GLIOBLASTOMA MULTIFORME: A CASE REPORT OF A RARE PEDIATRIC BRAIN TUMOR, MOLECULAR ANALYSIS, AND REVIEW OF THE LITERATURE

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Congenital brain tumors are rare, accounting for less than 4% of all pediatric brain tumors. Congenital glioblastoma multiforme (GBM) is rarer still, accounting for 3–15% of congenital brain tumors. There is literature to suggest that these tumors differ from pediatric and adult GBM clinically and molecularly, and as such should be treated as their own distinct entity. Our case is a 4 week old male who initially presented to his pediatrician for enlarging head circumference and upward gaze palsy. An MRI was obtained revealing a right parietal mass. He underwent gross total resection the following day with pathology revealing glioblastoma, WHO grade IV. Further analysis revealed ATRX retained, p53 immunoreactivity in 15–20% of nuclei, IDH1 and IDH2 wildtype, MGMT promoter not methylated, H3K27M wildtype, no 1p and/or 19q deletion/codeletion. Interestingly, RNA analysis of his tumor detected the PPP1CB-ALK fusion transcript as well as amplification of the ALK gene. Co-occurrence of these mutations has been reported in a small number of pediatric glioblastoma patients and PPP1CB-ALK fusions are one of the most common receptor tyrosine kinase fusions in infantile gliomas. ALK rearrangements and amplifications suggest a potential therapeutic target with tyrosine kinase inhibitors in glioblastoma. This patient serves as an example of a rare congenital glioblastoma with unique molecular features that may suggest novel treatment opportunities. We present his clinical course along with a pertinent review of the literature.

#### HGG-44. DEFECTS OF MISMATCH REPAIR PROTEINS IN PEDIATRIC HIGH GRADE GLIOMAS

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