Glioblastoma Multiforme with Complex Clinical Manifestations: Case Report and Literature Review

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Abstract:

Brain tumors in children account for 20% of all childhood malignancies. Most cases occur in the first decade of life, with the peak age at 5-9 years. The annual incidence is approximately 14 per 100,000 children younger than 15 years in the United States. Astrocytomas are classified according to the world health organization clinicopathologic grades from grave I and II which are considered an indolent low-grade astrocytoma and the more malignant astrocytomas grade III and grade IV. Glioblastoma multiforme (grade IV) is the most malignant form of astrocytoma. Prognosis is good with most low-grade tumors with surgical resection alone is curative. The 5-year survival rates as high as 95-100% without further treatment. Current operative mortality rates are less than 1%. The prognosis, however,

is poor for high-grade tumors. The 5-year survival rate is 15-30% for supratentorial lesions and less than 10% for pontine tumors. Seizure disorders might evolve thereafter depending on the astrocytoma site.

Key-words:

brain tumors, astrocytoma, childhood tumours, glioblastoma multiforme

Introduction:

Brain tumors in children account for 20% of all childhood malignancies. There are considered the most common malignant tumors after acute lymphoblastic leukemia [1].

Astrocytomas have wide clinical manifestations. They are classified based on location within central nervous system, potentiality of growth rate, invasiveness, morphological features, tendency for progression, and clinical course. The world health organization (WHO) clinicopathologic grades are: pilocytic astrocytoma (WHO grade I), diffuse astrocytoma

(WHO grade II), anaplastic astrocytoma (WHO grade III), and glioblastoma multiforme (WHO grade IV) [2].

Case History:

A female neonate was born by emergency lower-segment Caesarian section for non-reassuring cardiotocography at 40 weeks and 10 days. The pregnancy was not complicated by any medical illness. The mother is Blood Group O positive and rubella immune.

On day one of life, Apgar was 9 and 10 at 1 and 5 minutes, respectively. The patient was admitted to neonatal intensive care unit for 42 hours. Head circumference was 34 cm (25% centile). Birth weight was 2.78 kg (25% centile). Diagnosis was made as asymmetrical intra-uterine growth regression. She was pink in colour. Cardiovascularly stable. Neurologically stable, eyes opened spontaneously (E=4), sucking normally and crying (V=5), moving all four limbs (M=6), normal posturing (Glasgow coma scale is 15/15). She was crying. All primitive reflexes are elicited.

On day two of life, she had multiple generalized tonic-clonic seizures and episodes of apnea and desaturating to 60% in room air. The baby was place in continuous positive airway pressure. She received phenobarbitone and phenytoin. A septic workup was performed.

Lumbar tap was performed. Blood and lumbar culture found that no organisms were seen on gram stain and PCR. Intravenous antibiotics were empirically commenced. On day three of life, magnetic resonance imaging (MRI) to the brain was conducted. MRI report revealed that there is an extensive parieto-occipital intraparenchymal haemorrhage was found as well as a midline shift. Compression of the left lateral ventricles with left intracalcine herniation.

Two weeks later, surgical decompression and craniotomy was performed. Tissue was biopsied and sent to the pathology lab for further investigation. Post-operative MRI was done revealing the following: post surgical changes secondary to craniotomy. It is found that there was a large occipital cavity communicating with left lateral ventricle with surrounded oedema. Intraventricular and subdural blood was also found. Small post-operative axial air fluid collection and subgaleal fluid collection were also noted. MRI was repeated in a 6-week period. 3D MRA and 2D MRV have been performed. No abnormalities were found. Histopathological examination confirmed that patient has glioblastoma multiforme (WHO grade IV).

Three months later, patient had an MRI showing that a mass lesion at the site of the previous hemorrhage. The patient was admitted electively for craniotomy and debulking of a large parieto-occipital enhancing mass. Patient underwent craniotomy and the left occipital tumor was excised. A computerized topography revealed a large cavity at the site of excised mass and a small tentorial subdural hematoma in addition to pneumocephalus. A two-week MRI scanning showed a small post-operative psudomeningocele was noted, did not show any evidence of residual tumour.

She started the first cycle of chemotherapy (Regimen A: vincristine 0.065/kg, IV, taken on 1 day 1 and 4 day and cyclophosphamide 65 mg/kg, IV, taken on day 1. Regimen B: etopsie 6.5 mg/kg, IV, taken on day 3 and day 4 and cisplatin 4 mg/kg, IV, taken on day 1).

Regimen A was given for the first two months and regiment B was given in the third month.

Discussion:

The clinical manifestations of malignant gliomas are dependent upon the location and size of the lesion [3]. The spectrum of symptoms that malignant gliomas manifest as are: headache, seizures are a presenting symptom in approximately 20% of patients with supratentorial brain tumors [4]. As in our case report, the patient chiefly presented initially with seizures, which was described as generalized tonic-clonic.

GBM is considered as the most malignant type of cancer. The overall median survival is less than 1 year [5]. The most significant prognostic factors described in the literature are age at presentation, tumour location, tumour grade (GBM has the worst prognosis), and Karnofsky performance status (KPS; it is standard measure of the ability of patients with cancer to perform daily tasks, as well as extent of initial surgical resection [5, 6, 7, 8].

There is a compelling evidence suggesting that the greater the extent of resection, the more longer the survival for patients with malignant gliomas [9, 10, 11]. The malignant gliomas are rapidly progressive brain tumors that are divided into anaplastic gliomas and GBM based on

their histologic features [12]. They are best managed with a combined modality approach, initial surgical resection incorporated with adjuvant postoperative radiation therapy and adjuvant postoperative chemotherapy. The initial treatment for malignant gliomas is resection. There are many Adjuvant Postoperative Radiation Therapy (RT) techniques that have been described in the literature about the adjuvant postoperative radiation therapy. Whole brain RT (WBRT) was first technique that has been initially reported to be effective in the survival for GBM's patients. Focal external beam RT, termed involved field RT (IFRT), has replaced WBRT as the standard approach [13]. The addition of adjuvant WBRT to surgical resection increased median survival from 14 to 36 weeks [14]. Some studies succeeded to show that adequate doses of RT are required to maximize the survival benefit [15].

The effect on survival of maximal resection is uncertain. Although many studies failed to demonstrate a benefit with more extensive surgical resection [16], other reports suggested that maximal resection does lengthen survival [17, 18]. Temozolomide (TMZ): The benefit of adjuvant treatment with TMZ (as combination of TMZ and RT) was demonstrated in a phase

III trial [19]. In this study, patients who whose age is less that less than 50 years old, the five-year survival was 17 percent. Bevacizumab (BV): It is a monoclonal antibody that binds vascular endothelial growth factor (VEGF), which plays a critical role in the development of the abnormal vasculature observed in GBM. In a phase II study, patients who were treated with BV and TMZ during and after RT showed improved progression-free survival (=13.6 months) [20]. The survival benefit was shown unequivocally in a meta-analysis comparing RT alone or with chemotherapy [21]. Chemotherapy was associated with a 15 percent decrease in the risk of death (hazard ratio (HR) 0.85, 95% CI 0.78 to 0.91), which translated to a 6 percent absolute increase in one-year survival (from 40 to 46 percent) and a two-month improvement in median survival.

Reviewing the current literature, we would propose a treatment plan for this patient as follows. This patient shall start with an initial BV in combination with a standard regimen RT with concomitant followed by up to six cycles of adjuvant TMZ [19, 20]. This protocol has

been widely used so far [22]. This could not be assessed because the patient has not yet undergone her chemoradiotherapy.

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