

# Cerebellar High Grade Glioma in a 9 Year Old Female Child

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**Abstract:** *Glioblastoma multiforme is the most aggressive primary malignant tumor of brain which is uncommon in pediatric age group. 25 - 35% of these high grade gliomas are found in frontal lobe which is most common site of presentation. Treatment includes surgical excision followed by adjuvant radiotherapy and oral chemotherapy based on temozolamide. Despite treatment, GBM carries a dismal prognosis with mean survival of 1 year. We present a rare case study of a 9 year old female child with GBM in left cerebellar hemisphere with 2 years of follow up after treatment completion.*

**Keywords:** Pediatric GBM, glioblastoma multiforme, High grade glioma, H3K27M mutation, cerebellar Glioma

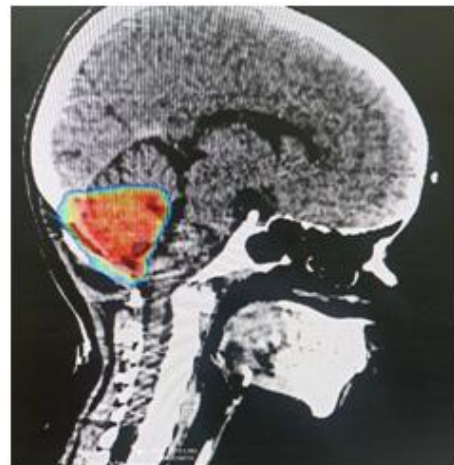
## 1. Introduction

Gliomas are the most common pediatric intra cranial tumors and approximately half of them are high - grade malignant tumors [1] Glioblastoma multiforme is the most aggressive primary malignant brain tumor characterized by nuclear atypia, cellular pleomorphism, mitotic activity, vascular thrombosis, microvascular proliferation and necrosis. It increases in frequency with age, mostly affecting adults between the 6th and 8th decade, and more commonly affecting men (male: female ratio of 3: 2) [2]. The GBMs are uncommon in children, accounting for only 3% of childhood brain tumors [3, 4, 5]. Here we present a rare case of cerebellar high grade glioma H3K27M positive in a 9 years old female child treated with surgical resection and adjuvant chemoradiotherapy with 2 years of follow up.

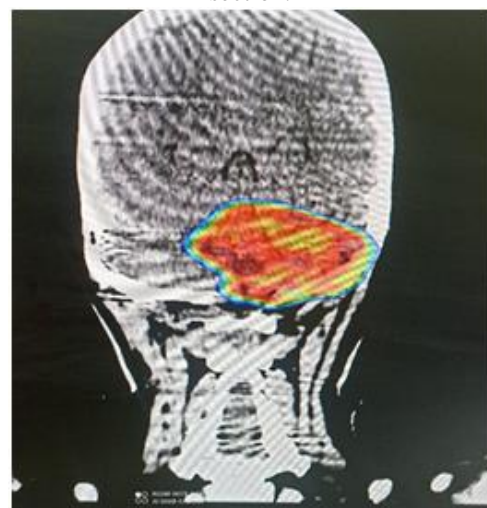
## 2. Case Report

A 9 year old female child presented with chief complaints of altered sensorium and difficulty in walking since 1 week. On examination cerebellar signs were positive including cerebellar ataxia, dysmetria and dysidiadochokinesia. Contrast enhanced MRI was suggestive of large left paramedian solid cystic infratentorial mass lesion of 4 x 4.7 x 4.2 cm in left cerebellar hemisphere with mild perilesional edema causing mass effect on brainstem, contralateral cerebellar hemisphere and compression of fourth ventricle. Suboccipital craniectomy was done with gross tumor excision of left cerebellar space occupying lesion. Post op MRI showed no residual tumor with post op gliotic changes and extra axial space collection likely seroma. Histopathological examination revealed astrocytic tumour with mild to moderate nuclear atypia with microvascular proliferation. Immunohistochemical stains were positive for GFAP, Olig2, S100 and H3K27M mutation which were suggestive of diffuse midline glioma grade IV. Radiotherapy was started after 2 weeks of surgery with a total dose of 41.4Gy in 23 fractions and boost dose of 12.6Gy in 7# to tumor bed along with oral chemotherapy temozolamide on radiation days. This was followed by adjuvant temozolamide in the dose of 150mg/m<sup>2</sup> for 8 cycles. CEMRI was done 2

months after completion of treatment and showed no residual or recurrent lesion. The patient is being reviewed with annual CEMRI and has completed 2 years of follow up with no recurrent lesion and no neurological deficit with a good performance status.



**Figure 1:** Color wash dose distribution of PTV in sagittal section.



**Figure 2:** Color wash dose distribution of PTV in coronal section

### 3. Discussion

Glioblastoma multiforme is the most common primary malignant brain tumor in adults, but is rare in children accounting for about 3% of all pediatric brain tumors [6]. The mean age of pediatric GBM is between 8.8–12.7 years [7] which is in accordance with our study where the patient is a 9 year old female child. In children, the frontal lobe has been found to be the most frequent location for GBM (25–35% of cases) [7]. However in our study, the lesion was present in left cerebellar hemisphere. A pediatric GBM study found that infratentorial lesions were exclusively found in patients <11 years old, whereas supratentorial lesions were found in patients ≥11 years old [8]. Children with high - grade gliomas present with a variety of signs and symptoms depending on their age and tumor localization. Common clinical manifestations include seizures, hemiparesis, visual deficit, headache, and sometimes, signs of intracranial hypertension. In our study, as the tumor was located in cerebellar hemisphere, patient presented with ataxia and other cerebellar signs. A contrast enhanced MRI brain is the investigational tool of choice for determining GBM [9], however, definitive diagnosis is established only histopathologically. The treatment of malignant gliomas is a challenge, particularly in pediatric age group as it associated with significant morbidity. GBM is treated with surgical removal of the lesion and adjuvant chemotherapy and Radiotherapy. Randomized trials have demonstrated a clear survival benefit to the use of radiotherapy after surgery [10]. In our study there was no residual tumor post surgery and adjuvant chemoradiotherapy was started 2 weeks after gross tumor excision. Literature suggests a better prognosis for complete resections [11] The current standard approach is to deliver a total dose of 59.4 to 60 Gy in 30 to 33 fractions at the rate of 1.8 to 2 Gy/fraction. Localized irradiation volumes are recommended despite the fact that GBM is usually more widely disseminated. In our study 41.4Gy/23# was delivered by VMAT followed by boost dose of 12.6/7# to tumor bed along with temozolamide. It was followed by 8 cycles of adjuvant temozolamide. The median survival for GBM is about 1 year. The median survival after GBM progression is 1.2 months. Recurrence is quite common in GBM patients with published recurrence rates of up to 90% [12]. According to the current literature, pediatric high grade glioma patients positive for the H3K27M mutation are more than 3 times more susceptible to succumbing to this disease, as compared to patients negative for the mutation [13]. On the contrary, in our study, patient was positive for H3K27M and had successfully completed treatment with no recurrence till date and follow up of 2 years with good performance status.

### 4. Conclusion

GBM in pediatric population is a rare entity that carries a poor prognosis. Pediatric GBM associated with H3K27M mutation has even worse outcome. We presented a rare case of 9 year old female child with cerebellar GBM and H3K27M mutation with 2 years follow up after treatment. Further investigation needs to be done in molecular studies and therapeutic options, for better understanding of disease course and improvement in survival.

### References

- [1] Reddy AT, Wellons JC. Pediatric high - grade gliomas. *The Cancer Journal* 2003; 9: 107 - 12.
- [2] Glioblastoma Multiforme. Brain tumour foundation of Canada; 2015. [Available at: <http://www.braintumour.ca/4869/glioblastoma-multiforme>]
- [3] Mahvash M, Hugo HH, Maslehaty H, Mehdorn HM, Stark AM. Glioblastoma multiforme in children: report of 13 cases and review of the literature. *Pediatr Neurol* 2011 Sep; 45 (3): 178–80.
- [4] Glioblastoma Multiforme. Brain tumour foundation of Canada; 2015. [Available at: <http://www.braintumour.ca/4869/glioblastoma-multiforme>]
- [5] Keith HM, Craig WM, Kernohan JW. Brain tumors in children. *Pediatrics* 1949 Jun; 3 (6): 839–44.
- [6] Stark AM, Fritsch MJ, Claviez A, Dörner L, Mehdorn HM. Management of tectal glioma in childhood. *Pediatr Neurol* 2005 Jul; 33 (1): 33–8.
- [7] Blondin NA, Becker KP. Anaplastic gliomas: radiation, chemotherapy, or both? *Hematol Oncol Clin North Am* 2012 Aug; 26 (4): 811–23.
- [8] Mahvash M, Hugo HH, Maslehaty H, Mehdorn HM, Stark AM. Glioblastoma multiforme in children: report of 13 cases and review of the literature. *Pediatr Neurol* 2011 Sep; 45 (3): 178–80.
- [9] Dropcho EJ, Wisoff JH, Walker RW, Allen JC. Supratentorial malignant gliomas in childhood: a review of fifty cases. *Ann Neurol* 1987; 22: 355 - 64.
- [10] Gorlia T, van den Bent MJ, Hegi ME, et al. Nomograms for predicting survival of patients with newly diagnosed glioblastoma: prognostic factor analysis of EORTC and NCIC trial 26981 - 22981/CE.3. *Lancet Oncol* 2008; 9 (1): 29–38.
- [11] Verla GT, Babu CR, Agarwal CV, Halverson CK, Adamson CD. 175 Treatment Outcomes and Prognostic Factors of Pediatric Glioblastoma Multiforme. *Neurosurg* 2014; 61 (1): 217–8.
- [12] Weller M, Cloughesy T, Perry JR, Wick W. Standards of care for treatment of recurrent glioblastoma—are we there yet? *Neuro Oncol* 2013 Jan; 15 (1): 4–27.
- [13] Lu VM, Alvi MA, McDonald KL, Daniels DJ. Impact of the H3K27M mutation on survival in pediatric high - grade glioma: a systematic review and meta - analysis. *J Neurosurg Pediatr*. 2018 Nov 30; 23 (3): 308 - 316.