Glioblastoma multiforme of the cerebellum

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ABSTRACT

تعد أورام الخلايا الدبقية متعددة الأشكال (GBM)، من الأورام الخبيثة جدا. وعادتاً ما تكون شائعة نصف الكرة المخية، ونادرا ما تنشأ في المخيخ. يمكن أن يصيب هذا النوع من الأورام أي من الفئات العمرية، ولكنه يشاهد بكثرة لدى الكبار في السن. وعلى الرغم من ندرته، إلا انه يجب التفكير به في حالة وجود كتلة في المخيخ. لا يوجد إجماع بشكل عام على العلاج الأمثل لمثل هذه الحالات، ولكن هناك اتفاق على أن تخضع هذه الحالات لخطة علاجية متعددة الجوانب، كالعلاج الكيميائي والإشعاعي المكثف، الذي قد يساهم في إطالة عمر المريض. وعلى الرغم من هذا العلاج المتعدد تبقى النتائج سيئة عموما، إلا انه يجب الأخذ بعين الاعتبار التخفيف عن المريض وإبقائه على قيد الحياة. نذكر في هذه المقالة حالتين تمت معالجتهم في مركزنا، وبين الفحص النسيجي للعينات إن هذا الورم هو من نوع أورام الخلايا الدبقية متعددة الأشكال (GBM). وسوف نقوم بمراجعة المقالات الطبية ذات الصلة بهذا النوع من الأورام.

Glioblastoma multiforme (GBM) is a highly malignant glial tumor seen commonly in the cerebral hemispheres, but rarely encountered in the cerebellum. It may occur at any age, but is seen more often in adult age groups. Despite its rarity, GBM should be considered in patients with a ring-enhancing lesion in the cerebellum. No consensus regarding the best management has yet been established. However, multimodal treatment is currently available to deal with these lesions: wide excision with radio-chemotherapy may improve and prolong the patient's life. Although the outcome remains dismal, we emphasize that timely multi modal treatment may provide the patient a better outcome and longer life. Herein, we report 2 new cases of cerebellar GBM and discuss their outcome and present a review of the relevant literature.

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Glioblastoma multiforme (GBM), the most common malignant astrocytic neoplasm, is associated with a grim outcome and low survival rate. It accounts for 20.3% of all primary intracranial neoplasms in the United States.[1] Although it can arise in virtually any part of the CNS, the cerebral hemispheres are the usual site, with predilection for the frontal and temporal lobes, while the brain stem, cerebellum, and spinal cord are unusual locations. Cerebellar GBM is extremely rare and may present at any age, but is less frequently observed in the very young and very old; slightly more males than females are affected.[2-4] Like other glial lesions, GBM does not present in any specific way, but the pattern of presentation depends on the site of the tumor and its rapidity of expansion. Sudden or swift progression at the time of presentation may be related to hemorrhage, infarction, or even acute hydrocephalus as seen in one of our cases.[3,4] The proximity of the cerebellum to the brain stem makes treatment options for cerebellar GBM a little different to those of supratentorial GBM. Various treatments for GBM have been adopted, including total surgical resection if anatomically and functionally feasible, conventional, or focused radiotherapy, and adjuvant chemotherapy. Despite these approaches, aggressive treatment has almost always failed to cure this malignancy because of its infiltrative and aggressive nature. However, life expectancy in patients with cerebellar GBM may be longer than in their counterparts with cerebral GBM, and this could be related to earlier neurological presentation, timely diagnosis, and surgical resection, basically gross resection followed by radio-chemotherapy.[4,5] In this report, we present 2 new cases and review the literature. Glioblastoma multiforme is to be considered in patients with cerebellar lesions;

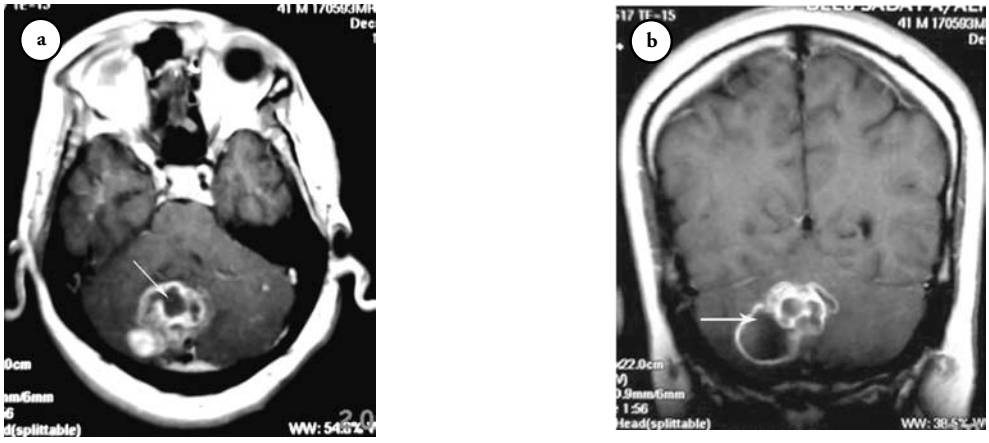

Figure 1 - Patient one. **a**) Axial T1-weighted and **b**) coronal T1-weighted MR scans of the brain with gadolinium contrast showing a vermian mass lesion with areas of necrosis and irregular ring enhancement (arrow), extending to the right hemisphere, the fourth ventricle is seen to be compressed by the lesion.

and multimodal treatment is highly recommended for patients with cerebellar glioblastoma to ensure better outcome.

Case Report. *Patient one.* In July 2005, a 41-year-old man suffered concussion after a motor vehicle accident. He was sent home from the Emergency Department with apparent full recovery, but without scanning. He then occasionally experienced headache and dizzy spells, which were initially attributed to the accident. Four months later, he was referred to our neurosurgical service with a 2-week history of worsening headache, vomiting, unsteadiness, and blurred vision. On examination he was lethargic with a Glasgow coma score (GCS) of 13/15, left partial abducens nerve palsy with double vision. An ophthalmology assessment confirmed papilledema. On the day of admission, he acutely developed delirium, and his level of consciousness declined to a GCS of 10/15, necessitating intubation and ventilation. An emergency CT brain scan demonstrated a cystic mass lesion located within the vermis, and the white matter of the right cerebellar hemisphere with irregular ring enhancement, obstructing the fourth ventricle, and causing hydrocephalus. He underwent an urgent insertion of external ventricular drain (EVD) from which he made a significant improvement, and he was able to be extubated in a couple of days. The CSF analysis showed no malignant cells. When his neurological status was optimized, an MRI with gadolinium was performed that confirmed a cystic mass situated deep in the vermis and right cerebellar hemisphere, with irregular ring enhancement, and edema causing mass effect on the brainstem (**Figures 1a & 1b**). There was no evidence of malignancy on the bone scan or CT of the chest, abdomen, and pelvis. A week later, he underwent

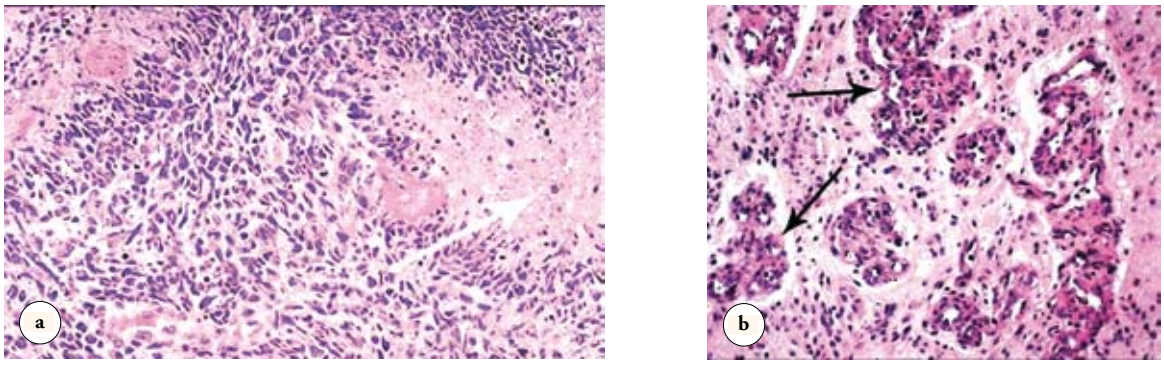

Figure 2 - Patient one. **a**) Photomicrographs of tumor biopsy specimens. Extensive proliferation of neoplastic glial cells with a mixture of atypical, multinucleated, hyperchromatic round and spindle cells are seen. Mitoses are widely apparent. Vascular proliferation can also be noted (arrow). **b**) Pseudo palisading and necrosis are evident (arrow). (Hematoxylin & eosin, x400, x200)

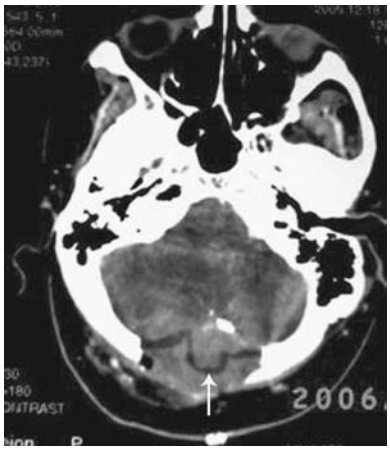

Figure 3 - Patient one. Postoperative CT scan with contrast showing adequate removal of the cerebellar tumor, the fourth ventricle is now patent.

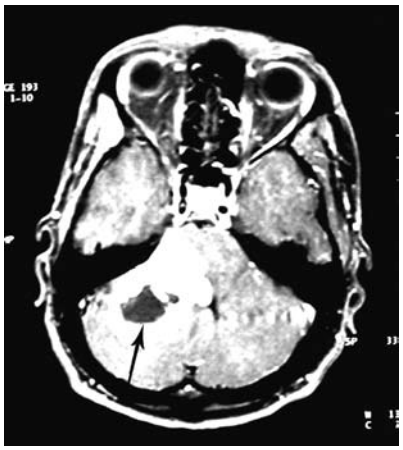

Figure 4 - Patient 2. Axial T1-weighted MR scan of the brain with gadolinium contrast showing a mass lesion involving the right cerebellar hemisphere, with central area of necrosis surrounded by enhancement (arrow). The fourth ventricle and brain stem are compressed by the lesion.

a suboccipital craniectomy for gross total resection of the cerebellar mass. Histopathology was consistent with GBM (**Figures 2a & 2b**). His postoperative course was uneventful. On the eighth postoperative day, the EVD was successfully taken out. He displayed some cerebellar signs on the right side and some unsteadiness on his feet for a while, but made a significant improvement during rehabilitation. A repeat scan with contrast revealed no identifiable gross residual tumor and resolution of hydrocephalus (**Figure 3**). He completed whole brain radiotherapy (WBRT) with focus on the posterior fossa, followed by temozolomide as per protocol in this center (150 mg/m^2/day for 5 days every 4 weeks for 6 cycles). He was neurologically stable on the monthly follow up as an outpatient for nearly 14 months. He then declined neurologically and succumbed to the disease 15 months after diagnosis.

Patient 2. A 29-year-old male presented in June 2006 with a 2-month history of headache and occasional attacks of vertigo associated with vomiting. Two weeks prior to admission he started to complain of unsteadiness and frequent falls to the right. On examination he had severe horizontal and vertical nystagmus, right sided dysdiadochokinesia and dysmetria, was unsteady on his feet and had a positive Romberg's sign to the right. An MRI of the brain with contrast revealed a right cerebellar hemisphere enhancing mass with a cystic component extending to the middle cerebellar peduncle and to the pons with mild obstructive hydrocephalus (**Figure 4**). A retroauricular suboccipital craniectomy for debulking of the tumor was effected; the tumor appeared greyish and soft with cystic necrosis and ill-defined edges. The histopathology confirmed GBM (**Figure 5**). He made an uneventful post-operative recovery, and his symptoms improved dramatically, but minimal residual cerebellar

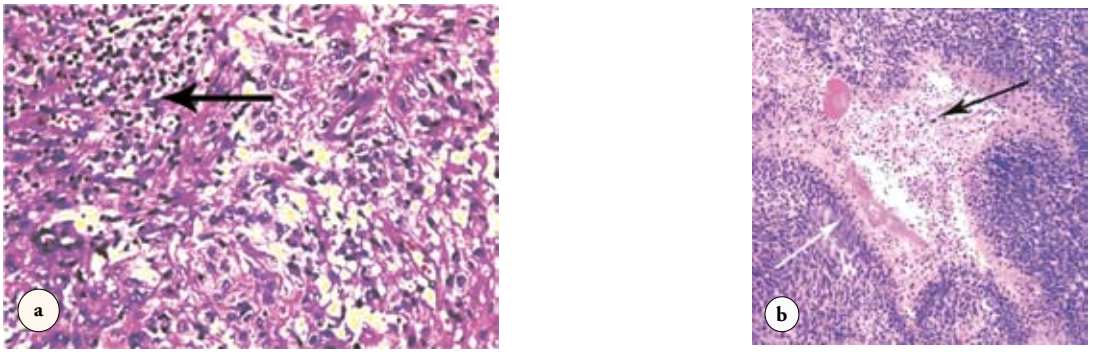

Figure 5 - Patient 2. **a**) Photomicrographs of tumor biopsy specimens. Again an extensive proliferation of neoplastic glial cells with an assortment of atypical, hyperchromatic cells is seen. Mitoses are widely apparent. **b**) Pseudo palisading (white arrow) and necrosis (black arrow) are evident. (Hematoxylin & Eosin x200)

signs remained. He received WBRT followed by temozolomide as per the protocol described for our first patient. He was well on the monthly follow up for 12 months; he then neurologically deteriorated and passed away 13 months after surgery.

Discussion. Glioblastoma multiforme was first described in 1928 by Carmichael[6] as "spongioblastoma" in the cerebrum. Glioblastoma multiforme in the cerebellum represents only a small percentage of all brain gliomas. The scarcity of cerebellar GBM is unexplained; one would anticipate these tumors to arise in this site at a rate of 10% as the cerebellum weight is 10% of the whole brain weight.[5] A small number of series illustrating cerebellar GBM are identified in the world literature. Djalilian et al,[4] reviewed 41 patients with cerebellar GBM from 1975 to 1998, while Chamberlain et al[3] found only 5 GBM out of 18 patients with anaplastic glioma treated between 1977 and 1987. In 1989, Rosenfeld et al[7] reviewed 86 cases with documented cerebellar GBM in the world literature. Having reviewed the world literature from 1989 to date, we found another 16 cases published with cerebellar GBM in adults (**Table 1**), bringing the total number to 104 cases including our cases.[2-4,7-12] As with cerebral malignant gliomas, the pathogenesis of these lesions is unknown. It is believed that some GBM may evolve from a low-grade glioma. Brain irradiation in the past is thought to have an etiological role in some cases. Genetic anomalies may play an important role in the development of these fatal neoplasms.[12-14] Patients with GBM, like other cerebellar lesions, may display a wide range of neurological conditions, but the cerebellar GBM can be detected earlier compared with cerebral GBM due to its effect on vital functions. However, rapid deterioration or even death due to massive bleeding or acute hydrocephalus is also mentioned in many instances.[2,6,8,9] The imaging scan appearance of GBM is non-specific for the cerebellum. There are a few reports on MRI imaging of cerebellar GBM. These lesions usually arise from the midline with extension to the hemispheres. On T1-weighted imaging the tumors appear to have irregular intensity with cystic components. The T2-weighted images show increased intensity associated with peritumoral edema. An irregular ring enhancement and heterogeneous enhancement of the solid part are evident after gadolinium injection. The lesion is usually compressing the fourth ventricle causing secondary ventriculomegaly and may compress the brain stem. However, cerebellar GBM is easily overlooked and mistakenly diagnosed on the imaging scans; the differential diagnosis includes metastatic tumors, medulloblastoma, abscess, or cystic astrocytoma.[15,16] More recently, magnetic resonance spectroscopy (MRS) is wildly applied in the diagnosis of variable CNS lesions; it is reliable in differentiating neoplasms from non neoplastic lesions.[17] Certain patterns can be illustrated in the presence of high grade gliomas, and this can be correlated with the histopathology findings.[10,17] The striking heterogeneity and pleomorphism of these tumors rationalize the term "multiforme". Grossly, areas of assorted colors - grey, yellow, brown, and red can be observed, and are attributed to necrosis, fatty degeneration, and old or new hemorrhage. Infiltration to adjacent structures is also seen. The most fundamental microscopic features of GBM are necrosis and microvascular proliferation; these are essential to differentiate GBM from anaplastic astrocytoma and other lesions. Although it is not distinctively characteristic for GBM, pseudopalisading around necrosis is seen frequently. Giant cell and gliosarcoma variants of GBM have been also described.[11,17] The strategy of cerebellar GBM management is similar to that used for cerebral GBM. Some differences in treatment options exist between these 2 locations; this is attributed to the rarity of cerebellar GBMs and the proximity of these tumors to the brain stem. The generally accepted treatment is to obtain as radical resection as feasible, followed by focal irradiation to the posterior fossa. Due to the sinister prognosis, some authors recommend partial resection or simply biopsy with or without radiotherapy, based on the patient's condition.[3,4,7] Generally speaking, variable concomitant chemotherapy protocols have been adopted to deal with GBM, their role is still under debate because of unsatisfactory results; this probably arises from the inability of the chemotherapeutic agents to penetrate the blood-brain barrier or chemoresistance, whereby gene expression in tumor tissue limits the effectiveness of chemotherapy in GBM in general. More recently, new regimens have been attempted to obtain more favorable

Table 1 - Number of cases with cerebellar GBM published or reviewed from 1989 to 2006.

Authors	Number of cerebellar GBM	Year of publication
Mattos JP, et al[10]	1	2006
Queiroz LS, et al[11]	1	2005
Tamaki T, et al[2]	1	2004
Ota T, et al[9]	1	2001
Djalilian & Hall[4]	4	1998
Schwartz & Ghatak[12]	1	1990
Aziz & Stoddart[8]	2	1990
Chamberlain MC, et al[3]	5	1990
Rosenfield J, et al[7]	86	1989

GBM - Glioblastoma multiforme

outcome. Temozolomide is a new oral chemotherapy agent that is now widely used and has been shown to improve quality of life and increase the survival rate of patients with GBM. Although examples of longer life have been reported, the prognosis of these tumors is almost always fatal within a short time.[18-20]

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CASE REPORTS

Case reports will only be considered for unusual topics that add something new to the literature. All Case Reports should include at least one figure. Written informed consent for publication must accompany any photograph in which the subject can be identified. Figures should be submitted with a 300 dpi resolution when submitting electronically or printed on high-contrast glossy paper when submitting print copies. The abstract should be unstructured, and the introductory section should always include the objective and reason why the author is presenting this particular case. References should be up to date, preferably not exceeding 15.