# Primary extraskeletal Ewing's sarcoma/primitive neuroectodermal tumor of breast

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## Abstract

Extraskeletal Ewing's sarcoma (EES) is a rare soft tissue tumor that is morphologically indistinguishable from skeletal ES. We report a case of a 25-year-old female with recurrent EES/primitive neuroectodermal tumor of right breast with imaging findings on mammogram, ultrasound, magnetic resonance imaging breast, and positron emission tomography–computed tomography.

**Key words:** Breast; extraskeletal Ewing's sarcoma; primitive neuroectodermal tumor

## Introduction

Ewing sarcoma (ES) is a highly malignant bone tumor of long bones occurring in children and young adults and was first described by James Ewing in 1921. However, there have been reported cases of malignant soft tissue tumors which are indistinguishable from ES and have been called extraskeletal ES (EES). These tumors are now classified as ES family of tumors (ESFT) and include ES, EES, and primitive neuroectodermal tumor (PNET), which shows more neural differentiation than ES.[1,2] EES is a rare, aggressive, malignant soft tissue tumor with high recurrence rate and mainly occurring in adolescents and young adults between 10 and 30 years of age. The breast is uncommonly involved.[3]

In 1975, Angervall and Enzinger reported the first case of extra-osseous ES. The most common sites are chest wall, paravertebral region, retroperitoneal space, lower extremities, and gluteal region. However, few cases have been reported in the kidney, breast, gastrointestinal tract, prostate, endometrium, the adrenal glands, brain, and lungs.[4]

We report the case of a 25-year-old female with recurrent EES/PNET of the breast with mammogram, ultrasound (US), magnetic resonance imaging (MRI) and positron emission tomography–computed tomography (PET-CT) imaging findings.

## Case Report

A 25-year-old female was referred to our institute with a history of diagnostic incisional lumpectomy for right breast lump in August 2014 which on histopathology was diagnosed to be a high-grade sarcoma. After surgery, there was a gradually increasing lump in the right breast.

Mammogram [Figure 1] revealed a large lobulated dense mass in the area of palpable abnormality in the upper inner quadrant of right breast.

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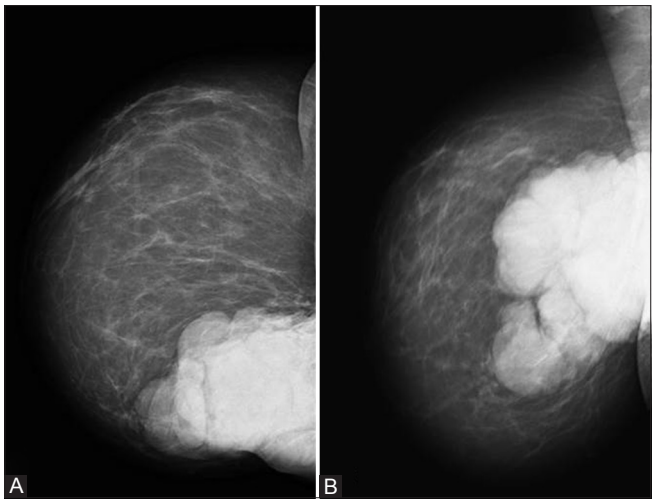

**Figure 1 (A and B):** Mammogram of right breast, cranio-caudal (A) and medio-lateral oblique (B) views shows a lobulated dense mass in the in the upper inner quadrant

US [Figure 2] showed a large multilobulated solid cystic mass in the upper inner quadrant of the right breast involving the overlying skin with high vascularity and subcentimeter sized lymph nodes were seen in the right axilla.

Contrast-enhanced MRI [Figure 3] of breast showed a large multi-lobulated heterogeneously enhancing mass lesion in the upper inner quadrant (1–4 o'clock position) of the right breast involving the overlying skin. The lesion appeared hypointense on T1-weighted and inhomogeneously iso- to hyper-intense on T2-weighted images. A cystic/necrotic component with peripheral enhancement was seen along the anterior aspect of the mass. Posteriorly, the mass was extending up to the pectoralis muscle.

PET-CT (performed at an interval of 10 days, Figure 4) revealed a large lobulated heterogeneously enhancing mass measuring approximately 11.6 cm × 9.2 cm × 6 cm in the medial half of the right breast reaching up to the presternal area and involving the overlying skin as well as underlying chest wall. The lesion showed intensely increased fluorodeoxyglucose (FDG) uptake with maximum standardized uptake values of 18.24. Two small indeterminate lung nodules were also seen in the right lung parenchyma which were too small to be characterized. No size significant hypermetabolic right axillary lymph nodes were noted.

US-guided biopsy revealed a tumor comprising of neoplastic cells arranged around blood vessels and in sheets. Individual cells were small with scant, pale eosinophilic to finely vacuolated cytoplasm and fairly uniform round nuclei with coarse chromatin and inconspicuous nucleolus [Figure 5]. Few mitotic figures were seen. Tumor cells demonstrate the presence of intracellular

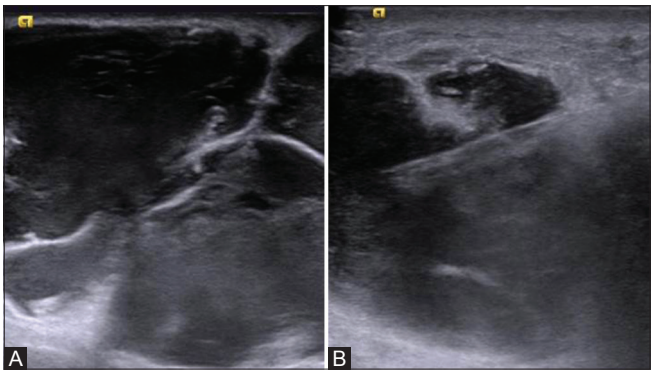

**Figure 2 (A and B):** Ultrasound (A) shows a large multilobulated hypoechoic to anechoic solid - cystic lesion. Ultrasound-guided biopsy (B) of the lesion was performed

glycogen. On immunohistochemistry (IHC): Tumor cells are: CD99 (Dako; 1.20E + 008): Positive, leucocyte common antigen (Dako; 21B11 + PD7/26): Negative, CK (Biogenix: AE1 + AE3): Negative, S-100 (Dako; IS504): Negative, Desmin (Dako; D33): Negative, Bcl-2 (Dako; 124): Positive. The morphological features and IHC profile favored an EES/PNET.

The patient was started on neoadjuvant chemotherapy (vincristine, cyclophosphamide, and doxorubicin) and post four cycles of chemotherapy there was more than 50% reduction in the size of the lesion [Figure 6].

The patient underwent a wide local excision of the right breast in February 2015.

## Discussion

ES and PNET form a single group of bone and soft-tissue tumors with typical undifferentiated ES at one end of the spectrum and PNET with clear evidence of neural differentiation at the other.[5] EES/PNET presenting as a breast mass is uncommon, with only a few cases been reported in the literature.[5,6] The majority of patients with EES/PNET are 10–20 years old, and other small studies of adult EES/PNET from the Royal Marsden, the Memorial Sloan Kettering, and the Dana Faber Cancer Centers have reported a median age of 24–27 years.[7-9] Our patient fell into the second age group.

Imaging modalities such as mammogram, US, MRI and PET-CT help in diagnosis, however, the imaging findings are nonspecific. The diagnosis is usually confirmed by histopathological and IHC examination.

Findings from mammography and ultrasonography breast images are variable as they could vary from a hypoechoic mass with a posterior enhancement to a heterogeneous mass with necrotic areas.[10,11] On mammography, a dense lobulated mass is usually seen. The reported CT

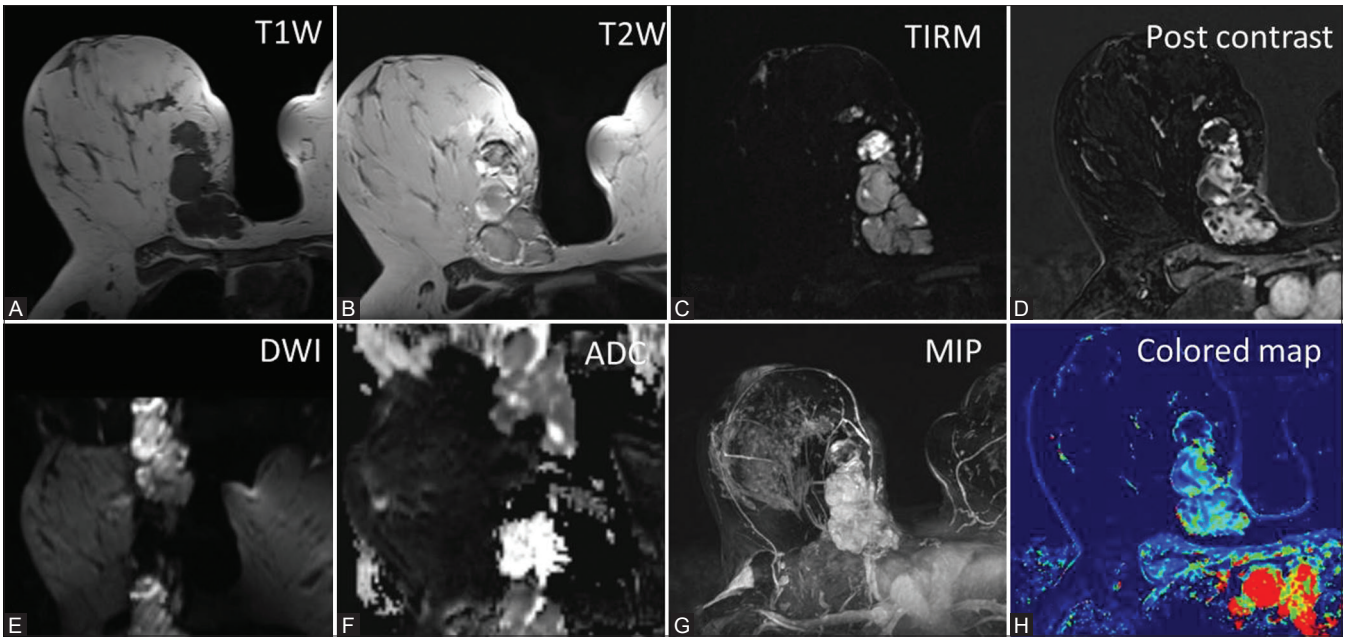


**Figure 3 (A-H):** The multilobulated lesion in the right breast appears hypointense on T1-weighted (A) and hyperintense on T2-weighted (B) and fat-saturated T2-weighted sequences (C) images and shows heterogeneous enhancement with few areas of necrosis within (D). It shows diffusion restriction on diffusion-weighted imaging and is dark on apparent diffusion coefficient maps (E and F). Maximum intensity projection (G) and colored maps (H) depicting the lesion

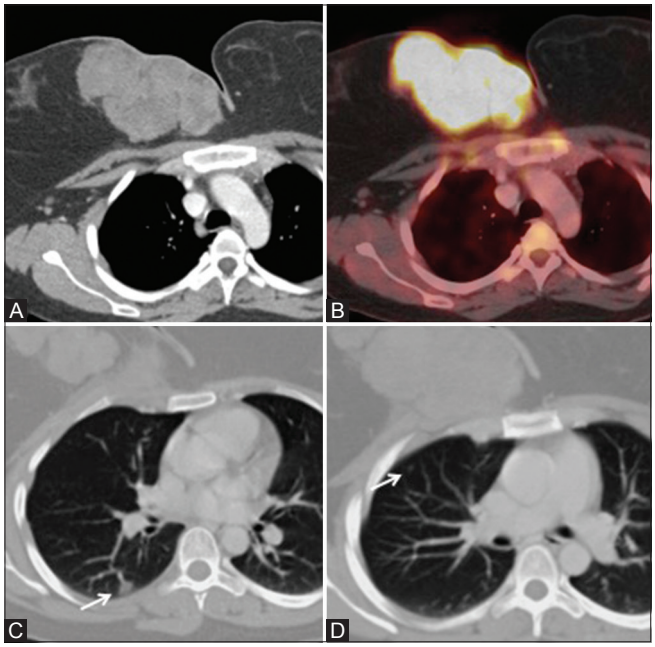


**Figure 4 (A-D):** (A and B) Positron emission tomography–computed tomography images revealed a large heterogeneously enhancing lesion in the right breast with intense fluorodeoxyglucose uptake, (C and D) two small indeterminate pulmonary nodules (white arrows) were seen in the right lung parenchyma

finding of EES is most commonly a heterogeneously enhancing mass.[12-14] Occasionally, a central, nonenhancing, low-density necrotic area is seen within the mass.[14] On MRI, EES is generally of low to isointense signal intensity compared to muscle on T1-weighted images, of high signal intensity on T2-weighted images, and exhibits heterogeneous enhancement.[15-17] Our case showed similar imaging findings on MRI. However, it is stated that the MR findings of this tumor are nonspecific.[3] In our case, the fat plane between the lesion and the chest wall was maintained on MRI, thus, ruling out the possibility of exophytic chest wall sarcoma. The utility of FDG-PET imaging has not been well established in the diagnosis and staging of soft tissue sarcoma. Our patient showed intensely increased FDG uptake. However, a case report of EES of the breast by Kim *et al*. showed falsely negative results on the PET scan.[18]

EES/PNET is an aggressive tumor with a high incidence of local recurrence and distant metastasis. A combination of multiple modalities, including surgery, chemotherapy, and radiation therapy, are the most appropriate treatment.[7]. All members of the ESFT tend to share the propensity for metastatic spread. Consistent use of systemic chemotherapy to treat localized ESFT effectively improved the 5-year survival rate from 5% to 10% to up to 65%, which is primarily due to the elimination of micrometastases.[19,20] In patients with unresectable or metastatic disease, palliative chemotherapy may be useful.

The role of radiation therapy in the treatment of ES/PNET is unclear. However, the use of radiation therapy combined with surgery, to control local disease, is proving to be helpful.[7] In our case, the patient was put on neoadjuvant chemotherapy which resulted in more

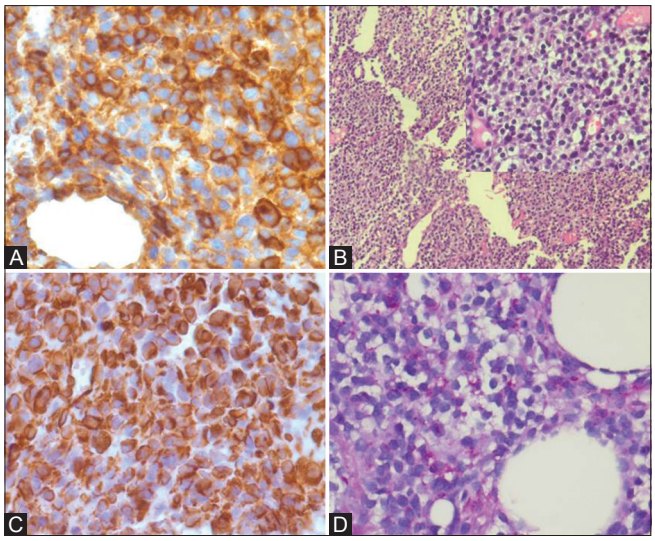

**Figure 5 (A-D):** Histology and immunohistochemistry (A) CD99-positive, (B) H and E, ×10: Small round cells arranged in sheets and perivascular location and inset picture H and E, ×40: Pale eosinophilic to clear cytoplasm and fairly uniform nuclei, (C) vimentin: Positive, (D) periodic acid-Schiff: Intracellular glycogen present

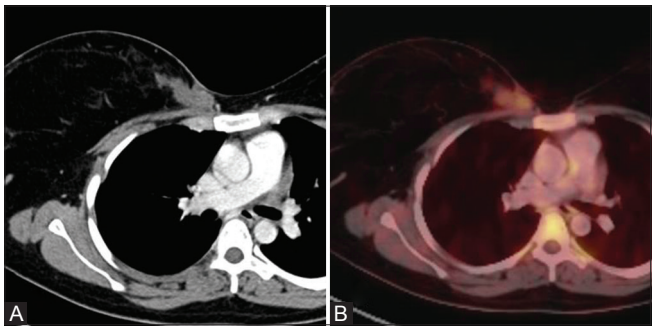

**Figure 6 (A and B):** (A and B) Positron emission tomography-computed tomography images postchemotherapy status showed reduction in the size and fluorodeoxyglucose avidity of the breast lesion

than 50% reduction of the tumor size and then a wide local excision of right breast was done. Bone scintigraphy has a role in ruling out local bone infiltration and skeletal metastasis.

## Conclusion

We report a case of recurrent EES/PNET presenting as a breast lump. Multiple imaging modalities such as mammogram, US, MRI, and PET-CT were used for diagnosis, and the definitive diagnosis was made by histopathological and IHC examination. MRI and PET-CT play a complimentary role in assessing local tumor resectibility and presence of metastatic disease. The EES/PNET of the breast is radiologically indistinguishable from other soft tissue tumors such as malignant phyllodes and therefore should be kept in the differentials for a recurrent/rapidly growing breast/chest wall soft tissue lesion.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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