Case Report

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# Axillary lesion in a young adult ends up to a peculiar diagnosis: primitive neuro-ectodermal tumor (PNET) of ulnar nerve: a rare case report

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**Introduction and importance:** Primitive neuro-ectodermal tumor (PNET) is a highly aggressive tumor composed of small round blue cells, mostly developing in children and young adults. Being a member of Ewing's Sarcoma Family of Tumors (ESFT); it has been discussed in two subcategories of central and peripheral PNET. PNETs of peripheral nerves are very uncommon pathologic findings, as to the best of our knowledge only 12 well-documented cases have been yet reported.

**Case presentation:** A 30-year-old male presented with progressive paresthesia of his right hand's little finger and painless swelling of the right axilla. Magnetic resonance (MR) neurography demonstrated a heterogeneous, high-signal, round mass within the right axilla fossa in proximity to the medial aspect of brachial plexus branches. The clinical and radiological study failed to an accurate diagnosis, thus surgical resection of the tumor was done for tissue evaluation. Histopathologic study of the lesion revealed a neoplasm comprising sheets of small, round, blue cells (Hematoxylin and Eosin stain), which immunohistochemically consisted with the diagnosis of PNET.

**Clinical discussion:** The differential diagnosis of axillary fossa masses, focusses on peripheral nerve tumors like Schwannoma and PNET. MR neurography aids in evaluation, but tissue diagnosis remains crucial. Treatment involves surgical resection, chemotherapy, and radiotherapy tailored to individual patients.

**Conclusion:** Although pPNET is not apparently the first differential diagnosis coming to mind when encountering a rapidly growing mass in the axillary fossa with peripheral nerve origin, its highly malignant behavior, makes it crucial to be considered in the differential diagnoses.

**Keywords:** peripheral primitive neuro-ectodermal tumor, pPNET, ulnar nerve

## Background and Importance

Primitive neuro-ectodermal tumor (PNET) was first introduced by Hart and Earle as a rare small round cell malignant tumor originating from neuroectoderm[1]. It is a member of Ewing's Sarcoma Family of Tumors (ESFT) and mostly develops in children and young adults. Based on differential classification, two subtypes of peripheral PNET (pPNET) and central PNET (cPNET) have been introduced. Evidence suggests that cPNET arises from precursor cells of the subependymal matrix of the central nervous system (CNS) or external granular layer of the cerebellum, pinealocytes, and subependymal cells of the ventricles. In contrast, pPNET originates from the neural crest located outside the CNS[2,3].

pPNET is responsible for about 4% of all soft tissue tumors and can appear in uncommon sites. Cutaneous localization of pPNET is very rare in adults and thus can easily be misdiagnosed[4]. No definitive diagnostic clue on radiologic findings or laboratory tests is known yet[2,5].

### HIGHLIGHTS

- This case report highlights a rare occurrence of Peripheral Primitive Neuro-Ectodermal Tumor (pPNET) in a 30-year-old male, adding to the limited documented cases of this entity.
- Despite initial diagnostic challenges, surgical resection confirmed the presence of PNET, emphasizing the importance of considering this highly aggressive tumor in cases of axillary masses with unclear etiology.
- The case underscores the significance of early recognition and appropriate management of pPNET due to its malignant potential and implications for patient care.

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*Key Clinical Message: Rare malignant neural tumors although are not the first differential diagnosis toward a rapidly enlarging peripheral subcutaneous mass lesion but should be kept in mind and ruled out using tissue diagnosis.*

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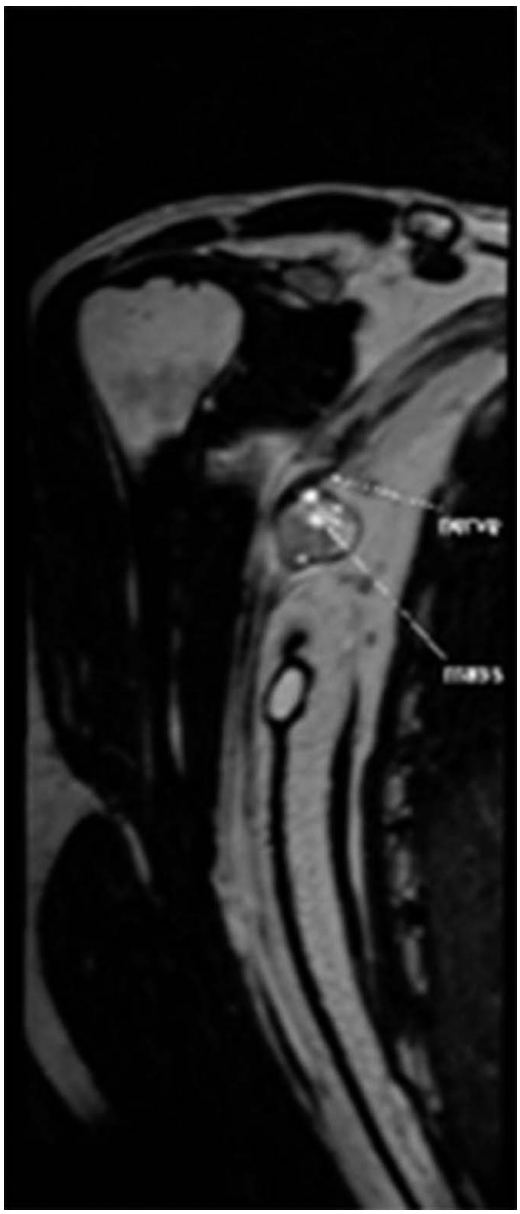

**Figure 1.** MR neurography: a spindled-shape space-occupying lesion adjacent to a peripheral nerve (a brachial plexus branch), near the anterior axillary line is detected. The lesion is heterosignal on fluid sensitive sequences (STIR: contains internal cystic-solid component). The ribs and chest wall subcutaneous soft tissue are intact. Above-mentioned descriptions are more suggestive of a peripheral nerve sheath tumor such as Schwannoma.

As the tumor occurs at a young age, long-term survival remains a challenge in patient management[1,2]. While a five-year survival is expected in about 70–80% of patients with localized PNET, it drops by less than 30% in patients with a metastatic disease[6]. Therefore, an early and accurate diagnosis is crucial for successful management of the patients.

The two subtypes of PNET are morphologically identical. The differential diagnosis of PNET includes other similar round blue cell tumors with the same histomorphological characteristics. Therefore, an Immunohistochemical study is mandatory for a definite diagnosis.

Differentiation markers such as CD99 (MIC2) when a positive membranous staining is seen, can distinguish PNET from other round blue cell tumors[7].

As PNETs are extremely invasive, they do not usually have a clear rim with the adjacent tissues. According to previous studies, PNET mostly shows mixed isointense to hypointense signals on T1-weighted imaging and isointense to hyperintense signals on T2-weighted imaging, with significant enhancement in contrast MRI. However, a definite diagnosis cannot be confirmed radiologically, indicating the necessity of other confirmative tests, such as pathological studies[1].

Chest computed tomography (CT) scan and MRI of the primary site, bone scan, and other metastasis investigations are strongly recommended for tumor staging[6]. We present a rare case of an axillary fossa mass with the diagnosis of Schwannoma in the primary needle biopsy followed by the diagnosis of PNET in the surgical excision sample. This case report has been reported in line with SCARE criteria[8].

## Clinical presentation

A 30-year-old male was referred with a one-year history of progressive tingling and numbness in the fifth finger of the right hand and a painless swelling in the right armpit. His past medical and medication history was unremarkable. He had no history of weight loss, night sweats and fever.

Physical examination revealed a non-tender, palpable enlarging mass in the right axilla fossa, characterized by firm consistency, adhesion to the overlying skin, smooth margins, and absence of involvement of adjacent tissues. No other peripheral lymphadenopathy was appreciated on examination.

MR neurography revealed a $30 \times 25 \times 24$ mm heterogeneous, high-signal, round mass within the right axilla fossa in proximity to the medial aspect of brachial plexus branches. The mass showed high-signal intensity on the T1 image, a very high T2 signal intensity, and no signal drop on the fat-saturated sequence with the fluid-fluid level (Fig. 1), indicating a hemorrhage in the tumor. Therefore, the surgical procedure was performed by a neurosurgeon and their team. Upon operation a well-circumscribed ovoid, solid, dark-blue tumor, originating from the ulnar nerve covered by the nerve sheath was seen. Some nerve bundles were encased in the tumor with no extra-neural invasion (Fig. 2).

Through a Frozen-section study a small, round, blue cell tumor was reported. Since all motor functions of the ulnar nerve were intact, total tumor resection with a wide margin of the sur-

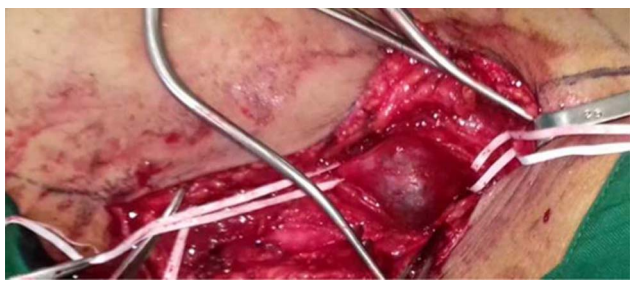

**Figure 2.** Intraoperative view of the tumor: a well-circumscribed ovoid solid tumor with dark-blue appearance.

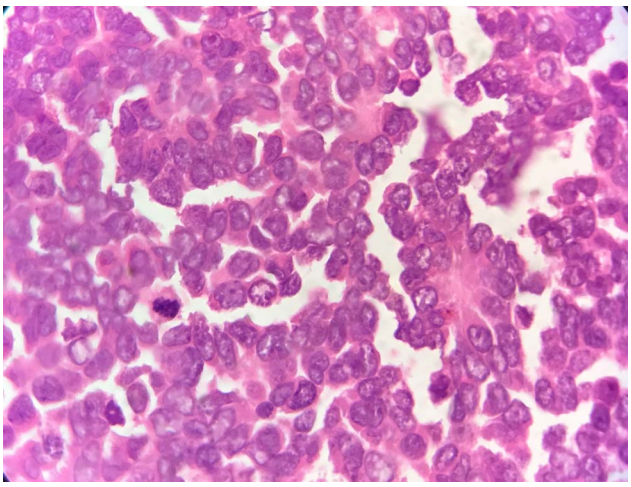

**Figure 3.** Histomorphologic study shows sheets of round blue cells with brisk mitotic figures and rosette formation (hematoxylin and eosin; 1000×).

rounding soft tissue was done.

Complementary investigations including histomorphological study (Fig. 3) and IHC staining (Fig. 4) revealed a high-grade malignant, small, round, blue cell tumor, with diffuse membranous staining for CD99, consistent with the diagnosis of pPNET. The patient was scheduled for chemotherapy as part of his treatment plan, but he did not comply with the prescribed treatment and missed follow-up appointments. Unfortunately, the only information available regarding the patient was that he passed away six months after the mass resection surgery.

## Discussion

An axillary fossa mass may have a wide range of differential diagnoses ranging from benign reactive lymphadenopathy to malignant neoplasms. While lymphadenopathies account for the vast majority of the cases, neural tumors can sometimes occur in this region. Not to mention, Schwannoma is the most common benign, slow-growing, peripheral nerve tumor in adults, originating from a single fascicle within the main nerve and displacing the nerve[9]; While Malignant neural tumors are very uncommon[10].

pPNET usually presents as a large soft mass (>5 cm) with undefined margins and local invasion into the surrounding tissue. Clinical presentation of pPNET mainly depends on the tumor site and the mass effects. It can present as a rapidly growing mass causing swelling and pain or the metastatic disease can be the initial presentation[11]. The most probable sites of metastasis are lungs, bone, and bone marrow[11]. Whereas a benign mass usually presents as a slow-growing mass taking several years to cause neurological symptoms. Macroscopic features of pPNET seen during surgery, unlike Schwannoma, lack the well-formed capsule, which is a very common and reassuring finding for the latter diagnosis[12].

When approaching a peripheral nerve tumor, MR neurography is a reliable technique to evaluate the anatomy and pathologies of a nerve, its regional muscle, and functional assessment. Although Schwannomas have characteristic MRI features, radiologic findings may not be of unequivocal diagnosis, especially when occurring in unusual sites[13]. Therefore, tissue diagnosis remains the gold standard diagnostic assessment emphasizing the importance of surgical removal of a suspicious lesion.

pPNET is associated with a significant mortality rate. Treatment includes total resection surgery with wide margins,

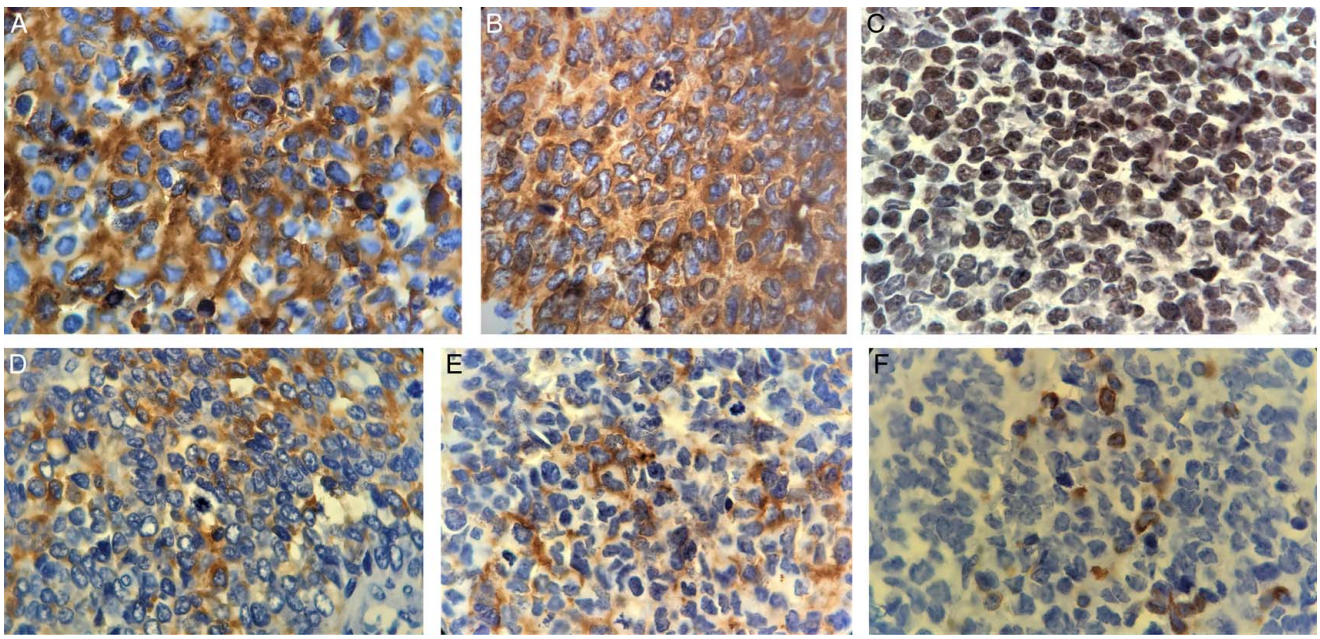


**Figure 4.** Immunohistochemistry study shows diffuse strong membranous staining for CD99; 1000× (A), diffuse strong cytoplasmic staining for NSE; 1000× (B), diffuse nuclear staining for FLI-1; 1000× (C), positive cytoplasmic staining for Synaptophysin; 1000× (D) and CD56; 1000× (E) in some tumor cells and positive cytoplasmic staining for CKAE1/3 in scattered tumor cells; 1000× (F).

chemotherapy, and radiotherapy, which should be individualized for each patient, based on the site and size of the tumor, metastasis, age, and health status.

Only 12 cases mentioned in the literature to date reported pPNET arising from the peripheral nerves[14] . Stout in 1918 first reported a case of a 42-year-old man with an ulnar tumor composed of small, round, blue cells forming rosettes but not confirmed by IHC or molecular studies[15]. Samuel *et al*.[16] in 1982 reported a primitive neuro-ectodermal tumor in a 59-year-old man, which arose from the ulnar nerve, but no confirmatory study was done either. Mohan *et al*.[17] in 2011 reported 2 cases of intraneural Ewing's sarcoma/PNET of the upper limb (ulnar and radial nerve) confirmed by IHC staining and fluorescent in situ hybridization (FISH) study. Akeyson *et al*.[18] in 1996 reported a median nerve PNET in an 80-year-old male, confirmed by pathological and cytogenetic studies. In the lower extremities, Lavorato *et al*.[14] in 2019 reported a rare case of a 46-year-old woman with an intraneural extraosseous ES of fibular nerve.

As the peripheral nerve location of ES is extremely rare, it is usually misdiagnosed by other types of more frequently observed tumors, such as Schwannomas. To end with, even when a preoperative tissue diagnosis is provided, there is sometimes a bonus in total excision of a clinically suspicious lesion for the surgeon and of course the patient.

## Conclusion

A rapidly growing painless mass with a superficial subcutaneous location may not be of serious concern. If arising from a peripheral nerve, a wide spectrum of tumors is considered. Although very rare, pPNET should be listed in the differential diagnoses due to its potential to alter the overall patient's outcome.

## Ethical approval

Not applicable.

## Patient consent

Written informed consent was obtained from the patient for probable publication of this case report and accompanying images in future. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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All authors contributed equally to this work.

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