East African Medical Journal Vol: 94 No. 2 February 2017
INFRATENTORIAL GLIOBLASTOMA MULTIFORME: CASE REPORT
M. A. A. Magoha, MBChB, Tutorial Fellow, T.L. Rowland, MBChB, Neurosurgical Resident, C.K Musau, MBChB, MMed (Surg.), Lecturer, Neurosurgery Unit, Department of Surgery, College of Health Sciences, University of Nairobi, P.O. Box 19676-00202, Nairobi and M.A. Omar, BSc (Physiology), MBChB, Medical Officer Intern, Armed Forces Memorial Hospital, P.O. Box 40668-00100 Nairobi, Kenya.

Requests for reprints: Dr. M. A.A Magoha, Neurosurgery Unit, Department of Surgery, College of Health Sciences, University of Nairobi, P.O. Box 19676-00202 Nairobi, Kenya.

INFRATENTORIAL GLIOBLASTOMA MULTIFORME: CASE REPORT

M. A. A. MAGOHA, T. L. ROWLAND, C. K MUSAU and M. A. OMAR

SUMMARY

Glioblastoma multiforme (GBM) is the most common and most malignant form of the gliomas. The tumour accounts for 45% of malignant primary brain and Central Nervous System (CNS) tumours, 54% of all gliomas and 16% of all primary brain and CNS tumours. We present a seven year old female child who presented with a one month history of right sided headache, progressive right sided hemiparesis, and tremor with no history of infection or trauma. Investigations included computerised tomography scanning, Magnetic Resonance Imaging, Magnetic Resonance Spectroscopy and Tractography. These revealed a homogenously hypo-dense mildly ring enhancing lesion in the right brain stem, with mass effect displacing the fourth ventricle to the left, among others. Retro sigmoid craniotomy and concurrent ventricular drain placement was performed with post-operative period being uneventful. Histopathology confirmed malignant Glioblastoma multiforme and the patient was commenced on Temozolimide and radiotherapy with satisfactory results.

INTRODUCTION

Glioblastoma multiforme (GBM) is the most common malignant tumour of the brain and is incurable (1,2). These tumours commonly occur in the supratentorial regions, however they have a prevalence of 0.4-3.4 % in the infratentorial regions (1,3).

Supratentorial tumours have a different epidemiology, and presentation when compared to infratentorial ones. In this case, we discuss a female patient who presented with an infratentorial gliobastoma multiforme.

CASE REPORT

On 26th of June 2016 a seven year old female child presented to Kenyatta National Hospital, with a one month history of right sided headache, progressive right sided hemiparesis and tremor with no history of infection or trauma. On examination she was in fair general condition, with central and right cerebellar signs and features of raised intracranial pressure.

An emergent computerised tomography scan revealed a homogenously hypo-dense mildly ring enhancing lesion in the right brain stem extending to the right CPA and middle cerebellar peduncle measuring 3x3x2 centimetres which exerts mass effect displacing and compressing the fourth ventricle to the left

Figure 1
Ct scan of brain T1 MRI images

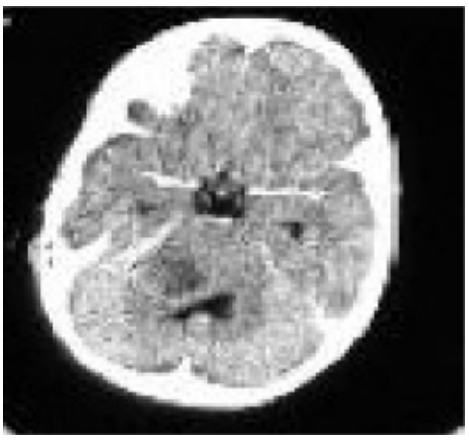
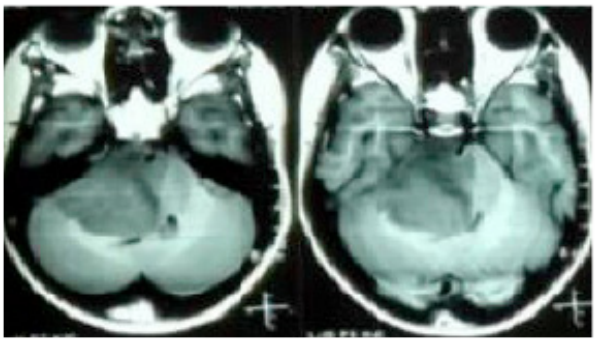


Figure 2A
T1 weighted MRI image



Magnetic resonance imaging revealed irregular eccentrically located brain stem mass with enlargement of the pons, hypo-intense on T1, hyper-intense on T2/flair sequences Irregular rim enhancement and Intra-lesional gradient blooming.(Figure 2A,B and C)

Figure 2B
T2 weighted image

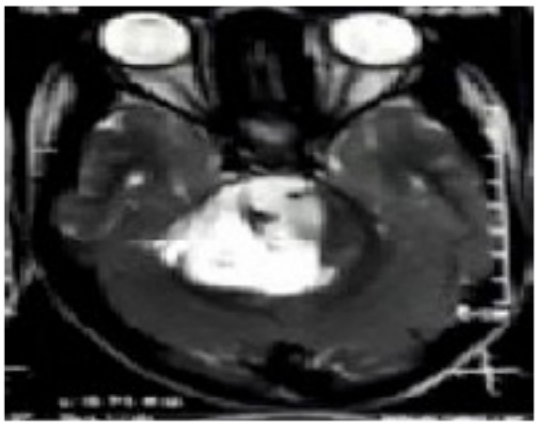
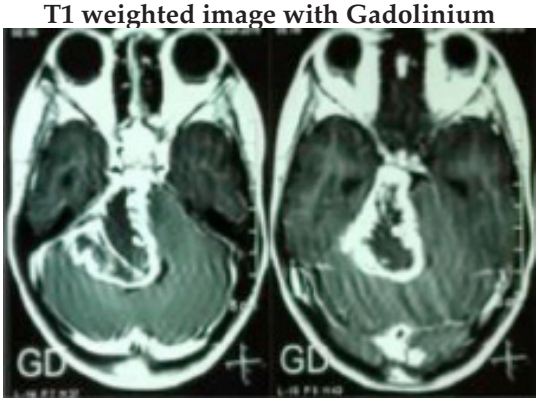
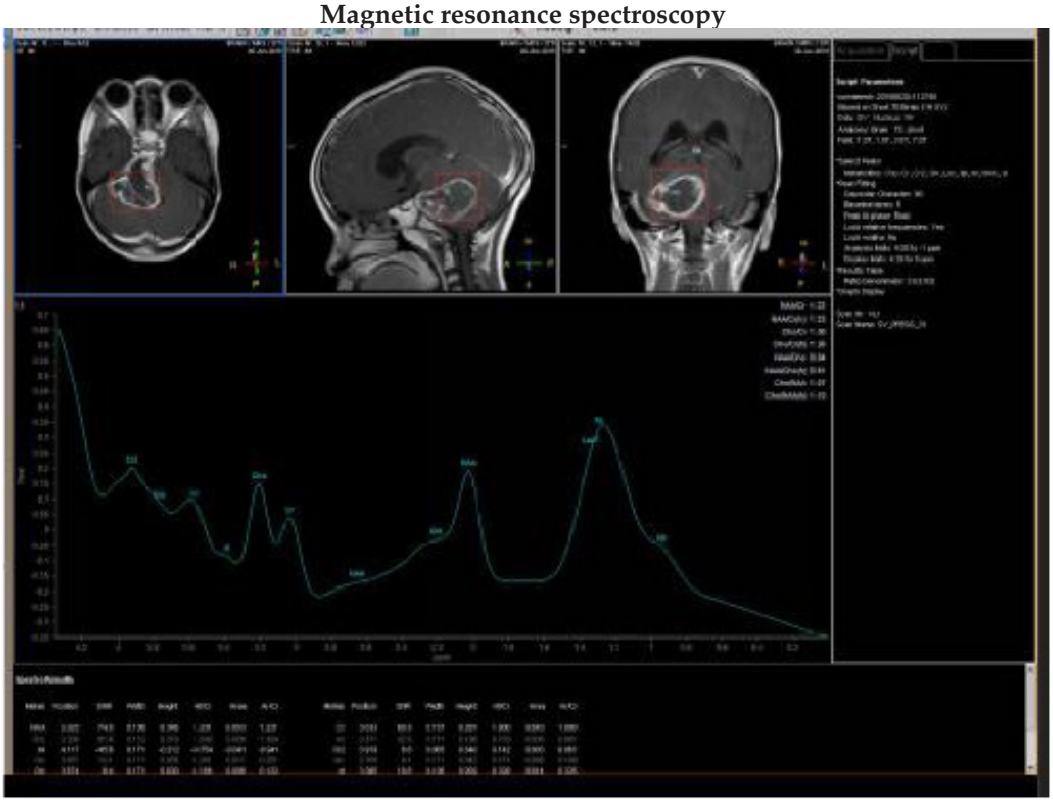


Figure 2C
T1 weighted image with Gadolinium



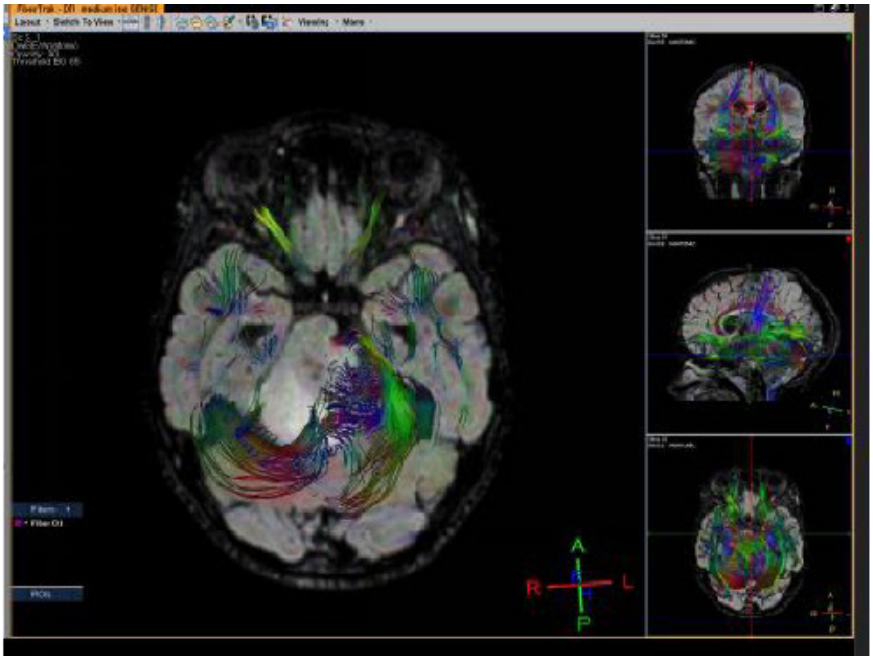
Magnetic resonance spectroscopy (Figure 3), revealed a choline rise suggestive of high cell membrane turn over, N-acetylaspartate was relatively depressed consistent with neuronal loss. Creatine was reduced implying depletion of energy stores by malignant highly metabolic tumour. Lipid-lactate doublet elevation consistent with anaerobic metabolism/ necrosis.

Figure 3
Magnetic resonance spectroscopy



Tractography (Figure 4) revealed there is discontinuation of the white matter tracts along the region of the lesion (corticospinal, corticobulbar and corticopontine).

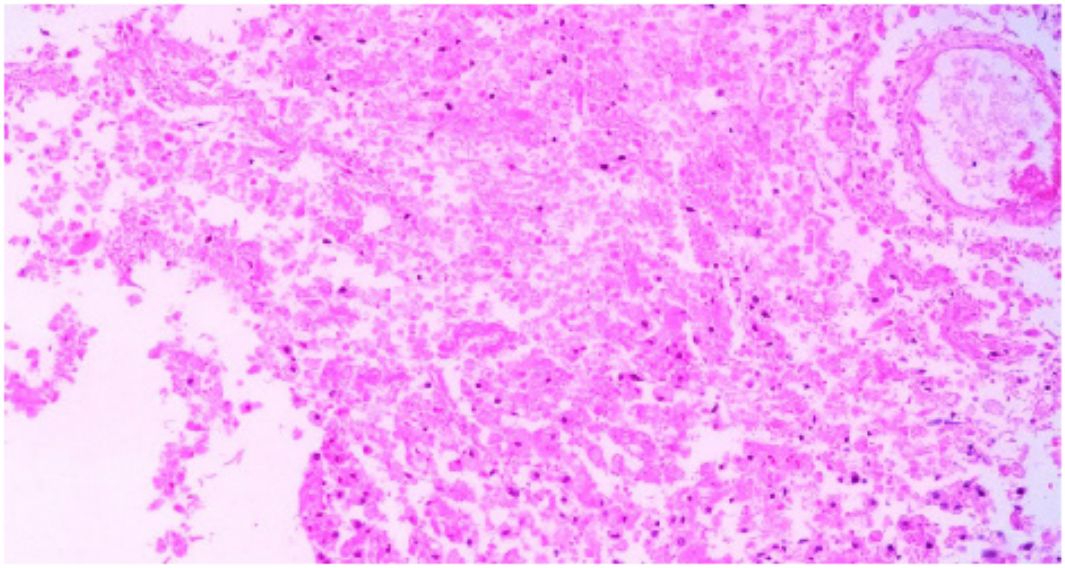
Figure 4
Tractography



Based on the above the patient was taken for a retrosigmoid craniotomy and concurrent external ventricular drain placement. The post-operative course was uneventful.

Histopathology revealed Sections of brain tissue with a high cellular tumour composed of sheets of astrocytic cells. The individual cells were exhibiting marked nuclear pleomorphism with the presence of bizarre cells. There were areas of coagulative necrosis and microvascular proliferation with some glomeruloid. Mitotic figures were demonstrable (Figure 5).

Figure 5
Histopathology



She was then started on Temozolamide therapy and radiotherapy.

DISCUSSION

Glioblastoma multiforme (GBM) is the most common and most malignant form of gliomas and is classified as Grade IV based on the World Health Organization (WHO) classification. This WHO grade is assigned to cytologically malignant, mitotically active, necrosis prone, neoplasms typically associated with rapid pre and post-operative disease evolution and a fatal outcome (4). These tumours can also widely infiltrate the surrounding tissue and disseminate to the spinal cord.

Glioblastoma multiforme accounts for 45.2% of malignant primary brain and Central Nervous System (CNS) tumours, 54% of all gliomas, and 16% of all primary brain and CNS tumours (1). The median age of diagnosis of this tumour is 64 years and only accounts for 3% of all CNS tumours reported among 0-19 year olds (1). The overall incidence rate is 1.6 times higher in males compared with females; with males having a higher frequency of primary GBMs while secondary GBMs are more common in females (1,5).

The highest incidence rates of glioblastoma multiforme are seen in whites, followed by blacks, then Asian/Pacific Islanders, and American Indians/Alaska natives in that order. Whites have two times higher incidence rates as compared to blacks (1,5). The tumours are located commonly in the supratentorial regions with rare occurrences in the cerebellum and brainstem; and very rare occurrences in the spinal cord. Overall, glioblastoma multiforme is one of the most aggressive brain tumours and is still considered to be incurable (2,3).

Infratentorial tumours can either be in the brain stem, the cerebellum or in the spinal cord. The brain stem tumours can be located in the medulla oblongata (6), in the pons and can metastasize to the sub-cutaneous tissues or in the pineal region and can metastasize to the leptomeninges (7,8). The brain stem tumours present with headache, nausea, vomiting, visual disturbance, symptoms related to Parinaud's palsy, symptoms of failure of the V, VI, and VII cranial nerves, pyramidal tract symptoms, ataxia and nystagmus, which can occur singly or in combination (8, 9).

The median survival of patients with brainstem tumours is 12.1 months (10). The location of the lesion in the brainstem, duration of symptoms and age greater than 40 years result in a significantly worse median survival (10).

Glioblastoma multiforme of cerebellum account for only 0.4-3.4 % of all and are more common in significantly younger patients (median age 50-60 years in contrast to 62-64 years for patients with supratentorial tumours (1,3). Cerebellar GBMs have also been reported in childhood, however these are more rare than in adulthood (11, 12). They occur less commonly in whites and are smaller in size (1, 3). The smaller size could be due to the fact that the posterior fossa is less accommodating to masses and thus patients with these tumours present earlier because of mass effects. Multicentric tumours involving both supratentorial and infratentorial regions are exceptional and have a reported incidence of between 0.15 – 10% (13–15).

Cerebellar glioblastomas are thought to arise from silent supra-tentorial glioblastomas that disseminate via the cerebrospinal fluid (3). Other hypotheses indicate that it may develop *de novo* or progress from lower-grade gliomas (3).

Genetic evaluation of patients presenting with cerebellar GBMs show that biopsies are immunopositive for p53, epidermal growth factor receptor and isocitrate dehydrogenase one which may be different from supratentorial lesions (3,16). Patients with cerebellar tumours may present in various ways. These patients may present with features of increased intracranial pressure such as sudden nausea and vomiting, headache, gait disturbances, ataxia, and Wallenberg syndrome (17,18).

When diagnosing these tumours, Magnetic Resonance Imaging (MRI) is favored among other diagnostic methods because of its high contrast resolution and multiplanar capability. Magnetic resonance spectroscopy and diffusion/perfusion imaging can also further assist in characterising the lesion. Glioblastoma multiforme appear as heterogenous masses on magnetic resonance imaging that may be due to necrosis or formation of cysts. On T1W magnetic resonance images, a hypointense area is visualised, surrounded by a thick irregular rim that is hyperintense and solid nodules that are isointense or slightly hypointense to surrounding cerebellar parenchyma (18). There may also be areas visualised that contain foci of bleeding or calcification.

T2W magnetic resonance images show a heterogenous hyperintense mass with variable signals surrounded by prominent oedema and enhances following intravenous gadolinium administration (18). Magnetic resonance spectroscopy differentiates glioblastoma multiforme from other diseases, with the choline (CHO)/creatine (Cr) ratio increasing over three to one and N-acetyl aspartate (NAA) peak being reduced. The tumours exhibit low signals on diffusion weighted images (DWI) while abscesses have high signal intensities (18). The segmentation of peritumoural oedema can also be used to differentiate brain metastasis from glioblastoma multiforme. Brain metastasis possess more extensive oedema with smaller tumour volume than does glioblastoma multiforme (19).

The differential diagnosis of infratentorial glioblastoma multiforme include; abscesses, hemangioblastomas, cystic astrocytoma, metastases, tuberculomas, and encephalitis (18). In patients with infratentorial tumours treatment modalities are varied across various centres because of the rarity of this condition. However, patients can be managed using a combination of surgery, radiotherapy or chemotherapy that may be neo-adjuvant or adjuvant.

A cerebellar location of a tumour independently predicts improved survival when compared to other locations (1,3). Younger age, larger extent of resection of the tumour and radiation therapy are associated with prolonged survival in patients diagnosed with cerebellar tumours (3,20).

Older patients have a decreased ability to with stand neurological insults or may have tumours with different molecular profiles and resistance genes thus creating a more aggressive tumuor (3). Radiation therapy prolongs survival in patients with cerebellar glioblastoma multiforme as is similar in supratentorial tumours.

There is a positive association between the extent of resection and survival as shown by Adams *et al*. However, other studies have varied results on the associations between surgical extent of resection and improvement in survival.

Tsung and his team found no association between the extent of resection and overall survival whereas Weber et al found that the extent of surgery was associated with a poorer survival (3,21,22).
The median survival rate of cerebellar GBMs was 8 months and 1-, 2-, 5- year survival rates of 21%, 13% and 2% respectively were demonstrated in a study by Adams *et.al* (3). Another study that reviewed both adult and pediatric cases showed that the median survival for patients with cerebellar tumours was 11 months, however this cohort had an earlier diagnosis and prompt intervention (23).

Weber *et al* evaluated outcomes in 45 patients that had brainstem GBMs, cerebellar gliosarcomas and giant cell GBMs and their median survival was 9.9 months with brainstem involvement being associated with poorer survival (3,21).

In conclusion, Infratentorial glioblastoma multiforme are less commonly reported in the literature relative to supratentorial tumours because of the rarity of this condition. They have a different epidemiological pattern and presentation in comparison to supratentorial glioblastoma multiforme and are diagnosed using imaging and histopathological techniques. The treatment modalities for these tumours are surgery, radiotherapy and chemotherapy with overall median survival rates ranging from 8- 12 months.

REFERENCES

1. Thakkar, J.P., Dolecek, T.A., Horbinski, C., Ostrom, Q.T. *et al.* Epidemiologic and Molecular Prognostic Review of Glioblastoma. Cancer Epidemiol Biomark Prev Publ Am Assoc *Cancer Res Cosponsored Am Soc Prev Oncol. 2014*; **2**:1985–96.
2. Tran, B. and Rosenthal, M.A. Survival comparison between glioblastoma multiforme and other incurable cancers. *J Clin Neurosci Off J Neurosurg Soc Australas*. 2010;**17**:417–21.
3. Adams, H., Chaichana, K.L., Avendanõ, J., Liu, B., Raza, S.M. and Quinõnes-Hinojosa, A. Adult Cerebellar Glioblastoma: Understanding Survival and Prognostic Factors Using a Population-Based Database from 1973 to 2009. *World Neurosurg*. 2013;**80**:e237–243.
4. Louis DN, Ohgaki H, Wiestler OD, Cavenee WK, Burger PC, Jouvet A, et al. The 2007 WHO Classification of Tumours of the Central Nervous System. *Acta Neuropathol (Berl)*.2007;**114**:97–109.
5. Ostrom, Q.T., Gittleman, H., Farah, P. *et al.* CBTRUS Statistical Report: Primary Brain and Central Nervous System Tumours Diagnosed in the United States in 2006-2010. *Neuro-Oncol*. 2013;**15**:ii1-ii56.
6. Luetjens, G., Mirzayan, M.J., Brandis, A. and Krauss, J.K. Exophytic giant cell glioblastoma of the medulla oblongata. *J Neurosurg*. 2009;**110**:589–593.
7. Kumar, V., Singh, D., Singh, H. and Saran, R.K. A case report of pontine glioblastoma presenting as subcutaneous metastasis in nape of neck in a child. *J. Pediatr. Neurosci*. 2015;**10**:386–388.
8. Matsuda, R., Hironaka, Y., Suigimoto, T. and Nakase, H. Glioblastoma Multiforme in the Pineal Region with Leptomeningeal Dissemination and Lumbar Metastasis. *J. Korean. Neurosurg. Soc*. 2015;**58**:479–482.
9. Strange P, Wohlert L. Primary brain stem tumours. *Acta. Neurochir. (Wien)*. 1982;**62**:219–232.
10. Babu, R., Kranz, P.G., Agarwal, V. *et al.* Malignant brainstem gliomas in adults: clinicopathological characteristics and prognostic factors. *J.Neurooncol*. 2014;**119**:177–185.
11. Fresh, C.B., Takei, Y. and O'Brien, MS. Cerebellar glioblastoma in childhood. *Case report. J. Neurosurg*. 1976;**45**:705–708.
12. Georges, P.M., Noterman, J., Flament-Durand, J. Glioblastoma of the cerebellum in children and adolescents. Case report and review of the literature. *J. Neurooncol*. 1983;**1**:275–278.
13. Dohrmann, G.J. and Dunsmore, RH. Gliobastoma multiforme of the cerebellum. *Surg. Neurol.1975*; **3**:219–223.
14. de Eulate-Beramendi, S.A., Piña-Batista, K.M., Rodrigo, V., Torres-Rivas, H.E. and Rial-Basalo, J.C. Multicentric spinal cord and brain glioblastoma without previous craniotomy. *Surg. Neurol. Int*. 2016 **7;7**(Suppl 17):S492–494.
15. Arcos, A., Romero, L., Serramito, R. *et al.* Multicentric glioblastoma multiforme. Report of 3 cases, clinical and pathological study and literature review. *Neurocir. Astur. Spain*. 2012 Sep;**23**:211–215.
16. Utsuki, S., Oka H, Miyajima, Y., Kijima, C., Yasui, Y. and Fujii, K. Adult cerebellar glioblastoma cases have different characteristics from supratentorial

glioblastoma. *Brain Tumour Pathol*. 2012;**29**:87–95.
17. Auff, E. and Vass, K. Cerebellar glioblastoma presenting clinically as Wallenberg's syndrome. *Arch Für. Psychiatr. Nervenkrankh*. 1981;**230**:361–364.
18. Demir, M.K., Hakan, T., Akinci, O. and Berkman, Z. Primary cerebellar glioblastoma multiforme. *Diagn. Interv. Radiol*. 2005;**11**:83–86.
19. Zhou, C., Yang, Z., Yao, Z. et al. Segmentation of peritumoural ooedema offers a valuable radiological feature of cerebral metastasis. *Br. J. Radiol*. 2016;**89**:20151054.
20. Babu, R., Sharma, R., Karikari, I.O. *et al*. Outcome and prognostic factors in adult cerebellar glioblastoma. *J. Clin. Neurosci. Off. J. Neurosurg. Soc. Australas*. 2013; **20**:1117–1121.
21. Weber, D.C., Miller, R.C., Villà, S. *et al*. Outcome and prognostic factors in cerebellar glioblastoma multiforme in adults: a retrospective study from the Rare Cancer Network. *Int. J. Radiat. Oncol. Biol. Phys*. 2006.1;**66**:179–86.
22. Tsung, A.J., Prabhu, S.S., Lei, X. *et al*. Cerebellar glioblastoma: a retrospective review of 21 patients at a single institution. *J. Neurooncol*. 2011;**105**:555–62.
23. Djalilian, H.R., Hall, W.A. Malignant gliomas of the cerebellum: an analytic review. *J. Neurooncol*. 1998 Feb;**36**:247–57.