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Peripheral primitive neuroectodermal tumor of the upper limb: A case report and review of literature

Sarah Afzal[1]*, Alen Thomas[1], Osamah Rahman Khan[2]

[1]Max Superspeciality Hospital, Shalimarbagh, Delhi, India.
[2]Holy Family Hospital, Okhla Delhi, India.

Email: Sarahafzalkhan@gmail.com

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Abstract

Peripheral Primitive Neuroectodermal Tumors (pPNET) are rare malignant tumors characterized by small round cells of neuroectodermal origin. They usually occur between the age of 6-25 years, mostly in soft tissues or bones and belong to the Ewing Sarcoma Family of Tumors (ESFT). We report an unusual case of pPNET of the upper extremity in a 24-year-old male. The purpose of reporting this case is it being a rare diagnosis which demands early detection and treatment as the presence or absence of metastasis is the most significant prognostic factor.

Introduction

Peripheral primitive neuroectodermal tumors (pPNETs) are a rare and highly malignant group of tumors composed of small, round neuroectodermal cells. They belong to the Ewing sarcoma family of tumors (ESFTs),[1] which share common genetic alterations and similar pathological features. pPNETs primarily arise in soft tissues but can also involve bone, distinguishing them from Ewing sarcoma, which predominantly affects osseous structures. These tumors exhibit aggressive clinical behavior and are often grouped with other small, round cell tumors due to overlapping histological features. Advances in molecular cytogenetics, particularly the identification of characteristic translocations like the (11;22), have been pivotal in distinguishing pPNETs from other poorly differentiated neoplasms.

Historically described in 1918, pPNETs were initially thought to arise from nerves.[2] Subsequent classifications have divided primitive neuroectodermal tumors (PNETs) into three subtypes based on their tissue of origin;[3]

1. Central nervous system (CNS) PNETs[4]
2. Neuroblastomas of the autonomic nervous system, and
3. Peripheral PNETs (pPNETs) arising outside these systems.

The broader ESFT group, which includes pPNETs, encompasses entities such as:

1. Ewing sarcoma (osseous and extraosseous forms)[5-6]

2. Askin tumors (peripheral neuroepithelioma of the thoracopulmonary region)[7]
3. Other neuroectodermal malignancies[8]

Although exceedingly rare, pPNETs are most commonly diagnosed in adolescents, with a slight male predominance and significant racial variability. These tumors frequently present in the thoracopulmonary region.[9], pelvis, abdomen, and extremities, with head and neck involvement being less common. [10-12]

Prognosis depends on factors such as tumor location, size, stage, and presence of metastases. Metastases are common at diagnosis, particularly to the lungs, bones, and bone marrow, contributing to poor survival outcomes. Reported long-term survival rates remain low, particularly in cases with metastatic disease.

Recent studies utilizing data from large registries have highlighted that tumor location, age at diagnosis, and racial disparities significantly impact survival. Additionally, patients with extraosseous tumors often face worse outcomes than those with osseous forms. These findings underscore the need for improved diagnostic precision and targeted therapeutic approaches for this aggressive and heterogeneous tumor group.

Recent analyses from large-scale registries, such as the Surveillance, Epidemiology, and End Results (SEER) database,[13], have identified additional factors affecting outcomes, including tumor size, axial versus appendicular location, and treatment modalities such as surgery. Patients with extraosseous pPNETs generally fare worse than those with osseous tumors. Racial and age-related disparities further impact survival, with younger patients and non-white populations exhibiting poorer outcomes. These findings underscore the urgent need for enhanced diagnostic precision, equitable treatment access, and the development of targeted therapies to address the challenges associated with this aggressive and heterogeneous group of tumors.

Case description

A 24-year-old male presented with swelling originating from the little finger of left hand and progressing to a size of about 13x11cm within a period of less than a month as per history (Figure 1). At the time of presentation, it was confused with a vascular swelling because of its firm consistency. Local examination revealed a firm, irregular mass involving the little and ring fingers (Figure 2). Other systemic examinations revealed no significant abnormalities. Plain X-ray of the left hand showed large soft tissue lesions with irregular contour involving the interdigital and web space of little and ring fingers and MRI findings included increased signal intensity on T2 and intense homogenous enhancement on post contrast. Significant vascularity was noted within the lesion on ultrasonography. Before excision was planned further investigations were done to rule out the metastasis and confirm the operability of the swelling. FNAC of the lesion suggested features of small round cell tumor. After thorough investigations, surgery was done and the mass along with the medial three fingers were excised with primary closure of the wound and excised tissue was sent for histopathological and cytological examination. (Figure 3) Subsequently, the patient received four cycles of multi-agent chemotherapy using the BEP regimen (Bleomycin, Cisplatin, and Etoposide). Gross appearance of the cut surface of tumor showed bony and tendinous connective tissue with areas of haemorrhage and necrosis. (Figure 4) H&E staining revealed sheets of small round blue cells with

hyperchromatic nuclei separated by fibrovascular stroma consistent with pPNET/ Ewing sarcoma. (Figure 5) Immunohistochemical profile with positive immunoreactivity for CD99 distinguished the PNET from other small round cell tumors. (Figure 6) Recurrence/metastasis cannot be commented upon as unfortunately, the patient was lost to follow up.

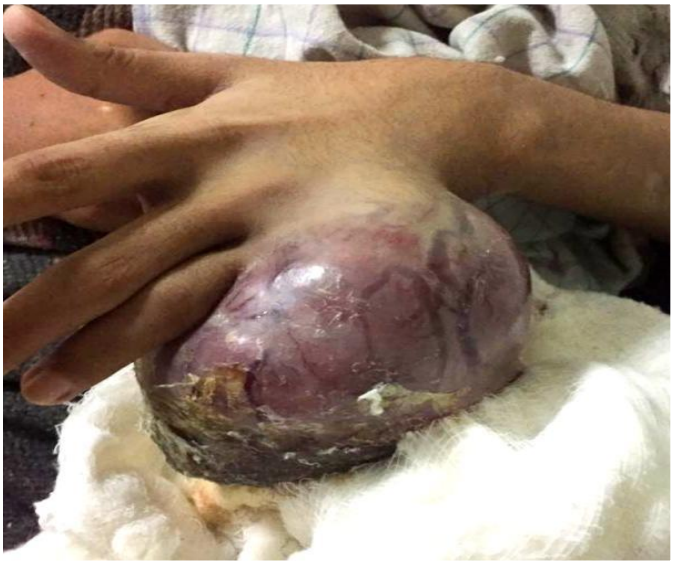

Figure 1: A swelling originating from the little finger of the left hand and progressing to a size of about 13x11 cm within a month.

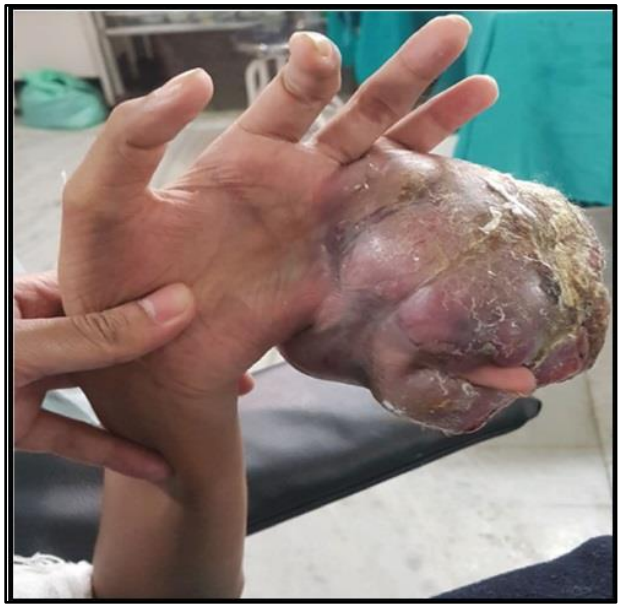

Figure 2: Local examination revealed a firm, irregular mass involving the little and ring fingers and had significant vascularity.

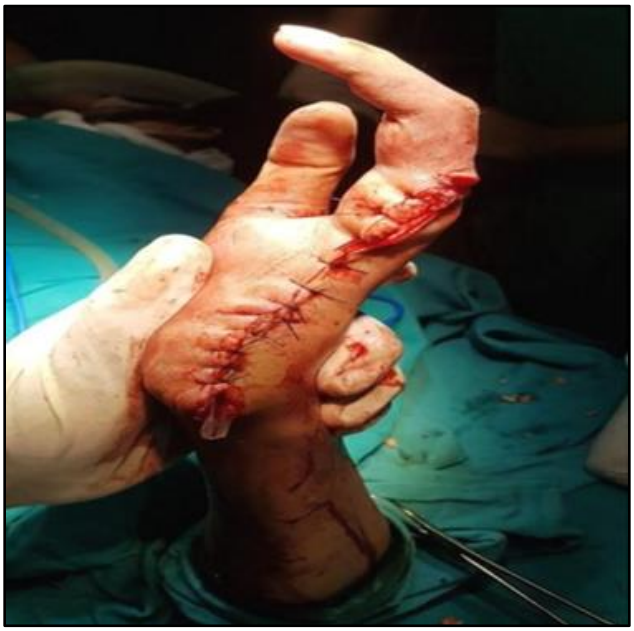

Figure 3: Mass along with the medial three fingers were excised with primary closure of the wound.

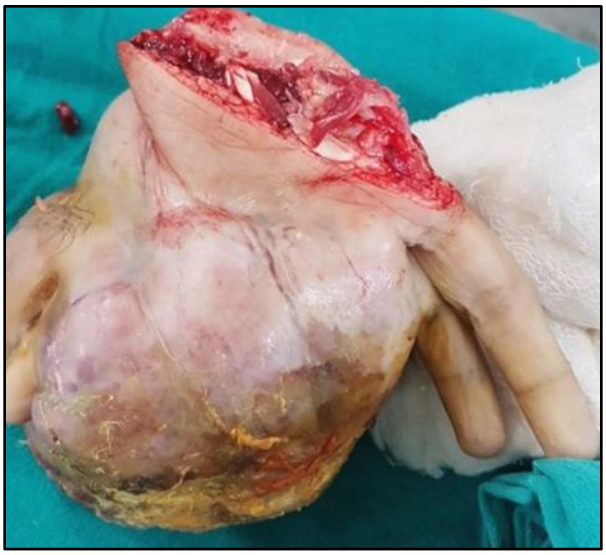

Figure 4: Gross appearance of the cut surface of tumor showed bony and tendinous connective tissue with areas of haemorrhage and necrosis.

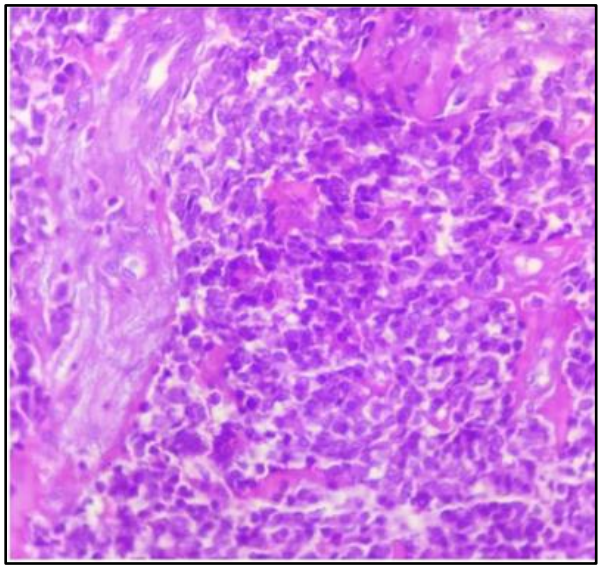

Figure 5: H&E staining revealed sheets of small round blue cells with hyperchromatic nuclei separated by fibro vascular stroma consistent with pPNET/ Ewing sarcoma.

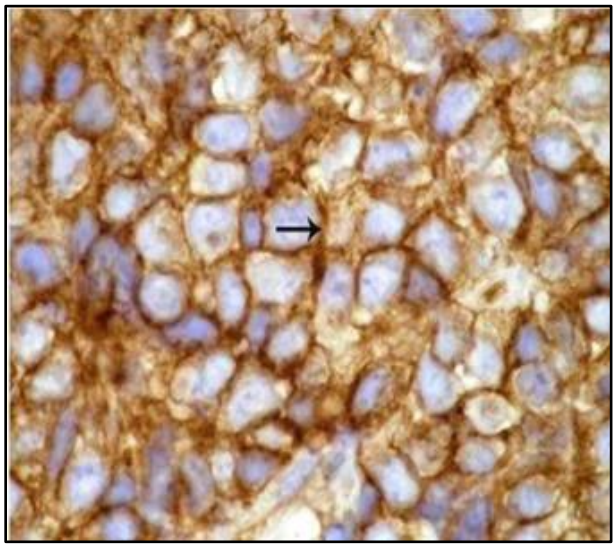

Figure 6: Immunohistochemical profile with positive immunoreactivity for CD99 distinguished the PNET from other small round cell tumors.

Discussion

The PNETs are aggressive tumors with almost inevitable recurrence and metastasis. These tumors share similar histology, immunohistology, and cytogenetics with Ewing's sarcoma so have been grouped into Ewing Sarcoma Family of Tumors (ESFT). Ewing sarcoma is the second most common malignant bone tumor in children, while the pPNET accounts for only about 4% of all soft tissue tumors.[14] Peripheral PNETS (pPNETs) typically occur in children or young adults, with a slight predilection in males.[15] The common sites involved are soft tissue of chest wall, abdomen, pelvis and the extremities.[16] Recent diagnostic advances including cytogenetic and immunohistochemically analysis have allowed these tumors to be distinguished from other small poorly differentiated round cell tumors such as Ewing Sarcoma, rhabdomyosarcoma, lymphoma and synovial sarcoma.[17] On immunohistochemical staining, over 90% of PPNETs are positive for CD 99 and FLI-1. Ninety-five percent of pPNETs express a characteristic translocation involving the EWSRI gene on chromosome 22.[18] A review of the literature revealed that primary PNET of the upper extremity is very rare and occurs predominantly in children and adolescents. Patients generally present with rapidly enlarging masses and symptoms related to tumor mass effects.[17] These tumors lack clinical and radiographic specificity. Thus, to confirm the diagnosis, histopathology and immunohistochemistry analysis are mandatory. Currently, the standard treatment of pPNET is complete surgical resection with an adequate margin with systemic chemotherapy and/or radiotherapy.[18] CT/MRI is useful in delineating distant metastasis, extent and resectability of the tumor and in monitoring the treatment.

Conclusion

PPNET of the extremities is a rare malignancy with only a handful of cases described in adult patients. Due to limited evidence regarding the therapeutic aspects of these tumors, no definite protocol has been formulated for their treatment, but resection, radiotherapy, and multipotent chemotherapy are the preferred treatment options. Clinical outcomes still need to be evaluated in prospective trial

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Conflict of Interest

None.

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