Case Report

Surgical experience with a huge supratentorial primitive neuroectodermal tumour in a 3 years old boy

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Abstract

The concept of Primitive Neuroectodermal Tumor (PNET) has been evolving for many years, since its nomenclature has been done. A 3 years old boy presented with unable to stand and walk, vertigo, vomiting and visual disturbances. MRI of brain revealed suggestive of malignant tumour with intratumoral hemorrhage involving the fronto-temporo-parietal region. A gross total removal of tumor was achieved through craniotomy. The pathological finding was consistent with PNET. This case is an exclusive one as it was huge size. Supratentorial PNETs are rare tumour and carry poor prognosis. Newer modalities of treatment should be tried to improve survival.

Key words: Supratentorial Primitive Neuroectodermal Tumour, Radiotherapy, Chemotherapy.

Introduction

Primitive neuroectodermal tumours (PNET) are the most common malignant tumors of the CNS in children. These lesions account for at least 30% of all childhood brain tumours[1]. They are diagnosed at a younger median age than medulloblastomas; more than 65% of supratentorial PNETs are reported in patients younger than 5 years of age with no significant sex predominance[2.] In one series, primitive neuroectodermal tumors (PNETs) are rare, representing less than 2.5% of childhood brain tumors.[3] However, collectively, supratentorial PNETs are relatively rare, representing approximately one tenth the frequency of medulloblastoma, and 3 to 7% of pediatric CNS tumours.[2]

PNETs are also rapidly growing tumors with a brief duration of symptoms and a rapidly progressive course[2(5)] and frequently metastasize via the CSF pathways to the spinal and cranial subarachnoid spaces and are highly malignant both histologically and clinically[4].

Hart and Earle, in 1973, described primitive neuroectodermal tumours (PNETs) as predominantly undifferentiated tumours with or without glial or neuronal differentiations occurring in the cerebrum of young individuals[5,6]. Subsequently, a number of investigators reported histological and clinical characteristics of PNETs. Tumors resembling each other histologically which are composed of primitive or embryonal neuroepithelial cells can occur in any site in the central nervous system and occasionally in the systemic organs[7,8,9]. PNETs most commonly occur in the cerebellum (medulloblastoms) but can arise in the pineal gland, cerebrum, spinal cord brain stem, and peripheral nerves[4] and also may arise in the basal ganglia, thalamus, or diencephalon. Because these tumors appear

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histologically identical, the treatment of SPNET has been extrapolated from the data on medulloblastoma.[10]. Although they are histologically very similar to medulloblastoma, supratentorial PNETs have markedly different clinical behavior and are generally considered to represent a more aggressive tumor group than medulloblastoma, with a frequently massive tumor burden and a higher incidence of disseminated disease at diagnosis, as reviewed in Jakacki.[2,9]

Several factors contribute to an increased risk of recurrence and poor clinical outcome of PNET e.g. an age less than 3 years the presence of spinal or CSF-metastases, glial differentiation, etc[11]. Thus, despite their smaller numbers, supratentorial PNETs are a significant therapeutic problem because these highly aggressive, therapy-resistant tumors primarily affect younger children, who are the most likely to suffer long-term damage due to radiation[2].

Though Supratentorial PNETs in children have a poor prognosis even after multimodal treatment including surgical resection, chemotherapy and radiotherapy, In the present study, we studied the clinical and histopathological features of PNET, therapeutical difficulties, and perspectives for the future, with reference to a case of unusual sized (huge) supratentorial PNET with the literature review.

Case Summary

A previously healthy 3 years old male child presented with complaints of unable to stand and walk, vertigo, vomiting and visual disturbance for 3 months. According to mother's statement, her child was reasonably well 3 months back. Then the child started facing difficulties in walking and occasional fall during walking. The child could not stand and walk for last one and a half months Patient also had occasional vomiting and visual disturbance for 15 days. Family history was unremarkable. There was no history of sphincteric disturbances, and weight loss.

Physical examination

On admission, vital parameters of the child were normal. The child was alert, oriented but irritated and not co operative. Cranial nerves were intact except the optic nerves. Visual acquity and field of vision could not asses properly due to non cooperation. Fundoscopic examination revealed bilateral papilloedema. Motor system showed weakness of all four limbs (grade IV in right upper and lower limbs and grade III in left upper and lower limbs) with exaggerated deep tendon reflex. Sensory system was intact. Finger-nose and toe-heel tests were normal.

Radiological investigation

Magnetic resonance (MR) imaging demonstrated the tumo to be mixed intensity (iso or hypo) on both T_1- and T_2-weighted images involving the right fronto-temporo-parietal region with midline shift to the opposite side, and not enhanced by intravenous infusion of gadolinium-diethylenetriamine pentaacetic acid (DTPA). No perifocal oedema was noted. The right frontal, temporal, parietal lobes and brainstem were markedly compressed and deformed. No evidence of tumor was detected in any other organ.

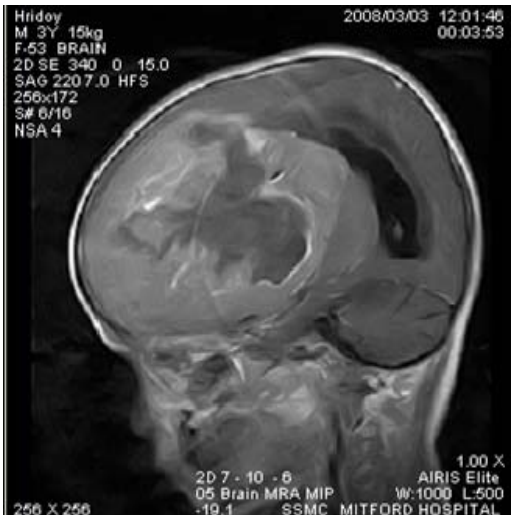

Figure 1

Preoperative MRI of brain

Figure 1 sagittal section and Figure 2 axial section of brain shows mixed intensity, irregular lesion occupying Right Fronto-temporo-parietal region compressing the brain parenchyma and the brain stem and obliterate the lateral and third ventricle. Midline also shifted grossly to the opposite side.

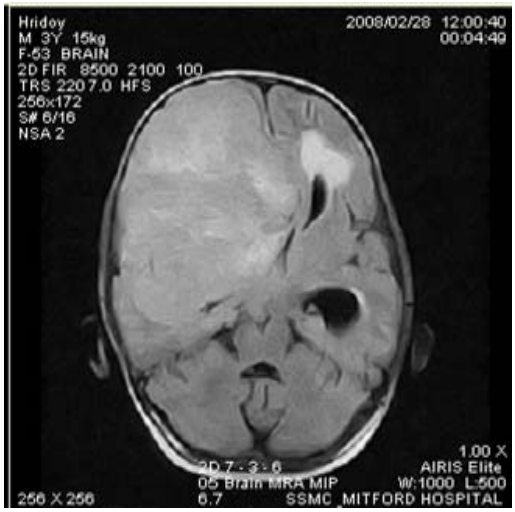

Figure 2

Operation

The patient underwent surgical removal of the tumor via a right fronto-temporal craniotomy. Curvilinear incision was given in the duramater. Tumour was found relatively avascular and suckable. The tumor was readily separated from the temporal, frontal, parietal lobes and brainstem, and was totally removed by piecemeal excision, leaving the arachnoid membrane intact. After ensuring heamostasis, wound was closed in anatomic layers.

Tumor was so huge that the remaining brain collapsed during and after surgery and the bridging veins from brain to superior sagittal sinus were found stretched.

Problems during surgery

1. Collapse of rest of the brain,
2. Bleeding due to large surface area of the exposed brain,
3. Stretching of the bridging veins.

During surgery meticulous approach was adopted to avoid any catastrophe. Tumour removal was done slowly and carefully to save the vital structures like blood vessels and cranial nerves. Patient was given transfusion peroperatively to replace the blood loss. Surgicell and Spongiostan were kept in situ to arrest bleeding from the brain surface and to support the collapse brain and sinuses.

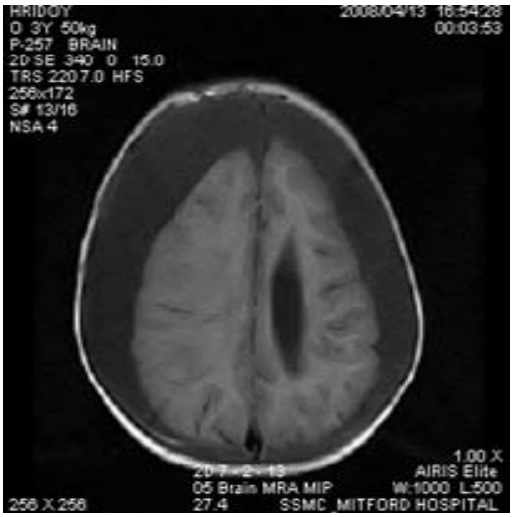

Figure 3

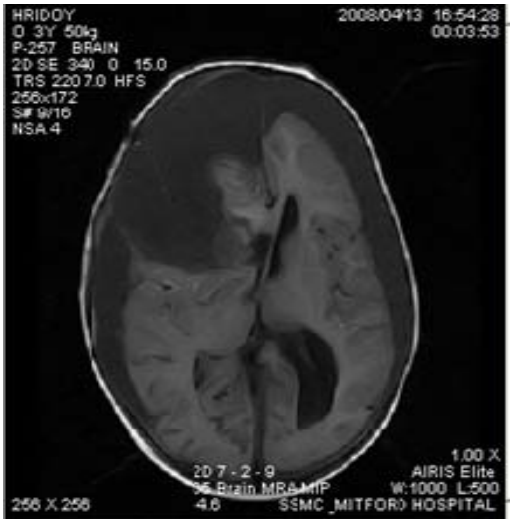

Figure 4

Postoperative course

The patient's postoperative course was uneventful. Magnetic resonance imaging yielded no evidence of a residual tumor mass. Post surgery neurological status showed slightly weakness in four limbs which improved with physiotherapy. A cerebrospinal fluid puncture procedure that was done before and after surgery revealed no evidence of leptomeningeal dissemination. Following surgery, he was asymptomatic, walked unsupported and had no neurological deficits.

Postoperative MRI of brain

Figure 3 showed hypo intense area around the brain parenchyma and Figure 4 showed irregular hypo intense area with the left lateral and third ventricle. No evidence of residual tumour was seen.

Pathological findings

On conventional light microscopy examination, the tumor tissue was found to be composed of small cells containing uniform round nuclei with minimal identifiable cytoplasm. According to histopathological pictures, it was compatible with primitive neuroectodermal tumour.

Discussion

PNET was first described as a tumor arising in peripheral nerve, and was called neuroepithelioma. Hart and Earle first introduced the term primitive neuroectodermal tumour in 1973 to describe predominantly undifferentiated tumours of the cerebrum (with 90-95% of the cells being undifferentiated) that did not fulfill the diagnostic criteria for neuroblastoma, ependymoblastoma, polar spongioblastoma, medulloepithellioma or pineal parenchyma tumours. In 1983, Rorke and Becker and Hinton independently reviewed this concept and published separate articles advocating that all central nervous system tumors predominantly composed of primitive neuroepithelial cells be called PNETs. They then further subclassified these tumours based on differentiation. This concept has been widely accepted, although it is still controversial[4]. In 1993, the World Health Organization (WHO) classification of brain tumors defined all PNETs of central nervous system as PNET, regardless of the location[7]. PNETs are clinically characterized by their aggressive clinical behavior and high incidence of leptomeningeal dissemination.[12]

There are conflicting data on the clinical outcome and prognosis and the impact of genetic lesions in childhood PNET and medulloblastoma and their putative role in tumorigenesis[11].

So far, the standard of care for supratentorial primitive neuroectodermal tumor (stPNET), medulloblastomas, and pineoblastomas in childhood comprises surgery, irradiation, and chemotherapy.[13] In spite of this, local and metastatic recurrences occur in 30–40% of patients, and such recurrences portend a poor prognosis for survival. Additional palliative therapeutic approaches are necessary when standard strategies fail[1].

The outcome of supratentorial PNETs are poor in spite multimodal treatments including surgical resection, radiation therapy and chemotherapy. Hart and Earle reported only one patient survived to 5 years and the remainder (five patients) were dead at an average of 10 months[4]. Kosnik et al reported 15 cerebral PNETs and 40% of the patients were alive at 6 months, only 10% at 1 year and all patients had died within 2 years after diagnosis[6]. Albright et al. reported patients of cerebral PNETs and overall 5 year survival rate was 34%3)[12].

sPNETs in adults and children are similar with regard to the clinical features and prognosis. Type of resection is the major prognostic factor. Presence of systematic

metastasis such as leptomeningeal metastasis and involvement of the lungs and the lymph nodes are poor prognostic factors. Prognosis of sPNETs is generally poor. Mean survival is 24 months in adults although 5-year survival was also reported in a few patients[14].

The current literature contains reports suggesting that metastatic disease, extent of surgery, and age at diagnosis may be of prognostic relevance in supratentorial PNETs. Several retrospective] and prospective studies have consistently reported significantly inferior outcomes for even localized supratentorial PNETs treated with high-risk medulloblastoma therapy. To date, the overall survival rate for supratentorial PNETs is substantially lower than that for medulloblastomas, with an expected 3-year progression-free survival of approximately 50% for localized supratentorial PNETs. These observations suggest intrinsic biological differences between supratentorial PNET and medulloblastoma.[2] According to Ghosh, recent series of low-risk cases with PNET, the 5-year survival rate has been reported to be 60-80% (or even higher)[15].

Over the past decades, survival of children with brain tumors has increased as a result of adding radiotherapy and chemotherapy to initial surgery, as well as optimizing treatment techniques[3].

We report on young children with stPNET of 03 years old boy who was treated by administering intensive postoperative chemotherapy and Radiotherapy (RT). Follow up after 06 month the scan of brain showed no recurrence and the child became near normal.

Supratentorial PNET (st PNET) is known to be more aggressive and is considered high risk regardless of stage. Unfortunately, only a few larger series have been reported because of the rarity of this tumor. RT has to be integrated in the primary treatment regimen after postoperative chemotherapy. Unfortunately, especially in young children, RT is associated with severe late effects. There still is some hope that high dose chemotherapy or new agents will be more effective. To achieve higher rates of complete resections without significant morbidity, surgery should be performed in experienced centers only and, neurosurgical guidelines should be established. Exhaustive documentation on all treatment modalities and late effects has to be carried out in every trial focusing on children.[13]

Conclusion

The optimal therapy for PNET is uncertain. We conclude that future advances in the treatment of PNETs must lie with chemotherapy and immunotherapy especially for those patients presenting with disseminated disease. This, combined with early detection, tumor identification and surgical removal and aggressive neuroaxis radiation, offers hope of long term and good quality survival.

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