Int J Cancer Manag. 2017 December; 10(12):e8100. doi: 10.5812/ijcm.8100.

Published online 2017 December 31. **Letter**

Clinical Experience with Glioblastoma Multiforme in Pediatric Patients

Mahmoud Reza Khalatbari,[1,*] and Yashar Moharamzad[1]

[1]Department of Neurosurgery, Arad Hospital, Tehran, Iran

[*]*Corresponding author*: Mahmoud Reza Khalatbari, MD, Neurosurgeon, Somayeh St, between Dr. Shariati and Bahar Ave, Tehran, Iran. Tel/Fax: +98-2177500958, E-mail: mrkhalatbari@hotmail.com

Received 2016 August 04; **Accepted** 2017 December 12.

Keywords: Glioblastoma Multiforme (GBM), Pediatric, Outcome, Temozolomide, Survival

Dear Editor,

Glioblastoma multiforme (GBM) is an uncommon and highly malignant tumor in children (1). There are limited reports (mostly in the form of case series) about evolution and prognosis of this tumor in children (2). Therefore, optimal treatment of pediatric GBM is still challenging. The outcome of surgical, radiotherapy plus chemotherapy treatment is generally poor. In a previous report from Iran reporting 23 pediatric (younger than 20 years) GBM patients with a mean age of 15 years, the median survival rate was reported as 11 months. In 12 patients, only stereotactic biopsy was done, all received radiotherapy and some received chemotherapy. Only two patients survived more than 5 years (3). According to the children's cancer study group (CCG) study, only 16% of children with GBM had 5-year progression-free survival (4).

We decided to report our clinical experience regarding GBM in pediatric (< 18 years old) patients. From 2003 to 2013, 13 GBM cases (6 males and 7 females) with histopathological confirmation were treated in our tertiary referral neurosurgery center.

Mean age upon diagnosis was 11.3 years (range, 4 - 17). Most common symptoms were headache, seizures, and hemiparesis. Loss of consciousness (one case) and intratumoral bleeding (one case) were also recorded. Surgical interventions performed included gross total resection (9 patients), subtotal resection (one patient), and stereotactic biopsy for 2 patients (lesions were located in the left thalamus). Ventriculoperitoneal shunt was placed for an 8-year-old patient with quadrigeminal plate tumor who presented with hydrocephalus and died 3 days later due to severe intratumoral hemorrhage (5). Radiotherapy with chemotherapy was done for most patients. Mean follow-up time was 25.2 months (3 days to 72 months). Of 13 cases, 4 survived (Table 1) with a mean follow-up of 39 months (range, 18 months to 6 years). Temozolomide had been administered in all of them who survived at the last follow-up. Nine patients died after a mean follow-up period of 19.1 months (range, 3 days to 36 months). Temozolomide was used just in 3 out of 9 patients who died.

Consistent with previous reports (1, 2), unfortunately, prognosis of pediatric GBM is very poor. The common point between the four survived patients here was the treatments applied which included temozolomide for all of them. Due to low sample size, it was not feasible to do statistical analyses to reach prognostic factors. It was also not possible to explicitly assess the role of temozolomide here as per low sample size. In a previous report by Cohen et al. (6), from the Children's Oncology Group, temozolomide failed to improve outcome in 55 children with GBM. In their study, radiotherapy consisted of 54.0 Gy to the preoperative tumor volume plus a 2-cm margin in 1.8 Gy fractions delivered once daily, with an additional 5.4-Gy boost in 3 fractions to any residual disease on postoperative MRI scan plus a 1-cm margin. Temozolomide was administered as 90 mg/m^2/day for 42 days. Four weeks later, adjuvant temozolomide was given (200 mg/m^2/day) for 5 days (in 10 cycles). They reported that the 3-year EFS (event-free survival) rate for GBM was 7% $\pm$ 4% in the children's oncology group study ACNS0126 compared with 15% $\pm$ 5% in the Children's Oncology Group study CCG-945. These results that temozolomide had no superiority to conventional treatments were reported as well in another study (7).

Experts who express favor in use of temozolomide in high-grade pediatric gliomas often refer to the results of trials carried out in adults. In a previous systematic review of eight eligible clinical trials (adult patients) by the Cochrane Collaboration, the authors concluded that temozolomide in both concomitant and adjuvant phases was ef-

Table 1. Information of the Survived Pediatric Patients with the Diagnosis of Glioblastoma Multiforme

Age/Gender on Presentation	Tumor Location	Treatments	Follow-Up
16/M	Right parietal lobe	Gross total resection, radiotherapy (5,400 cGy), and chemotherapy with temozolomide (Temodal®) and BCNU (carmustine)	39 months
14/F	Right parietal lobe and centrum semiovale	Same as above	27 months
7/F	Left parietal lobe and centrum semiovale	Same as above	6 years
17/M	Left occipital lobe and corpus callosum	Subtotal resection, radiotherapy, chemotherapy with temozolomide (Temodal®) and BCNU (carmustine)	18 months

fective in comparison to radiotherapy alone (8).

In our opinion, conducting meta-analyses on the role of temozolomide in prognosis of pediatric GBM would yield better information regarding whether temozolomide has a beneficial role in pediatric high grade gliomas or not.

Acknowledgments

None declared.

Footnotes

Authors' Contribution: MKh developed the concept of this letter and provided the data. YM drafted the letter and performed the literature review.

Conflict of Interests: None declared.

Financial Disclosure: None declared.

References

1. Khalatbari MR, Hamidi M, Moharamzad Y. Glioblastoma multiforme with very rapid growth and long-term survival in children: report of two cases and review of the literature. *Childs Nerv Syst*. 2011;**27**(8):1347–52. doi: 10.1007/s00381-011-1492-z. [PubMed: 21656012].
2. Sanchez Herrera F, Castro Sierra E, Gordillo Dominguez LF, Vaca Ruiz MA, Santana Montero B, Perezpena Diazconti M, et al. Glioblastoma multiforme in children, experience at hospital infantil de Mexico Federico Gomez. *Childs Nerv Syst*. 2009;**25**(5):551–7. doi: 10.1007/s00381-008-0780-8. [PubMed: 19148652].
3. Ansari M, Nasrolahi H, Kani AA, Mohammadianpanah M, Ahmadloo N, Omidvari S, et al. Pediatric glioblastoma multiforme: A single-institution experience. *Indian J Med Paediatr Oncol*. 2012;**33**(3):155–60. doi: 10.4103/0971-5851.103142. [PubMed: 23248421].
4. Finlay JL, Boyett JM, Yates AJ, Wisoff JH, Milstein JM, Geyer JR, et al. Randomized phase III trial in childhood high-grade astrocytoma comparing vincristine, lomustine, and prednisone with the eight-drugs-in-1-day regimen. Childrens Cancer Group. *J Clin Oncol*. 1995;**13**(1):112–23. doi: 10.1200/JCO.1995.13.1.112. [PubMed: 7799011].
5. Khalatbari MR, Khalatbari S, Moharamzad Y. Fatal intratumoral hemorrhage in tectal plate glioblastoma multiforme following ventriculoperitoneal shunt. *J Pediatr Neurosci*. 2014;**9**(2):192–5. doi: 10.4103/1817-1745.139366. [PubMed: 25250086].
6. Cohen KJ, Pollack IF, Zhou T, Buxton A, Holmes EJ, Burger PC, et al. Temozolomide in the treatment of high-grade gliomas in children: a report from the Children's Oncology Group. *Neuro Oncol*. 2011;**13**(3):317–23. doi: 10.1093/neuonc/noq191. [PubMed: 21339192].
7. Broniscer A, Chintagumpala M, Fouladi M, Krasin MJ, Kocak M, Bowers DC, et al. Temozolomide after radiotherapy for newly diagnosed high-grade glioma and unfavorable low-grade glioma in children. *J Neurooncol*. 2006;**76**(3):313–9. doi: 10.1007/s11060-005-7409-5. [PubMed: 16200343].
8. Hart MG, Garside R, Rogers G, Stein K, Grant R. Temozolomide for high grade glioma. *Cochrane Database Syst Rev*. 2013;**30**(4):7415. doi: 10.1002/14651858.CD007415.pub2. [PubMed: 23633341].