

Case Report

An Unusual Tumor of the Breast - Extraskkeletal Ewing Sarcoma

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ABSTRACT: Extraskkeletal Ewing's Sarcoma/Primitive Neuroectodermal Tumor presenting as a breast mass is uncommon. It may pose a diagnostic challenge. In order to increase awareness and identify potential diagnostic pitfalls, we report a 24 year-old woman extraosseous Extraskkeletal Ewing's Sarcoma/Primitive Neuroectodermal Tumor arising in the breast.

KEYWORDS: Extraskkeletal Ewing's Sarcoma, Primitive Neuroectodermal Tumor, Breast

Introduction

Ewing sarcoma (ES) is the most frequent malignant tumor under ten year-old children. In the second decade of life it is the second malignant bone tumor exceeded by osteosarcoma [1,2]. It was first described by Dr. James Ewing in 1921 [1,2,3]. Extraosseous Ewing's sarcoma (EES) was introduced by Tefft in 1969 [4].

Initially, the histopathological diagnosis was made when a tumor consisted of blue small round cells on heamatoxylin-eosin staining with no evidence of a cell origin. A number of reports have characterized the histological and electron microscopic appearance of EES, differentiating it from other small, round cell soft tissue malignancies such as rhabdomyosarcoma, peripheral primitive neuroectodermal tumor and malignant lymphoma. Despite these diagnostic difficulties, EES has been accepted as a distinct clinicopathological entity. EES has been identified in the chest wall, pelvis, lungs, paravertebral tissues etc.[2] According to our knowledge, there are few cases that have been described as Extraskkeletal Ewing's Sarcoma/Primitive Neuroectodermal Tumor (ES/PNET) arising in the breast [5, 6].

This study reports a case of a 24-year old woman with ES/PNET of the breast.

Case Report

A 24-year-old woman is presented with a 2 month history of lump in her right breast. Physical examination revealed a hard, painful mass, measured approximately 10 cm in the right breast. Ultrasonographic examination disclosed 13x11x9 cm solid mass lesion replacing almost the entire breast which was

macrolobulated. In the right axillary region lymphadenopathy measured as 16x8 mm was identified. Thru-cut biopsy from mass lesion was performed. Since on histopathological examination the biopsy was entirely necrotic, re-biopsy was recommended. Following this, a wide excisional biopsy was performed.

Macroscopically the cut surface of the tumor was lobulated, which was grayish-white and measured as 11x10x9 cm. Necrotic and hemorrhagic areas were also seen. Microscopic examination showed monomorphic population of small blue cells with variably conspicuous nucleoli and scant cytoplasm (Fig.1, 2).

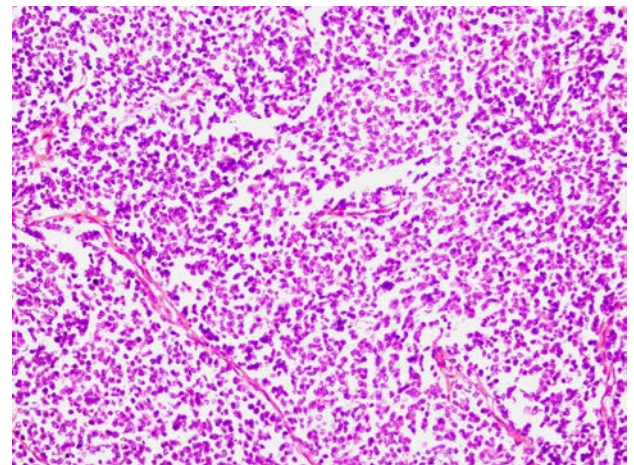


Fig.1. Tumor is composed of small, round cells with inconspicuous nucleoli and scanty cytoplasm, which are arranged in sheets or solid nests (Hematoxylin-Eosin staining, X400).

Atypical mitotic figures and necrosis were also seen. Some of the cells had clear cytoplasm secondary to glycogen deposition, which was positive for Periodic Acid Schiff (PAS) stain. Immunostaining was positive for neuron-specific enolase, S-100, synaptophysin and

strong membranous CD99 positivity (Fig.3) and negative for pancytokeratin, epithelial membrane antigen, leukocyte common antigen, CD3, CD79a, tdt, myeloperoxidase, chromogranin A, desmin, actin, HMB45, CD34, CD57, CD10, CD56 and CD117. Staging evaluation which was consisted of a whole-body bone scintigraphy, cranial and thorax CT was negative. The morphologic characteristics and the immunohistochemistry were compatible with ES/PNET.

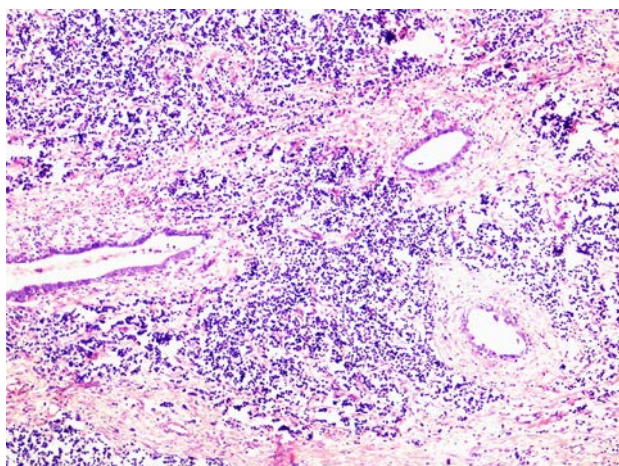


Fig.2. Tumor displays a diffusely infiltrative growth pattern. Rare residual breast ducts are also seen (Hematoxylin-Eosin staining, X100).

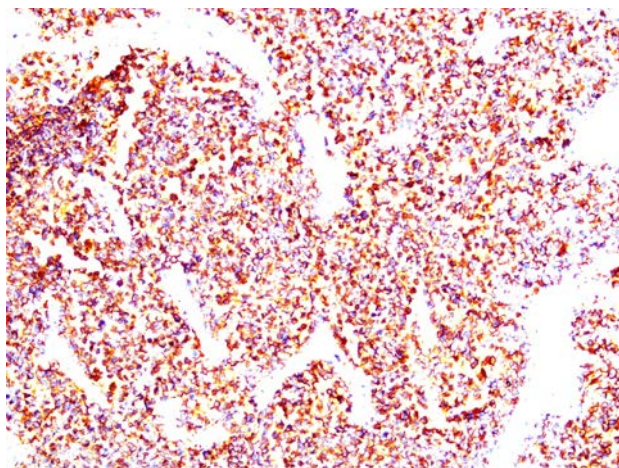


Fig.3. On immunohistochemistry, the tumor cells show strong membranous staining for CD99 (CD99, X400).

The patient received multi-agent chemotherapy with vincristine, doxorubicin, cylophosphamide, ifosfamide and etoposide. After chemotherapy she was treated with radiotherapy. Two months following the radiotherapy as she developed local recurrent disease, modified radical mastectomy and axillary lymph node dissection were performed. Macroscopic examination revealed mass

measured as 11x10x6 cm. Histopathological and immunohistochemical findings were the same as excisional biopsy. Resected axillary nodes were positive for tumor. The patient died 8 months after the first surgery of disease progression.

Discussions and conclusion

Ewing's sarcoma and PNET form a single group of bone and soft-tissue tumors with typical undifferentiated Ewing's sarcoma at one and of the spectrum and PNET with clear evidence of neural differentiation at the other [5]. ES/PNET presented as a breast mass is uncommon, with only few cases have been reported in the literature [5, 6].

The histology of EWS/PNET ranges from small, round cells with round nuclei, fine chromatin, scant cytoplasm, and indistinct cell borders to larger, more irregular nuclear contours, pseudorosettes, a nesting pattern, and in some instances, spindle cells. Necrosis may be present [3]. ES/PNET should be differentiated from other small round cell tumors for therapeutic approaches [7]. Tumor cells are positive for vimentin, CD99, FLI1. Reactivity for neuron-specific enolase, CD57, synaptophysin, and cytokeratin may vary. Rare cases may be positive for desmin and glial fibrillary acidic protein, but not typically for leukocyte common antigen or actin. CD99 (MIC 2) shows a membranous staining. It was initially thought to be highly specific for EWS/PNET, but it is now recognized that, although its sensitivity ranges from 84% to 100% in EWS/PNET, the specificity is limited [3].

CD99 is sometimes expressed in non-epithelial and epithelial tumours other than EFT, which include acute lymphoblastic leukemia, alveolar rhabdomyosarcoma, granulocytic sarcoma, synovial sarcoma, solitary fibrous tumour, meningioma, and neuroendocrine tumours. Invasive ductal carcinomas also can be positive for this antibody [5]. Routine histologic and immunohistochemical examinations are sufficient to render a correct diagnosis of ES/PNET in most cases. When morphology is not conclusive, or when these tumors appear in an unusual clinical setting, genetic analysis is very helpful. Molecular techniques used for detection of the EWS translocations associated with PNET are important tools for the confirmed diagnosis. The methods include DNA- and RNA-based polymerase chain reaction, Southern blotting, and FISH [8]. In the case we report, the diagnosis of PNET/Ewing's sarcoma of the

breast was established on morphologic and immunohistochemical findings. We could not perform molecular cytogenetic analysis, because of the lack of technical structure.

In conclusion, ES/PNET can occasionally involve the breast as an isolated mass. Careful histological examination and appropriate immunohistochemical studies are often necessary to confirm the diagnosis. Awareness of this as a possibility will help distinguishing this tumor from other neoplasms.

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