

An Interesting Case of Spinal Primary Peripheral Primitive Neuroectodermal Tumor: Rarest of the Rare

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ABSTRACT

Primitive neuroectodermal tumors (PNETs) are fast-growing undifferentiated tumors that share a common cell of origin. Primitive neuroectodermal tumors constitute less than 1% of all primary spinal tumors. They are further classified into central and peripheral types. Peripheral PNETs are considered to belong to Ewing's sarcoma family of tumors. After the advent of immunohistochemistry and cytogenetic analysis, differentiating central and peripheral PNETs becomes possible. We are reporting the second case of extradural peripheral PNET occurring in the cervical spine after Pinelopi et al. Though rare, primary PNET should be considered as differentials in an adult patient presenting with a spinal mass lesion. Surgical excision followed by chemoradiation is the treatment of choice with 5 years survival of about 50%.

Keywords: Ewing's sarcoma, Extradural, Primitive neuroectodermal tumor.

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INTRODUCTION

Primitive neuroectodermal tumors (PNETs) are fast-growing undifferentiated tumors that share a common cell of origin according to the World Health Organization (WHO) classification of brain tumors.¹ Primary PNETs occurring in the spinal canal are very rare. According to a study by Engelhard et al,² PNETs constitute less than 1% of all primary spinal tumors. They are further classified into central and peripheral. Of all the spinal primary PNETs, peripheral PNETs constitute less than 25% of tumors.³ Both the types of spinal PNETs can occur extradurally, extramedullary, or intramedullary,⁴ of which extradural location is still more rare constituting less than 25% of peripheral PNETs. Though there are

several reports of spinal PNETs available in the literature since 1969, only after early 2000s, after the advent of immunohistochemistry and cytogenetic analysis, differentiating central and peripheral PNETs becomes possible. We are reporting the second case of extradural peripheral PNET occurring in the cervical spine after Pinelopi et al.⁵

CASE REPORT

An 18-year-old girl was admitted with complaints of neck pain radiating to left upper limb of 2 weeks duration. She also gave H/O painful neck movements. On examination she had shoulder abduction weakness of grade 4 power, sensory blunting along C4-5 on the left side. Examination of the lower-limb power was normal. All reflexes were exaggerated with plantar-flexor. There was no evidence of neurocutaneous markers. Patient underwent magnetic resonance imaging (MRI), which revealed T1 hypointense, T2 heterointense lesion with peripheral hypointensity and central mild hyperintensity in the cervical spine at C3-4 level in extradural space located anterior to the cord and extending bilaterally more toward the left side. C4 body showed signal changes. The lesion was enhancing well with the contrast (Figs 1A to D).

SURGERY

With the clinical diagnosis of Pott's spine with extradural abscess, patient underwent C4 corpectomy with excision of the lesion and spacer and plating (Fig. 2). Intraoperatively, the lesion was firm, well-encapsulated, moderately vascular, and total excision was achieved in piecemeal manner. No pus was seen.

POSTOPERATIVE

Patient was extubated on the table, and no fresh neurologic deficit. Patient was mobilized the next day and was able to walk without any support with normal bladder bowel function.

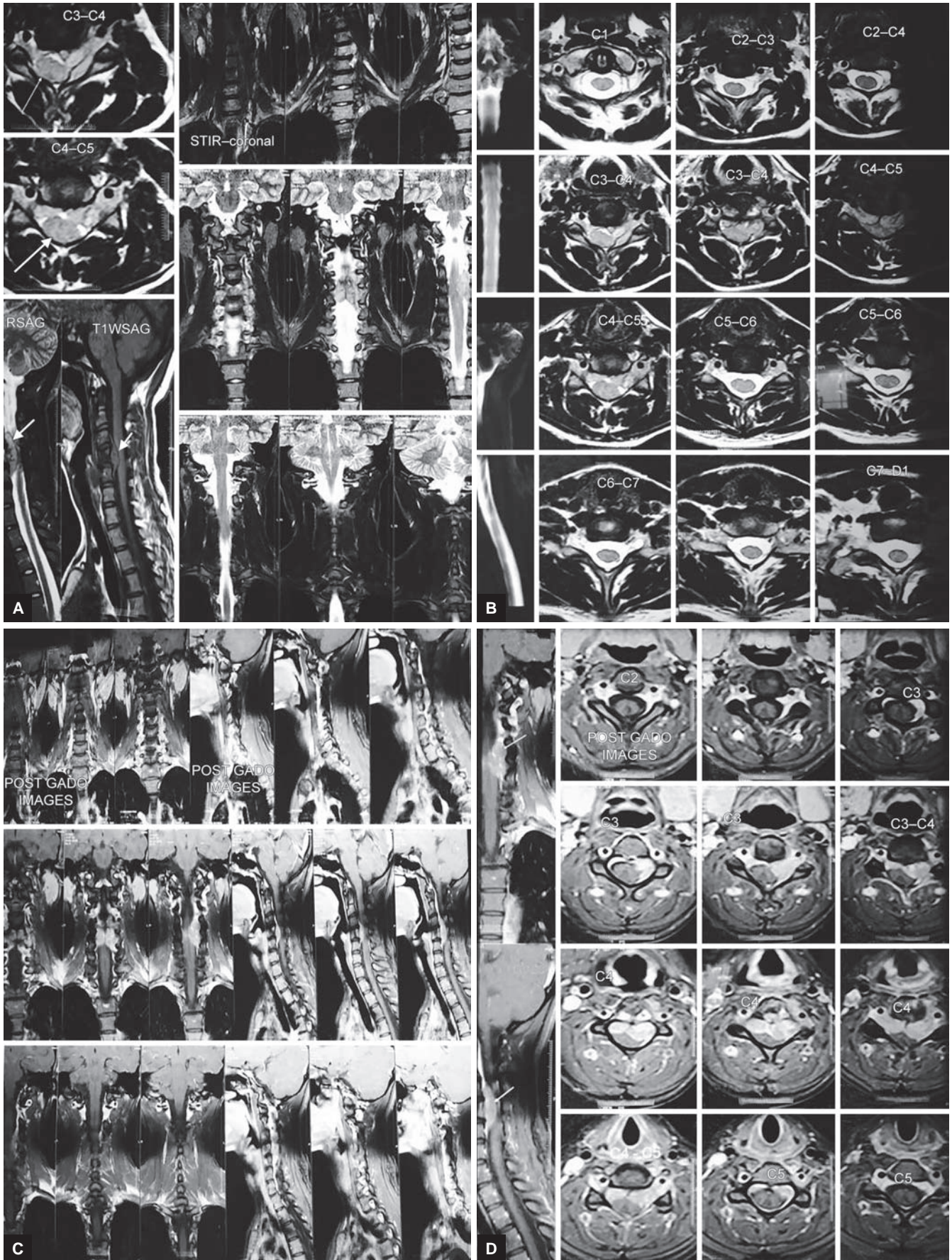
PATHOLOGY

Histopathologic examination revealed tumor with small, round cells with hyperchromatic nuclei, inconspicuous nucleoli, and scant cytoplasm arranged in

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Figs 1A to D: (A) Magnetic resonance imaging plain showing T1 iso, T2 heterointense lesion at C4, C5 level located anterior to the cord; (B) MRI T2 axial section showing anterior location of the lesion with myelogram showing typical brush border appearance; (C) MRI T1 contrast showing homogenous contrast enhancement; and (D) MRI T1 contrast axial section shows the extent of the lesion anterior to the cord

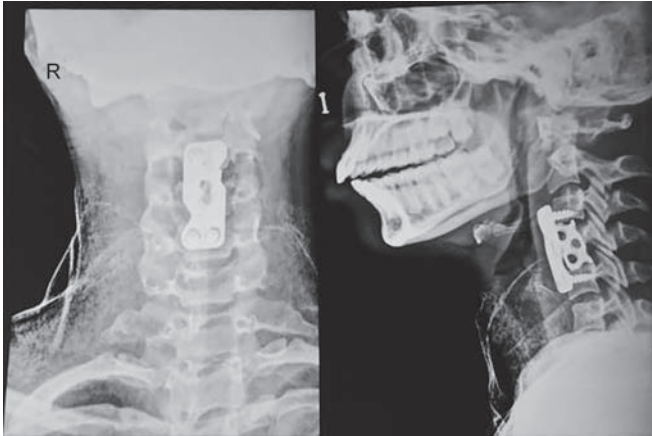


Fig. 2: Postoperative digital X-ray showing spacer and plating in position

sheets, pseudopapillae and pseudorosettes (Figs 3 and 4) with foamy histiocytes consistent with PNET. Immunohistochemistry showed strongly positive CD 99, vimentin, Friend leukemia integration-1 positivity, negative for cytokeratin, leukocyte common antigen, Desmin, Synaptophysin, CD 56, and Terminal deoxynucleotidyl transferase (TDT), suggestive of peripheral PNET.

METASTATIC WORKUP

Positron emission tomography scan was done, which showed physiological increased metabolic activity in the postoperative site and uterus (Fig. 5). Computed tomography brain was done and intracranial mass lesions ruled out.

ADJUVANT THERAPY

Patient was referred to oncology department for chemotherapy. Patient is currently undergoing chemotherapy with vincristine, cisplatin, and cyclophosphamide and planned for craniospinal irradiation.

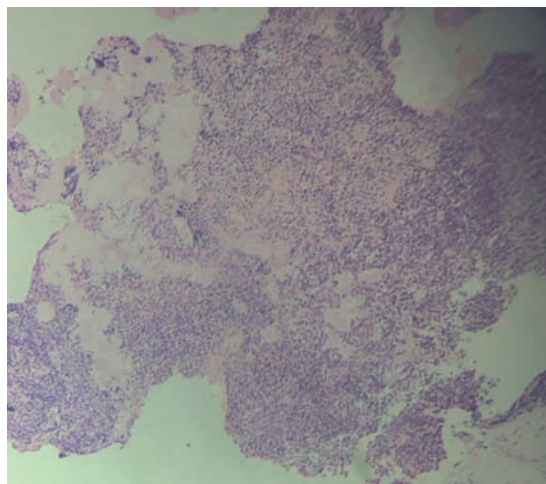


Fig. 3: Low power field shows small, round cells arranged in sheets

DISCUSSION

All PNETs arise from common neuroepithelial cells. They are further classified into central PNET (cPNET) and peripheral PNET (pPNET)⁶ based on their embryological origin. Moreover, PNETs have a male preponderance and are more common in 1st and 2nd decade. Central PNET arises from subependymal germ-cell matrix and are seen within the central nervous system (CNS), whereas peripheral PNET arises from neural crest cells⁷ and is seen outside the CNS. Differentiation of central and peripheral PNET is particularly important and difficult when they occur in meninges and spinal canal due to the overlapping of central and peripheral nervous system.^{8,9} Central PNET commonly spreads through cerebrospinal fluid and rarely metastasizes outside CNS and pPNET frequently metastasizes outside CNS and may involve bone, lung, lymph nodes, and liver.³ Thus central and peripheral PNETs are differentiated only by immunochemical and genetic studies and not merely by location. Both central and peripheral PNETs are aggressive tumors with similar survival rates. However, they differ in the way they clinically present, their spread pattern, treatment protocols, immunohistochemical profiles, and genetic structure.⁸ Thus differentiating these two is important for tailoring treatment protocols.

DIAGNOSIS

Immunohistochemistry and fluorescent *in situ* hybridization (FISH) techniques are particularly important in differentiating central and peripheral PNETs. Peripheral PNETs strongly expresses CD 99 in immunohistochemical studies; at the same time, negative for synaptophysin or glial fibrillary acidic protein. They have a high MIB-1 (Ki 67) proliferation index

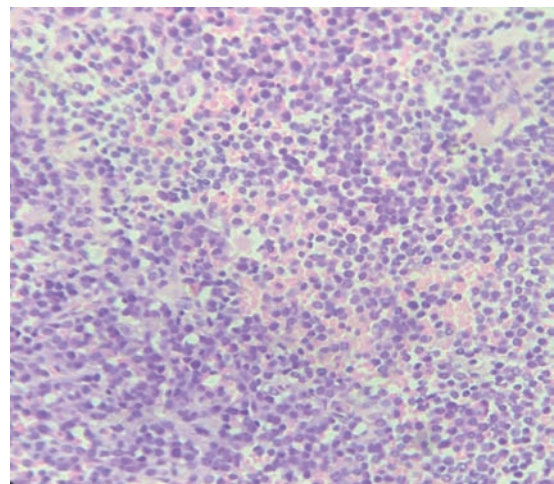


Fig. 4: High power field shows round cells with hyperchromatic nuclei with scanty cytoplasm

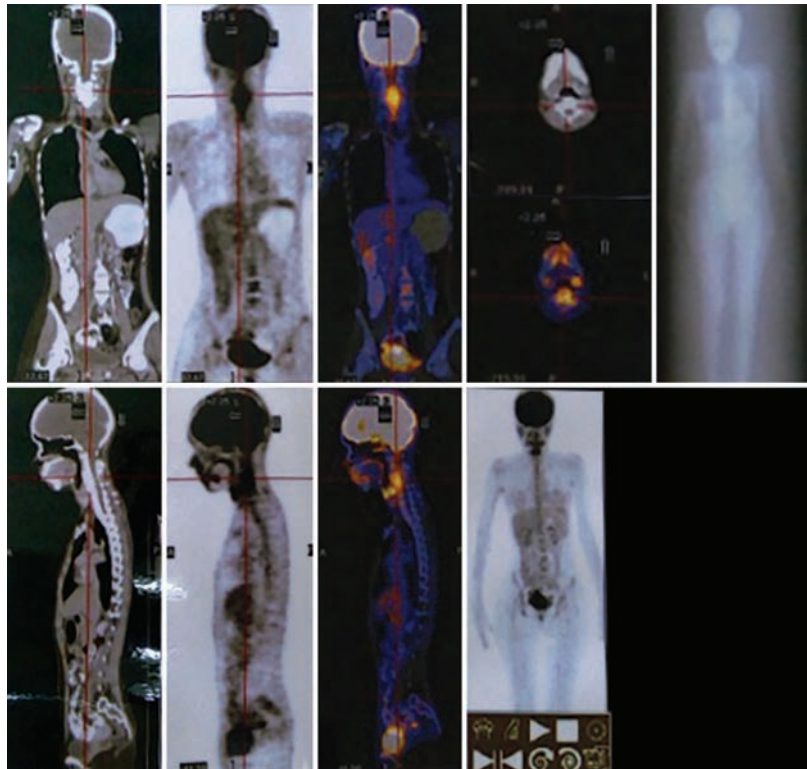


Fig. 5: The PET CT scan showing physiological increased uptake at postoperative site and endometrium

of 20 to 30%. The FISH analysis identified reciprocal translocation between chromosomes 11 and 22 {t(11;22)(q24;q12)}. In contrast, cPNETs lack CD99 expression and the cytogenetics revealed normal chromosomal arrangement.

TREATMENT

Treatment is multimodal involving surgical removal followed by adjuvant chemotherapy and radiation therapy. Surgery is the mainstay of treatment in reducing the tumor bulk decompression of the cord and establishing tissue diagnosis.^{10,11} So, PNETs are both chemosensitive and radiosensitive tumors; hence they form the major adjuvant therapy.¹² The most commonly used chemotherapeutic drugs are vincristine, adriamycin, cyclophosphamide, ifosfamide, and actinomycin-D, and their combination called VAIA regimen.¹³⁻¹⁵ Radiation therapy is another important modality of treatment for PNETs, particularly in patients where complete excision is not possible. Postoperative radiation therapy targeting the entire neuraxis with doses up to 50 Gy is usually considered to achieve local control and also reducing the risk of distant metastasis.^{4,12} The results of various studies are promising and raising hopes on the use of autologous stem cell rescue concurrent to surgery and radiation therapy.¹⁶

FUTURE TREATMENT OPTIONS

Adoptive Immunotherapy

Adoptive immunotherapy is being investigated widely as a possible therapy for PNETs. Lymphokine-activated killer cells are the most preferred cells as it possesses various attributes that would render them useful in adoptive immunotherapy. They are highly potent against cancerous cells, does not require prior antigen exposure to initiate its oncolytic property. These lymphokine killer cells can differentiate normal cells from malignant cells and thereby expresses its oncolytic activity only against the tumor tissues and sparing normal cells.¹⁰ Musahl et al¹⁰ designed a study to assess the potential sensitivity of the tumor cells derived from PNETs. The results were rewarding and favors adoptive immunotherapeutic approach as an adjunct in the management of PNETs. The study recommends intrathecal administration of IL-2 and LAK cells as an adjuvant to the treatment of PNET. This form of therapy not only eradicates residual tumor but also avoids the harmful side effects of radiation and chemotherapy.

Peripheral Blood Stem Cell Transfusion

The role of peripheral blood stem cell transfusion (PBSCT) is also studied in PNETs. They are primarily advocated for chemosensitive tumors or in patients who had remissions. The PBSCT use after remissions helps

in preventing relapse. In a trial, PBSCT was employed in 21-year-old male with PNET of chest wall stage-IV. More studies are required to explore the role of PBSCT in controlling the disease, stopping the progression and improving the survival in these group of patients.

CONCLUSION

As PNETs affect younger population and are more aggressive in nature, high index of suspicion is necessary for diagnosis. There is a need for research to support the use of newer adjuvant therapies in the management of these aggressive tumors to improve the longevity of these patients.

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