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Case Report

Primitive Neuroectodermal Tumour (PNET) With Divergent Differentiation In Frontal Lobe

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Abstract

Primitive neuroectodermal tumors (PNETs) of brain are childhood tumours which are frequently located in cerebellum. Supratentorial PNETs are uncommon. These tumors are composed of undifferentiated or poorly differentiated cells of neuroectodermal origin, with the capacity for differentiation along neuronal, astrocytic, ependymal, and melanocytic cell lines. PNET with divergent differentiation in frontal lobe of brain is a rare phenomenon. A case of 6 years old female child having PNET with divergent differentiation (ependymal and neuroblastomal differentiation) in frontal lobe of brain is reported.

Key words: Primitive neuroectodermal tumor (PNET), divergent differentiation, frontal lobe of brain.

Introduction

Primitive neuroectodermal tumors (PNETs) are malignant tumors composed of small round cells that affect soft tissues and bone.

CNS PNET is a brain tumor composed of undifferentiated or poorly differentiated cells of neuroectodermal origin, that may differentiate along neuronal, astrocytic, ependymal and melanocytic cell lines. They are common in children, and rare in adults.[1] Infratentorial PNETs (medulloblastomas) are common. Supratentorial PNETs are very rare.

Children present with signs and symptoms of raised intracranial pressure (headache, vomiting), localizing signs(motor and sensory loss) and non-localizing signs(behavioral change)

Diagnostic modalities include biopsy and imagingstudies.Immunohistochemistry confirms the diagnosis.Radiographic diagnostic clue is the presence of a mass with minimal peri-tumor edema. On CT scan, these lesions appear isodense or hyperdense. On MRI, these tumors appear inhomogeneous and variably contrast enhanced lesions. Furthermore, they appear hypo intense on T1 weighted images, hyper intense on T2 weighted images.

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CNS-PNET can show positivity for synaptophysin, GFAP and occasionally dot-like cytoplasmic EMA, according to differentiation.[2] There is total negativity for CD99 in contrast to the peripheral type PNET tumors.[3]

Supratentorial PNET express two neurogenic transcription factors i.e. NeuroD family and HASHI.[4,5,6]

Children with supratentorial PNET have a worse overall 5 year survival.[7]

Supratentorial PNET with divergent differerntiation has very limited data in the literature.

According to our knowledge, there is no report on a supratentorial PNET with divergent differentiation in frontal lobe of brain.

In this case, we report a patient with supratentorial PNET in frontal lobe of brain, showing ependymal and neuroblastomal differentiation.

Case Report

A 6 years old female child presented with fits for last 2 years, associated with behavioral changes, vomiting and headache.

Neurological examination showed a GCS of 15/15. MRI brain was done and it showed bifrontal tumour.

The patient underwent craniotomy and surgical removal of lesion was done.The tissue was sent for histopathology.

Gross examination: Multiple white soft brain tissue fragments (4x3x1 cm each) were received in formalin. Entire substance was submitted. Slides were processed and stained with routine hematoxylin and eosin stain. Slides were examined by the resident and Histopathologist.

Microscopic Examination: Sections revealed fragments showing malignant neoplasm composed of sheets of round blue cells , having indistinct cytoplasm ,high N/C ratio , and pleomorphic nuclei showing irregular chromatin (Figure 1).

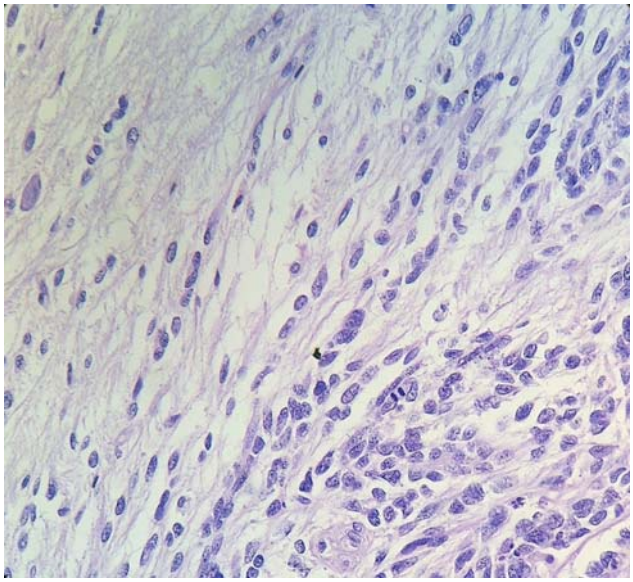

Figure 1: Photomicrograph (hematoxylin-eosin stain , x400) showing small round blue tumor cells with round to oval hyperchromatic nuclei and scant cytoplasm with distinct outline.

Foci show ependymal and neuroblastic differentiation at places.

Tumour cells form Homer-Wright rosettes (Figure 2 and 3) as well as Flexner-Winteresteiner rosettes at places (Figure 4 and 5). Scattered mitotic figures with areas of calcification and necrosis are seen.

On the basis of these findings, final diagnosis of PNET with ependymal and neuroblastic differentiation was made.

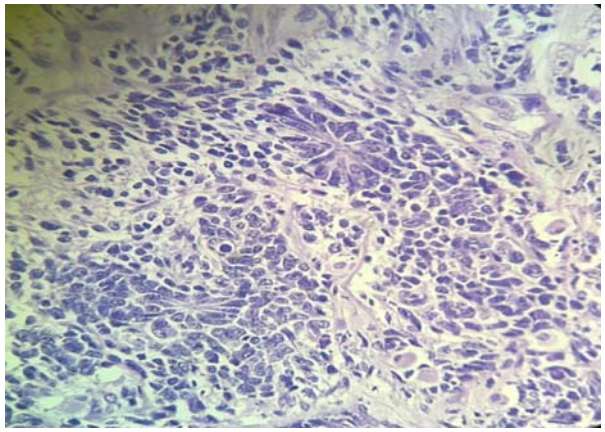

Figure 2: Photomicrograph showing Homer Wright rosette (hemotoxylin-eosinstain,x400).

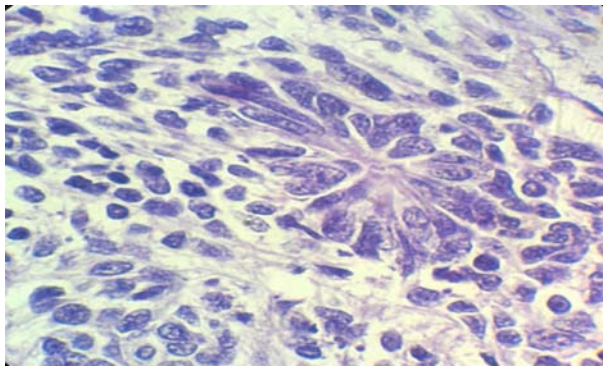

Figure 3: Homer Wright rosette(hemotoxylin-eosinstain,x1000).Tumour cells surround a central region containing neuropil

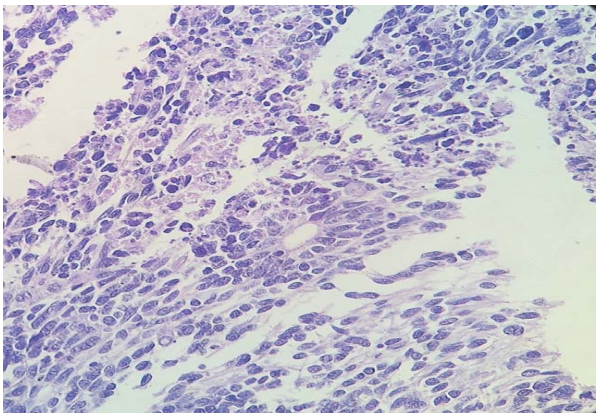

Figure 4: Photomicrograph showingFlexner-Wintersteiner rosette(hematoxylin-eosin stain , x400).

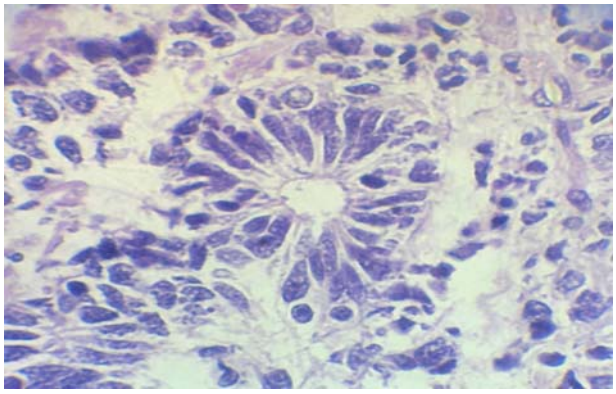

Figure 5 : Flexner-Wintersteiner rosette(hematoxylin-eosin stain ,x1000). Tumour cells surround a central lumen that contains cytoplasmic extensions of tumour cells

Histopathology Diagnosis: Small round blue cell tumor. Immunohistochemistry:Tumour cells were positive for synaptophysin (Figure 6) and GFAP (Figure 7); and negative for chromogranin and EMA.

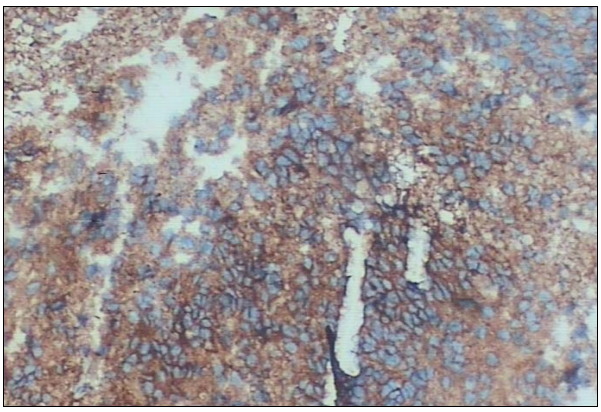

Figure 6: Photomicrograph of Immunohistochemical stain showing positivity for synaptophysin

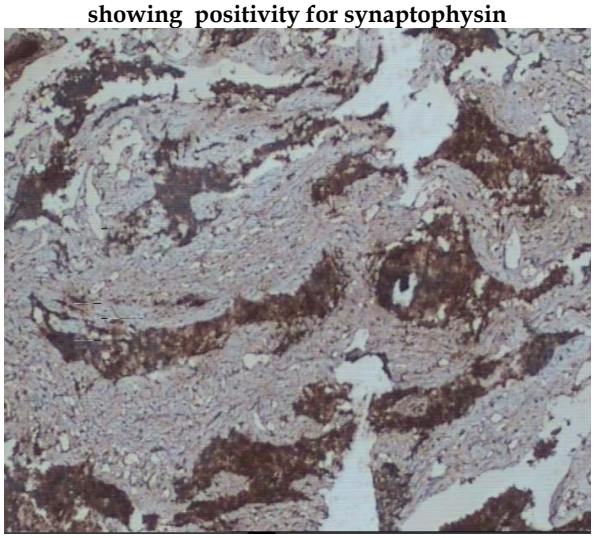

Figure 7 :Photomicrograph of Immunohistochemical stain showing positivity for GFAP

Discussion

The term PNET was introduced in 1973 by Hart and Earl, for describing supratentorial, pediatric brain tumors that were highly undifferentiated or primitive but contained small foci of glial or neuroblastic differentiated cells of primitive neuroectodermal origin.[8]

CNS-PNETs include neuroblastomas, ganglioneuroblastomas, medulloepitheliomas, ependymoblastomas, embryonal tumors with abundant neuropil and true rosettes, and not otherwise specified PNET tumors.[9]

They primarily occur in children,[10,11,12] ranging between the ages of 4 weeks to 10 years, with a mean of 5.5 years.[13]

On macroscopic examination, PNETs usually appear as lobulated, purple grayish or pinkish masses.

On histology, the tumor has undifferentiated small cells with scanty cytoplasm, and round or oval cells with hyperchromatic nuclei.[1,9] Mitotic activity is variable. Microscopic calcifications, necrosis and Homer Wright rosettes are also observed.

The vascularity of the tumors varies, whereas endothelial cell proliferation within the vessel wall is regularly observed.[1,9,14] Divergent differentiation in cells is most reliably identified by use of various antibodies such as GFAP, neurofilament protein and desmin.[13]

Newer genetic analysis studies have demonstrated that PNETs are characterized by MYCN or MYCC gene amplifications and polysomies of chromosomes 2 and 8.[1]

MYCN or MYCC gene amplifications and polysomies of chromosomes 2 and 8 have been individually associated with decreased survival in children, and the combined presence appears to be an even more unfavorable prognostic factor.[1]

Chromosomal translocation of chromosome (11;22) is unique to central and not peripheral PNETs.

There is total negativity for CD99 in contrast to the peripheral type PNET tumors.[3]

Conclusion

It is rare to encounter PNET with divergent differentiation in frontal lobe of brain.

We report a case of PNET with divergent differentiation in frontal lobe of a 6 years old female child, and propose that supratentorial primitive neuroectodermal tumours should be considered in differential diagnosis of space occupying lesions in frontal lobe of brain.

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