Primitive neuroectodermal tumor of ulnar nerve: A rare case

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Abstract

Primitive neuroectodermal tumor (PNET) is a highly aggressive tumor and mostly develops in children and young adults. PNETs of peripheral nerves are uncommon. Ulnar nerve, in particular, is an extremely peculiar origin for PNET and to the best of our knowledge only few well-documented cases have been yet reported.

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Abstract

Primitive neuroectodermal tumor (PNET) is a highly aggressive tumor and mostly develops in children and young adults. PNETs of peripheral nerves are uncommon. Ulnar nerve, in particular, is an extremely peculiar origin for PNET and to the best of our knowledge only few well-documented cases have been yet reported.

Background and Importance

Primitive neuroectodermal 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 (ES) family 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[4,5] and can appear in uncommon sites[6]. Cutaneous localization of pPNET is very rare in adults thus can easily be misdiagnosed[7]. No definitive diagnostic clue on radiologic findings or laboratory tests is known yet[2,8].

As the tumor occurs at young age, long-term survival remains a challenge in patients management[1,2,9]. 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[10]. Therefore, an early and accurate diagnosis is crucial for successful management of the patients.

The two subtypes of PNET are morphologically identical[5,11]. The differential diagnosis of PNET includes other similar round blue cell tumors with the same histomorphological characteristics. Therefore, Immunohistochemical study is mandatory for definite diagnosis[12].

Differentiation markers such as CD99 (MIC2) when a positive membranous staining is seen, can distinguish PNET from other round blue cell tumors[12,13].

As PNETs are extremely invasive, they do not usually have a clear rim with the adjacent tissues[14]. 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 on contrast magnetic resonance imaging (MRI). However, definite diagnosis cannot be confirmed radiologically, indicating the necessity of other confirmative tests, such as pathological studies[1,5,6].

Chest computed tomography (CT) scan and MRI of the primary site, bone scan and other metastasis investigations are strongly recommended for tumor staging[10,15]. We present a rare case of an axillary fossa mass with the diagnosis of schwannoma in the primary needle biopsy following the diagnosis of PNET in the surgical excision sample.

Clinical Presentation

A 30-year-old male presented with a one-year history of right little finger progressive paresthesia and a non-tender palpable enlarging mass in the right axillary fossa.

MR neurography revealed a 30×25×24 mm heterogeneous, high-signal, round mass within the right axillary fossa in proximity to the medial aspect of brachial plexus branches. The mass showed high-signal intensity on T1 image, a very high T2 signal intensity and no signal drop on fat-saturated sequence with the fluid-fluid level (Figure 1), indicating a hemorrhage in the tumor. On 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 (Figure 2).

Frozen-section study revealed a small, round, blue cell tumor. Since all motor functions of the ulnar nerve were intact, total tumor resection with a wide margin of the surrounding soft tissue was done.

Histomorphological study (Figure 3) and IHC staining (Figure 4) revealed a malignant, small, round, blue cell tumor, consistent with primitive neuroectodermal tumor.

Discussion

An axillary fossa mass may have a wide range of differential diagnosis from a reactive lymphadenopathy to malignant neoplasms. While lymphadenopathy accounts for the vast majority of cases[16,17], neural tumors can sometimes occur in this region. Schwannoma is the most common benign, slow-growing, peripheral nerve tumor in adults, originating from a single fascicle within the main nerve and displaces the nerve[18]. Malignant neural tumors are very uncommon developing from primitive, undifferentiated, small, round cells[19].

pPNET is usually a large soft mass (>5 cm) with an undefined margin and local invasion to the surrounding tissue[20-23]. Clinical presentations of pPNET depend on the tumor site and mass effects. It can present as a rapidly growing mass causing swelling and pain[24,25]. Sometimes the metastatic disease can be the initial presentation[24]. The most probable sites of metastasis are the lungs, bone and bone marrow[11,24,26,27]. On the other hand a benign mass usually presents as a slow-growing mass taking several years to cause neurological symptoms[28,29]. In addition, the macroscopic features of pPNET seen during surgery were unlike those of schwannoma,lacking the well-formed capsule which is a very common and reassuring finding for the diagnosis[30]. Therefore, despite previous biopsy diagnosis, a frozen section study was requested upon surgery. The frozen section diagnosis was small round blue cell tumor.

In peripheral nerve tumors, MR neurography is a reliable technique for evaluation of anatomy and pathology of a nerve, regional muscle and functional assessment[31]. Although schwannomas have common MRI characteristics, radiologic diagnosis is not reliable on its own, especially when occurring in unusual sites[32].

pPNET is associated with significant mortality rate[33]. Treatment should be individualized for each patient, based on the site and size of tumor, metastasis, age and health status, including total resection surgery with wide margins and chemotherapy. Radiotherapy may also be done[34].

Only few well documented cases of pPNET arising from the peripheral nerves have been yet reported. 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[35]. Samuel et al. in 1982 reported a primitive neuroectodermal tumor in a 59-year-old man, arose from the ulnar nerve, but no confirmatory study was done neither[36]. Mohan et al. in 2011 reported 2 cases of intra-neural 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. in 1996 reported a median nerve PNET in an 80-year-old male, confirmed by pathological and cytogenetic studies[38].

Conclusion

A rapidly growing mass within the axillary fossa arising from the peripheral nerves may be a similar presentation of wide spectrum of tumors. Highly malignant behavior of pPNET makes it an important differential diagnosis to be considered despite its low incidence.

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Figure legends:

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 peripheral nerve sheath tumor such as schwannoma.

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

Figure 3: Histomorphologic study shows sheets of atypical round blue cells with brisk mitotic figures and rosette formation (Hematoxylin and Eosin; x1000).

Figure 4: Immunohistochemistry study shows diffuse strong membranous staining for CD99; x1000 (A), diffuse strong cytoplasmic staining for NSE; x1000 (B), diffuse nuclear staining for FLI-1; x1000 (C), positive cytoplasmic staining for Synaptophysin; x1000 (D) and CD56; x1000 (E) in some tumor cells and positive cytoplasmic staining for CKAE1/3 in scattered tumor cells; x1000 (F)

List of abbreviations:

PNET: Primitive Neuroectodermal Tumor

pPNET: peripheral Primitive Neuroectodermal Tumor

cPNET: central Primitive Neuroectodermal Tumor

E/S: Ewing Sarcoma

IHC: Immunohistochemistry

CT scan: Computed Tomography scan

MRI: Magnetic resonance imaging

FISH: Fluorescent In Situ Hybridization