Primary cutaneous Ewing’s sarcoma/primitive neuroectodermal tumor manifested as huge ulcerated mass on posterior thigh region: Case report and review of literature

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ABSTRACT

Introduction: Ewing’s Sarcoma (ES) and Primitive Neuroectodermal Tumor (PNET) are thought to have a common origin as these tumors share identical clinical and histological properties and are often interchangeably used in literatures. Extraskeletal ES/PNET is rarely found especially on cutaneous region and primarily manifests as a single small lesion in the mid-to-deep dermis. Case Report: We reported an unusual presentation with MRI findings of cutaneous ES/PNET case on 19-year-old presenting as a single huge ulcerated mass that was initially mistaken as arteriovenous malformation. Conclusion: Magnetic resonance imaging provided excellent depiction in suggesting the diagnosis of cutaneous ES/PNET. Surgical excision followed by chemotherapy were successful in treating this case with no local recurrence or distant metastasis was observed after one year of follow-up.

Keywords: Cutaneous, Ewing’s sarcoma, Magnetic resonance imaging, Primitive neuroectodermal tumor

INTRODUCTION

Extraskeletal Ewing’s Sarcoma (ES) and Primitive Neuroectodermal Tumor (PNET) share identical clinical and histological properties as both the tumors consist of small blue round cells and often referred to interchangeably in the literature. They represent different manifestations of the same tumor and have similar genetic alterations [1]. Immunohistochemistry and cytogenetic studies suggest that these tumors have a common origin [2]. Most literature report extraskeletal involvement of ES/PNET to be rare but it was likely under reported as recent diagnostic advances have allowed such tumor to be distinguished from other small, poorly differentiated round cell tumor [3, 4]. Extraskeletal ES/PNET usually manifest as a 5–10 cm tumor and might manifests at any part of our body, usually at deep soft tissues and muscles, such as paraspinal muscles, or chest wall (Askin Tumor). However, cutaneous regions are rarely affected by ES/PNET with most cases are reported to have small size (2–3 cm), singular, tumor mass [1, 2, 5].
Due to its small size, number of lesion, and superficial location, most cutaneous ES/PNET underwent excisional biopsy without investigated earlier by advanced imaging. It has also been reported to have more favourable outcome and prognosis. Bigger and more deeply located lesion are more resembling to malignant soft tissue sarcoma and are usually more well documented. We report an unusual presentation with MRI description of a histopathologically confirmed cutaneous ES/PNET case on 19-year-old, presenting as a single huge ulcerated mass that was firstly mistaken as arteriovenous malformation.

CASE REPORT

A 19-year-old female presented with progressively enlarging mass on posterior left thigh that developed since 12 months ago. Mass was about 15 cm diameter in size, dense, well defined margin, with increasing pulsatile pain, marked gradual discoloration, and auscultated bruit. Patient was referred from primary health care to vascular surgeon, where she was treated with arteriovenous malformation as working diagnosis. Patient was lost to follow-up due to pregnancy before further advanced investigation was performed. By the time patient readmitted to our emergency department (due to obstetric problem), the lump had reached the size of 22 cm, ulcerated and actively bleeding (Figure 1). No compromised distal neurovascular status. Patient underwent emergent caesarean section along with bleeding-source control and biopsy. The histopathologic exam resulted as Ewing’s Sarcoma and the patient was referred to us.

Plain radiograph showed soft tissue tumor on posteromedial side of left thigh with no radiological abnormality on left femur (Figure 2). Bone survey and a chest radiograph were performed to rule out multicentric disease and pulmonary metastasis. Magnetic resonance coronal T1-weighted image shows a fungating mass with the size of 22 x 14 x 8 cm of low intensity that is restricted to cutaneous-subcutaneous region with clearly demarcated border, some skin thickening was observed on the peripheral tumor, with lack of soft tissue envelope at the centre-superficial lesion suggesting ulcerated tumor (Figure 3A). Tumor enhancement was observed after contrast was introduced, showing lobulated structured inside the tumor (Figure 3B). Sagittal T2-weighted image showed large lobulated mass with heterogeneous signal intensity (Figure 3C). Axial T1, T1 contrast, T2-weighted represented similar finding of three previous slice, depicting better the depth and base of the tumor. Interestingly the tumor itself was restricted in cutaneous-subcutaneous level of left thigh with no infiltration to the muscle, bone, and neurovascular bundle (Figure 3D-F).

Histopathologic examination showed solidly packed, dense, lobular, round cell pattern of striking uniformity, on low magnification. Round or ovoid nucleus with a distinct nuclear membrane on each tumor cell, chromatin of fine texture, and marked nucleoli. Immunohistochemistry examination of sample confirmed strong and diffuse reaction to CD99 staining Figure 4(A–B).

Patient underwent wide excision of tumor lesion as the mean of immediate local control to the huge, ulcerated, fragile-bleeding tumor Figure 5(A–D). Immediate post-operative condition was uneventful, with the patient discharged with bilateral crutches to assist mobility. Postoperative chemotherapy was conducted using vincristine, doxorubicin, and cyclophosphamide regimen. During short term one year of follow-up, no local recurrence or distant metastasis was observed.

DISCUSSION

Extraskeletal Ewing’s Sarcoma (ES) and Primitive Neuroectodermal Tumor (PNET) both share identical clinical and histological properties as both tumors consist of small blue round cell and often interchangeably used in the literature [1]. Angervall and Enzinger (1975) first
described Extraskeletal ES on 39 cases of extraskeletal neoplasms with uniform histologic features that were indistinguishable from skeletal ES [6]. Jaffe et al. (1984) also reported four cases and suggested that some ES of bone and soft tissue in children were of neuroectodermal nature and that monoclonal antibodies usage in the future would explain the similarity and correlation between the two tumors [7]. In general, ES and PNET represent different manifestations of the same tumor and have similar genetic alterations. However, ES are more commonly associated with bone tumor, while PNET tumors are more commonly associated in soft tissue tumor. Although the name of ES are widely known as bone tumor that frequently extends to surround soft tissue by destructing the bone cortex first, it may develop as a primary soft tissue tumor without the involvement of bone at all. Extraskeletal ES/PNET occurrence is at the highest on second decade of life, with median age 17 years, affecting female more than male by the ratio of 2:1, unlike classical skeletal ES which affect more male population [8].

Most literature conclude that extraskeletal involvement of ES/PNET is rare. However, recent diagnostic advances have allowed such tumor to be distinguished from other small, poorly differentiated round cell tumor. It was thought that the rarity was probably caused by under reported cases. The tumor has similar appearance with other tumor including rhabdomyosarcoma, neuroblastoma, and non-Hodgkin lymphoma. In extraskeletal ES/PNET, Homer-Wright rosettes was absent. Electron microscopy examination of PNET reveals neurosecretory granules with microtubules and microfilaments with short dendritic processes lying in between cells in PNET. In addition, short dendritic processes lie between cells in PNET, in contrast to ES

Figure 2: (A) Anteroposterior view of the femur. (B) Lateral view of the femur. Pictures showed marked soft tissue tumor with no extension to femur.

Figure 3: Magnetic resonance imaging of the left thigh coronal T1 (A), coronal T1 with 286 contrast (B), sagittal T2 (C), axial T1 (D), axial T1 contrast (E), and axial T2 (F). Pictures showed a solitary low-intensity fungating mass with the size of 22 x 14 x 8 cm, that is restricted to cutaneous-subcutaneous region with clearly demarcated border. Contrast enhancement showed large lobulated mass with heterogeneous signal intensity.

Figure 4: Histopathologic examination (A) HE staining and (B) CD99 immunohistochemistry staining. Pictures showed solidly packed, dense, lobular, round cell pattern of striking uniformity, round or ovoid nucleus with a distinct nuclear membrane on each tumor cell, chromatin of fine texture, and marked nucleoli that also showed strong and diffuse reaction to CD99 staining, confirming the ES/PNET origin of the tumor.

Figure 5: Wide excision of tumor (A, B). Macroscopic view of tumor (C, D). Magnetic resonance imaging depiction was confirmed intraoperatively as the tumor was lobulated and restricted to cutaneous region.
which processes are absent [3, 4]. Immunohistochemistry and cytogenetic studies had suggested that these tumors all have a common origin with common cytogenetic abnormality of t(11;22) (q24;q12) [4].

Reports have showed that ES/PNET might manifests at any part of our body although the occurrence outside of the head and neck area has been matter of debate over time. Several proposals of the original site to harbour the neuroectodermal tissues have been put forward, which include the origin from abnormally migrated neural crest cells or germ cells that have been misplaced during embryonic migration [2]. ES/PNET might manifest at deep soft tissues, such as muscles of the paraspinal region, chest wall (Askin Tumor), or even at the lesser extent site on cutaneous, and even eye lid [1, 2]. Cutaneous ES/PNET are rarely found and primarily manifests as a single small lesion in the mid-to-deep dermis. Some case series have reported this unique character of cutaneous lesion, including: a series of 14 cases in which all presented as a single mass with median diameter of 3 cm; a review of 23 cases from the literature, confirming the same solitary lesion and median value of 3 cm (in exception of one case with multiple nodules); and a series by Ehrig et al of 13 cases of single tumor with a median size of 1.5 cm, halve the previous two [1, 9]. Review by De La Place showed that tumors were mainly located (in order of frequency) on lower limb (38%), upper limb (26%), head (20%), and trunk (16%) [8].

The ideal treatment for skeletal ES/PNET comprises multimodality treatment that includes wide excision to ensure clear margin, chemotherapy, and radiotherapy. Limb ablation surgery should always be reserved as the last resort, whereas either neurovascular structure had already been invaded or the limb integrity would be severely compromised if we perform wide excision [2, 10]. In accordance to this approach, the 5 and 10 years’ overall survival rates ranges as high as 69.7% and 65.2%, respectively, for patients with localized tumors [2, 9, 10]. However, extraskeletal ES/PNET has not reached definitive consensus for treatment modality. De La Place et al raised the hypothesis of treating cutaneous ES/PNET with surgery alone because multimodal treatments are associated with late and severe complications [8]. Nonetheless, more conservative treatments are still expected and yield more favourable outcome at bigger or deeper cutaneous ES/PNET [9]. Survival within 10-year was expected to be as high as 91% with overall survival to be 93%. Earlier time to diagnosis, size of tumor and superficial location are thought to hold important role. Tumor volume >100 cc is associated with poorer prognosis as often found in ES of the bone. This is contrary with the average size of cutaneous ES/PNET of size diameter 2-3 cm [8].

We performed wide excision and defect closure using primary suture followed by chemotherapy using vincristine, doxorubicin, and cyclophosphamide. The surgical procedure provided excellent local control as the outcome was good both aesthetically and functionally. No local recurrence or distant metastasis was observed after one year of follow-up.

CONCLUSION

In summary, this is a case of an extraskeletal ES/PNET affecting cutaneous region of posterior left thigh manifested as single huge ulcerated mass which was initially mistaken as arteriovenous malformation. Magnetic resonance imaging provides excellent depiction in suggesting the diagnosis of cutaneous ES/PNET.

REFERENCES


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**Conflict of Interest**
Authors declare no conflict of interest.

**Data Availability**
All relevant data are within the paper and its Supporting Information files.

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