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INFRATENTORIAL GLIOBLASTOMA MULTIFORME: CASE REPORT AND REVIEW OF LITERATURE
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ABSTRACT

Glioblastoma multiforme (GBM) is the commonest 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 which included computerized 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 4th 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

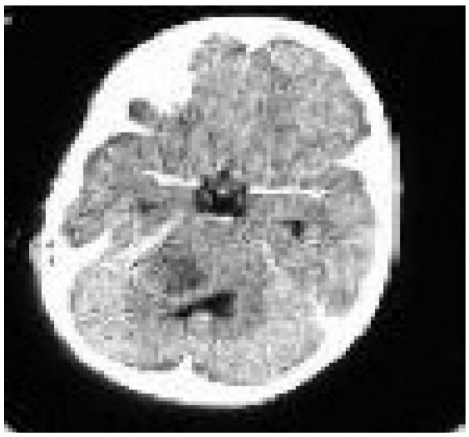
Glioblastoma multiforme (GBM) is the commonest malignant tumour of the brain and is incurable (1,2). These tumours commonly occur in the supratentorial regions, however they have a prevalence of 0.4-3.4 % in the infratentorial regions (1,3). Supratentorial tumours have a different epidemiology, and presentation when compared to infratentorial ones. In this case, we discuss a female patient who presented with an infratentorial gliobastoma multiforme, followed by review of the literature.

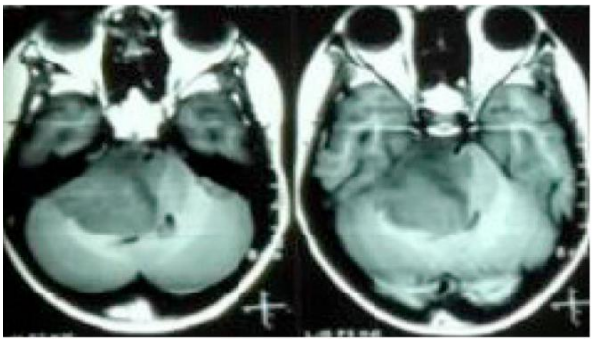
CASE REPORT

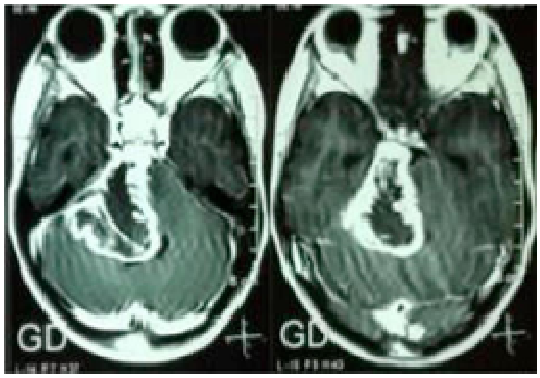
On 26th of June 2016 a 7yr old female child presented to Kenyatta National hospital, with a one month history of right sided headache, progressive right sided hemiparesis and tremor with no history of infection or trauma. On Examination she was in fair general condition, with central and right cerebellar signs and features of

raised intracranial pressure. An emergent computerized 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 3 x 3 x 2 cm which exerts mass effect displacing and compressing the 4th ventricle to the left (Figure 1A).

Figure 1A
CT Scan of brain TI MRI images







Magnetic resonance imaging revealed irregular eccentrically located brain stemmas with enlargement of the pons, hypo-intense on T1, hyper-intense on T2/ flair sequences Irregular rim enhancement and Intra-lesional gradient blooming.

Figure 2
T1 MRI images with gadolinium T2 MRI image right enhancement left

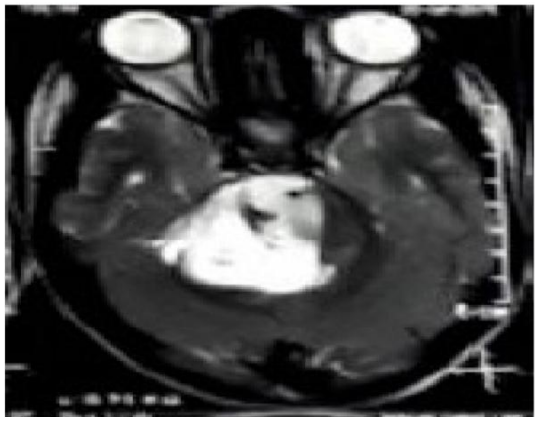
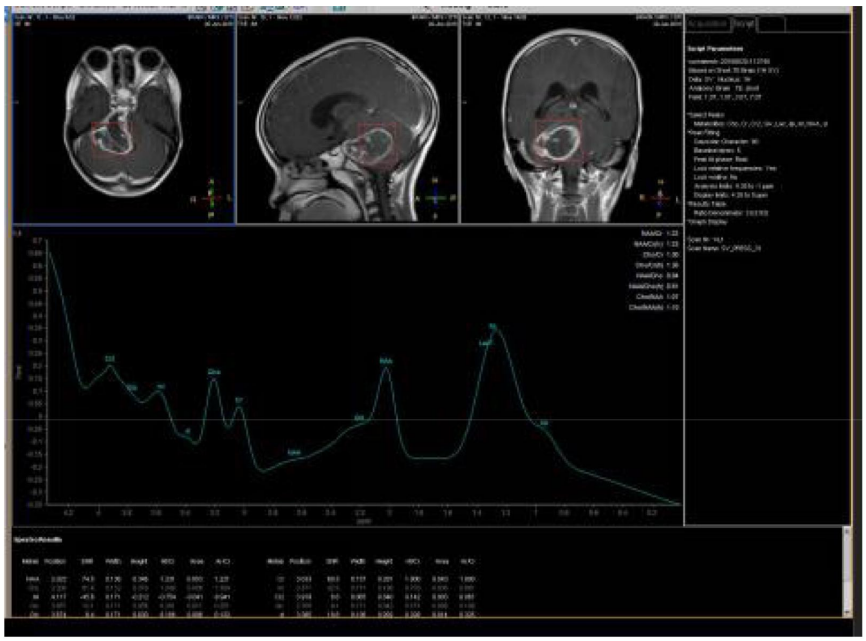
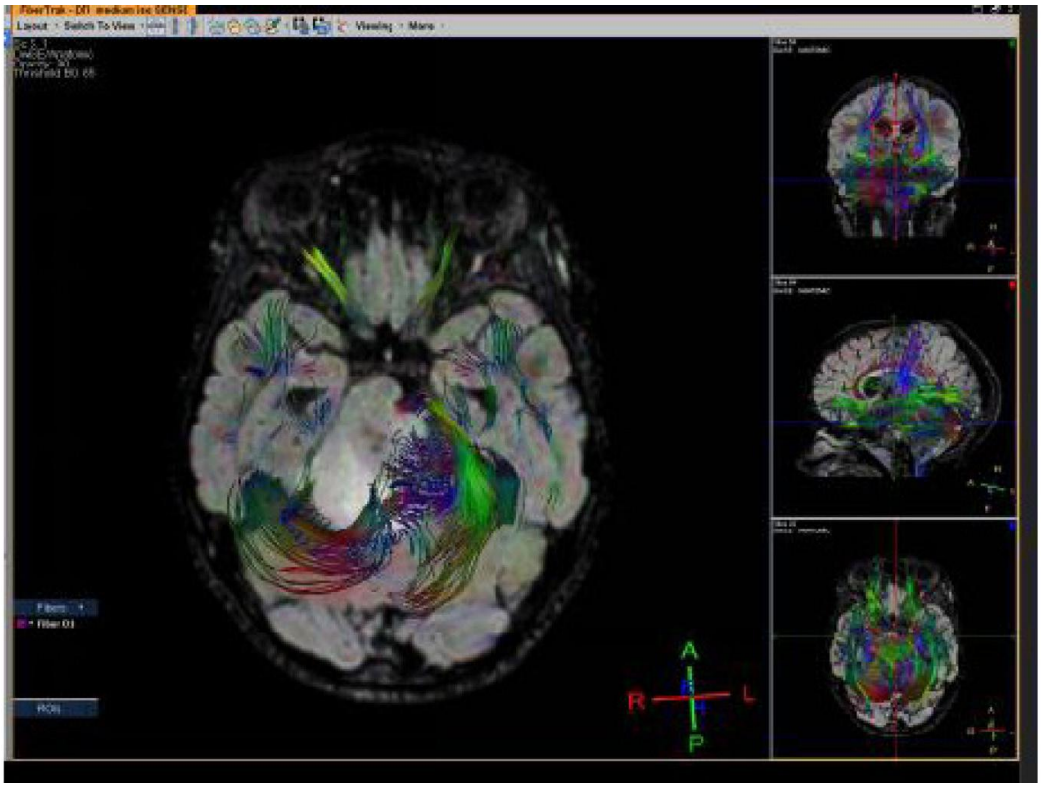


Figure 3
Magnetic resonance spectroscopy



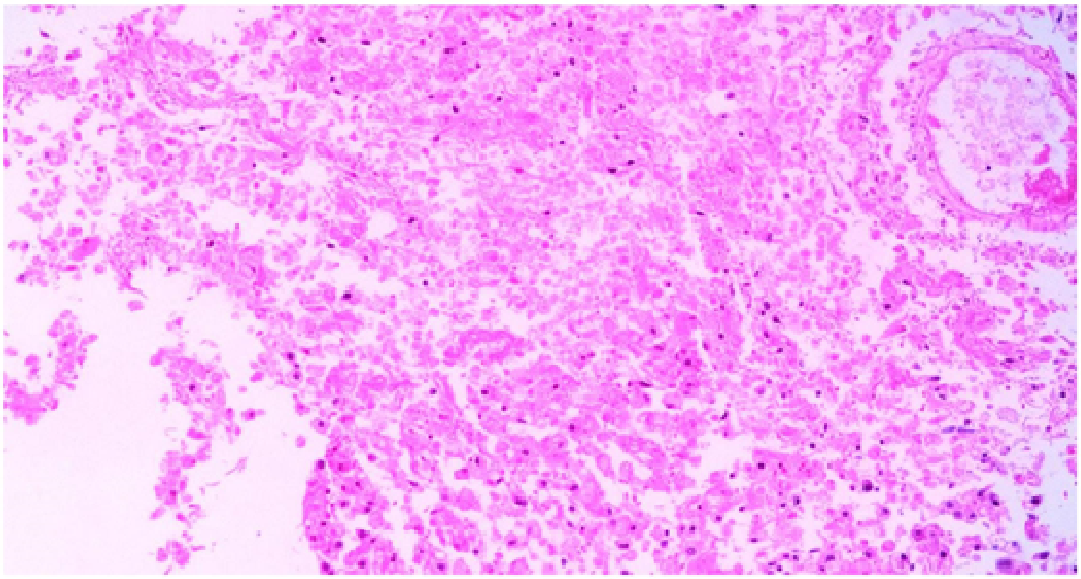
Magnetic resonance spectroscopy (Figure 3), revealed a choline rise suggestive of high cell membrane turn over, N-acetylaspartate was relatively depressed consistent with neuronal loss. Creatine was reduced implying depletion of energy stores by malignant highly metabolic tumour. Lipid-lactate doublet elevation consistent with anaerobic metabolism/ necrosis. 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 commonest 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 postoperative 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 commoner 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 2 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 brainstem, 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 subcutaneous tissues or in the pineal region and can metastasize to the leptomeninges (7,8). The brainstem 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 cerebellar account for only 0.4-3.4 % of all and are commoner 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 1 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 favoured 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 characterizing 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 visualized, 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 visualized 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 3 to 1 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 centers 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 withstand neurological insults or may have tumours with different molecular profiles and resistance genes thus creating a more aggressive tumour (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 paediatric 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).

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.

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