



Primitive Neuroectodermal Tumour in Young Adults - A Report of two Rare Cases and Review of Literature

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ABSTRACT

Primitive Neuro Ectodermal Tumours' (PNET) are highly aggressive embryonal tumours of presumed neural crest origin. They are derived from neoplastic transformation of common progenitor cells in the sub ependymal matrix layer. They are more common in children. They are small round cell tumours affecting the central nervous system (CNS), others being Ewing's sarcoma, medulloblastoma, lymphomas etc. They are classified based on their immune histochemical characteristics- neuronal, astrocytic, ependymal, retinal photo receptor, undifferentiated. Undifferentiated variety carries better prognosis. GFAP expression is an important prognostic factor. Presence of p53 germ line mutation indicates an increased risk for developing PNET. Spinal PNET are secondary to CSF metastasis from cranium commonly. Primary spinal PNET tumours are rare and extradural location is extremely rare. PNET needs multimodality approach but carries poor prognosis when compared to other CNS tumours.

Keywords: PNET, Small cell tumors, Immunohistochemistry, GFAP expression, p53 mutation

INTRODUCTION

A group of malignant neoplasms of presumed neural crest origin previously termed as "Neuroepithelioma" were termed as primitive Neuroectodermal tumour (PNET) by Hart and Earl in 1973. They are small round blue tumours which are sub classified based on differentiation and occurs mostly in brain and very rarely in the spinal cord. These tumours are more common in children than in adults. Here we report two cases of primitive Neuroectodermal tumours in young adult females [1,2].

CASE PRESENTATION

Case 1

A 28-year-old female patient presented to the hospital with complaints of neck pain radiating to left upper limb associated with left upper limb weakness for duration of 4 months. She had left sided flaccid weakness and left sided sensory impairment at C5-C7 level. MRI cervical spine revealed an anteriorly placed small extra dural lesion at C6-C7 level with involvement of vertebral body on the left side with extra spinal extension and minimal contrast enhancement. Anterior cervical discectomy and biopsy of extradural granulation tissue was done. Histopathological examination was inconclusive of any definite pathology (Figure 1).

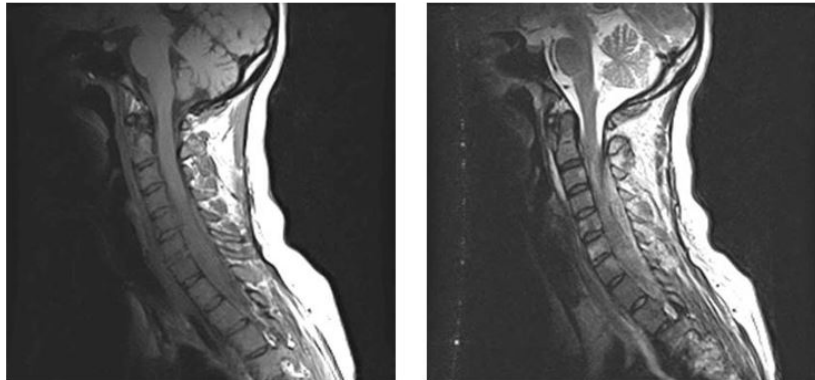


Figure 1 MRI cervical spine minimally contrast enhancing, left sided anterolateral extra dural lesion extending from C2-D1 level with maximum involvement around C4-C6 level with displacement and compression of cord involving the bone

Four months later she presented with torticollis to the right side with pain increasing in severity. On examination she had lower motor neuron weakness at C5-C7 in left upper limb and upper motor neuron weakness right upper limb and both lower limbs. Her erythrocyte sedimentation rate (ESR) was elevated. The ancillary tests done for Myeloma and tuberculosis were negative. Repeat MRI showed a minimally contrast enhancing left sided anterolateral extra dural lesion extending from C2-D1 level with maximum involvement around C4-C6 level with displacement and compression of cord involving the bone.

Left sided C4-C6 hemi laminectomy was done and it revealed a yellowish, fleshy, moderately vascular tumour plastered to the dura, extending to the neural foramina and involving the bone. Microsurgical excision of the tumour was done. Histopathological examination of the mass revealed an infiltrating and necrotic tumour destroying the bone, cartilage, and muscle fibers. The tumour was composed of closely packed small round cells with scant cytoplasm, round nuclei with stippled chromatin, mitosis, and pseudo rosettes. Periodic acid Schiff (PAS) positive globules were seen in the cytoplasm of few of these cells. The cells showed negative Immunohistochemical staining for Leukocyte Common Antigen (LCA) and exhibited strong positivity for CD 99 (Figure 2).

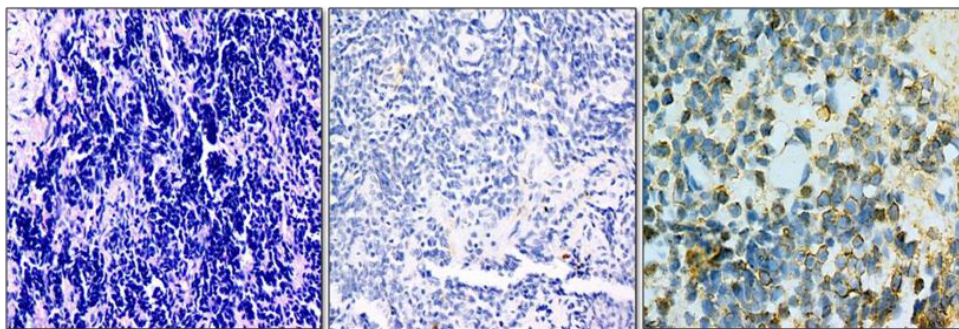


Fig 2 (a)

Fig 2 (b)

Fig 2 (c)

Figure 2 (a) Closely packed small round cells with scant cytoplasm, round nuclei with stippled chromatin, mitosis and pseudo rosettes, H&E, 400X (b) Immunohistochemical staining for Leukocyte Common Antigen (LCA) showing tumour cells are negative (c) Tumour cells expressing strong membrane staining for the immunohistochemical marker CD 99

The patient was referred for radiotherapy and chemotherapy. On follow up, there was significant neurological improvement and no evidence of recurrence after three months.

Case 2

A 21-year-old young female came to the neurosurgery outpatient department with complaints of head ache in occipital region - 2 yrs. She also complained of decreased sensation in the right half of face associated with slurring of speech and decreased taste sensation. She had weakness of left upper & lower limbs and nasal regurgitation of fluids for one

week. She denied history of hearing deficit, double vision, and projectile vomiting. There was no preceding trauma or tuberculosis. On examination, patient's higher mental functions were normal. Bilateral papilloedema was present. She had right sided V, VI, VII, IX and X cranial nerve palsy and left hemiparesis. The cerebellar signs were positive on the right side. The working clinical diagnosis of a right sided cerebello pontine lesion was made.

MRI brain showed a large lesion involving mid brain, pons and upper medulla with extension through cerebellar peduncles. The lesion was hypo intense in T1 weighted image and hyper intense in T2 weighted images (Figure 3).

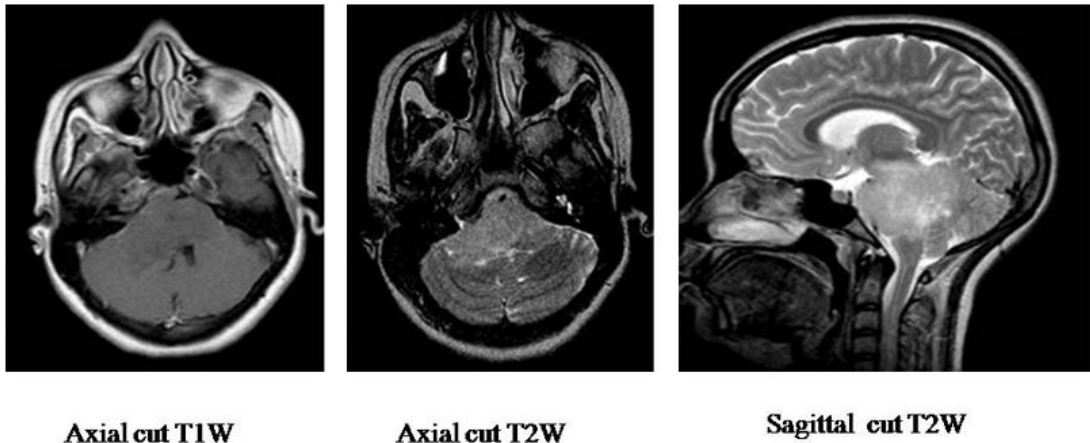


Figure 3 MRI brain showing lesion involving Mid Brain, Pons & upper Medulla with extension through cerebellar peduncles

Through right retro mastoid-retro sigmoid approach the tumour was debulked after placing an external ventricular drain. Per operatively, the lesion was greyish pink, soft to firm in consistency, moderately vascular and seen in relation to pons and medulla, infiltrating into the right-side cerebellum and growing around the cranial nerves.

Histopathology of the lesion showed a highly cellular tumour involving the cerebellum composed of sheets of relatively uniform round to oval cells with scant cytoplasm, hyper chromatic to vesicular nuclei, stippled chromatin, occasional mitotic figures. Perivascular pseudo rosettes and Homer Wright rosettes were seen. Thin walled capillaries devoid of endothelial proliferation, haemorrhage & necrosis were noted in a fibrillary background (Figure 4).

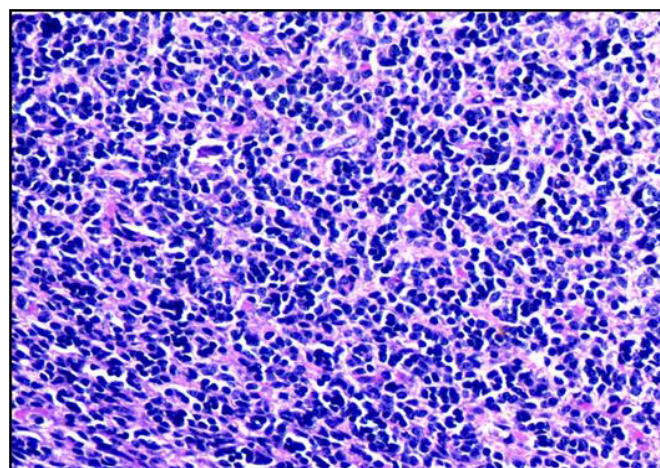


Figure 4 Highly cellular tumour with rosettes in a fibrillary background, (H & E x 400)

Immunohistochemistry using a panel of markers revealed that the tumour cells showed strong membrane staining for CD 99, focally positive for Synaptophysin and negative staining with leukocyte common antigen (LCA). There were many cells showing peri nuclear cytoplasmic staining with Glial fibrillary acidic protein (GFAP) marker. A diagnosis of primitive Neuroectodermal tumour with Neuroglial differentiation was made and patient was referred for chemotherapy (Figure 5).

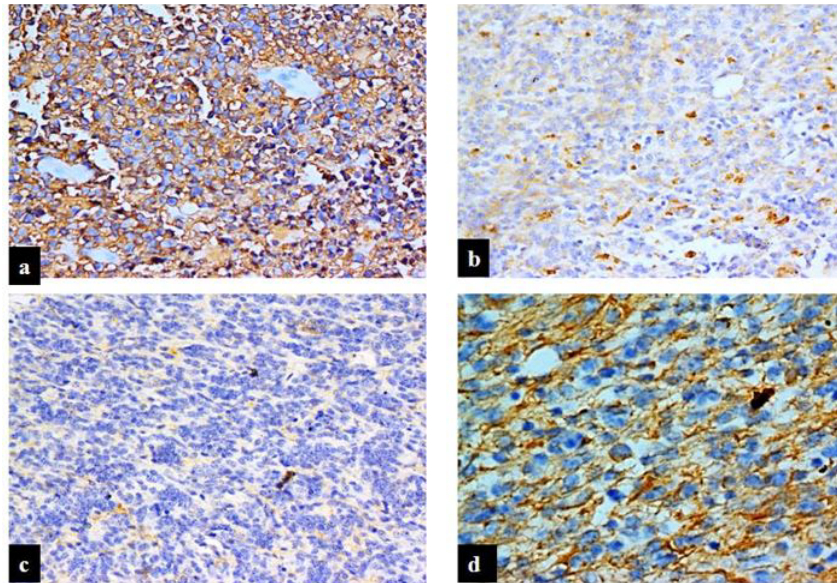


Figure 5 (a) Strong membrane staining with CD 99, (b) Focal positivity with Synaptophysin (c) Negative for Leukocyte common antigen (d) Peri nuclear cytoplasmic staining with Glial fibrillary acidic protein (GFAP)

DISCUSSION

Primitive Neuro Ectodermal Tumour (PNET) are the embryonal neoplasms outside the cerebellum, but morphologically similar to medulloblastomas [3]. These tumours that have chromosomal translocations identical to Ewing's sarcoma. They are highly aggressive embryonal tumours, manifesting preferentially in children. PNETs are derived from neoplastic transformation of common progenitor cells in the sub ependymal matrix layers. They most commonly occur in the cerebellum (medulloblastomas) but can arise in the pineal gland, cerebrum, spinal cord brain stem, and peripheral nerves [4]. Primitive neuroectodermal tumours frequently metastasize via the CSF pathways to the spinal and cranial subarachnoid spaces and are highly malignant both histologically and clinically

These tumours are composed of primitive small round blue cells forming Homer Wright & Peri vascular pseudo rosettes [5]. They have a capacity for divergent differentiation into neuronal, astrocytic, ependymal or retinal photo receptors [6]. Undifferentiated variety of PNETs carries a better prognosis than the differentiated ones. Expression of GFAP in PNETs has prognostic power comparable with the most significant clinical factors currently used to predict clinical outcome [3]. A diagnosis of Primitive Neuro Ectodermal tumour is usually made based on the morphological and immunohistochemical examination. PNETs in children and adults following chemotherapy, including alkylating agents [7] and radiotherapy as treatment for leukaemia or lymphomas have been published. Other risk factors for PNET/EWS include a possible genetic predisposition. Those individuals with Li-Fraumeni syndrome with germline p53 mutations have an increased risk for primitive neuroectodermal tumour.

Spinal PNETs are mostly due to metastasis via CSF pathways from cranial origin. Primary spinal primitive Neuroectodermal tumours are relatively rare [4]. They may be intramedullary, extramedullary or extradural in location. Extradural location is rare; only 4 such cases have been reported. Radical Surgery with combined radiotherapy and chemotherapy is the preferred treatment. In spite of multimodality management, the prognosis is poor. The causes of death in these patients include pneumonia, metastatic disease, aggressive local spread of the disease and progressive spinal cord involvement [2]. Some early reports had suggested that adults with Ewing's sarcoma/PNET have a less favourable outcome than children, but a study of adult patients performed in the Department of Cancer Therapeutics, Institute of Cancer Research, Sutton, United Kingdom [8] has suggested that adults may have a similar outcome to children.

CONCLUSION

Primitive neuroectodermal tumours are rare but have a highly aggressive clinical course with a poor outcome in spite of multimodality treatment options [5]. PNETs in adults are extra ordinarily rare. Histopathological,

immunohistochemical and molecular studies are important for correct diagnosis. Our case 1 was a primary extra dural spinal primitive neuroectodermal tumour which has been rarely reported in the literature. So spinal PNET has to be thought of as a differential diagnosis for any spinal lesion with rapidly progressive course [9]. Our case 2 was a primitive neuroectodermal tumour with neuroglial differentiation which imparts a poor prognosis. This case report emphasizes the many faces of this aggressive tumour and the need for research towards a better theragnostic approach [10,11].

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