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## Oncology

# Peripheral primitive neuroendocrine tumor of the chest wall—A case report with pathological correlation

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## ABSTRACT

Primitive neuroectodermal tumor is a high-grade malignant tumor originating from the neural crest and neuroectoderm, which can be subdivided into central and peripheral categories. Peripheral primitive neuroectodermal tumor is thought to be identical to Ewing's sarcoma, and falls under a broader category of Ewing's sarcoma family of tumors. Very rarely, it may present without osseous involvement, known as extraosseous Ewing's sarcoma. Here we present a case of a 38-year-old woman, who presented with several-month history of a slow-growing chest wall mass, initially thought to be a breast mass. The mass was diagnosed as extraosseous Ewing's sarcoma upon tissue biopsy. The patient was started on a dose-intensified neoadjuvant therapy, based on protocol from pediatric population given rarity of this tumor in the adult population. While the patient was initially planned for surgical resection, the tumor showed excellent response to chemotherapy on follow-up imaging, and radiation therapy was elected in lieu of resection.

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## Background

Primitive neuroectodermal tumor (PNET) is a high-grade malignant tumor originating from the neural crest and neuroectoderm. These tumors are separated into 2 broad classifications: central PNET and peripheral PNET [1]. Central PNETs occur primarily in the brain and spinal cord, with cells originating from the neural tube [2]. Peripheral PNETs, which are now thought to be virtually identical to Ewing's sarcoma (ES), originate from neural crest cells and occur outside the CNS [2]. Both tumors have a similar neural phenotype, share an identical

chromosome translocation t(11;22), and vary only by their degree of differentiation [3].

ES falls under a broader category of Ewing's sarcoma family of tumors, a family of morphologically similar small round-cell neoplasms [2]. It is the second most common malignant bone tumor of children and young adults. Rarely, it occurs as a primary soft tissue neoplasm without bone involvement, known as extraosseous ES (EO ES).

EO ES remains rare. There have been case reports of EO ES occurring in the kidney [4–6], GI tract [7–9], thyroid [10,11], vagina [12–14], and other more unusual locations such as the orbit [15], adrenal gland [16], and tonsil [17]. Fewer are seen in the

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thoracic region, with 1 reported case in the supraclavicular fossa [18], and a few seen in the lung [19,20]. Peripheral PNET or EO ES originating from the chest wall was previously classified as Askin tumor [21]. Here we report a case of EO ES in the anterolateral chest wall.

## Case report

A 38-year-old woman first presented to an outside hospital in August 2016 with a left lateral chest wall mass. The mass was firm, painless, and nonmobile. This was originally thought to be a breast mass, and patient underwent ultrasound-guided biopsy. During the biopsy, the mass was discovered to be deep to the breast tissue and within the chest wall. The mass slowly grew and, at the time of her presentation to Tufts Medical Center, the mass measured approximately 4.5 cm × 2.5 cm on palpation.

Patient's family history was significant for lung cancer in patient's grandfather, who was a lifetime smoker, and patient herself was a former 8-pack-year smoker. Otherwise no risk factor for malignancy was identified. Patient's review of systems was negative aside from the mass. Laboratory workup was unremarkable.

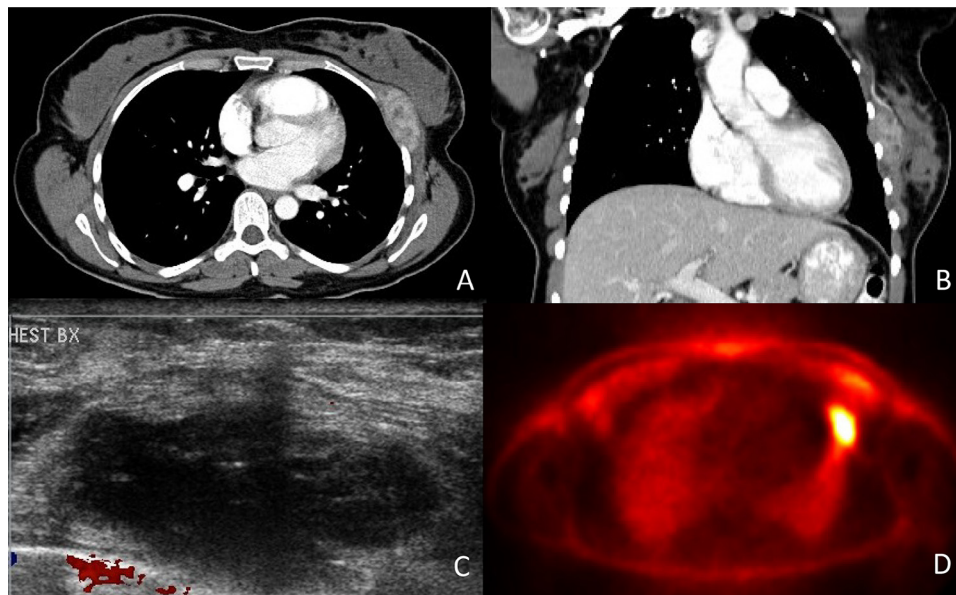
Ultrasound-guided biopsy of the mass and imaging workup revealed an EO ES of the left chest wall. The mass appeared oval, lobulated, and well-demarcated with heterogeneous hypoechoic echotexture during the ultrasound. Mild vascularity was demonstrated. On initial contrast-enhanced computed tomography (CT) of the chest, it appeared as a lobulated, heterogeneously enhancing mass in the left chest wall musculature without surrounding bony erosion, measuring 3.6 cm × 5.2 cm × 2.4 cm (Fig. 1). Biopsied tissue sample was

strongly and diffusely immunoreactive for CD99 and synaptophysin, and patchily positive for vimentin and CAM 5.2 (Fig. 2). The tumor cells were otherwise negative for pan Cytokeratin, epithelial membrane antibody, smooth muscle actin, Desmin, S100, chromogranin, CD45, CD3, and CD20. Positron-emission tomography-CT was performed for staging indicating SUV 7.53 within the left chest wall mass and no additional evidence of abnormal Fluorodeoxyglucose 18F uptake (Fig. 1). There was no apparent pathologic lymphadenopathy, involvement of the adjacent ribs, or distant metastasis. The tumor was staged as T4N0M0.

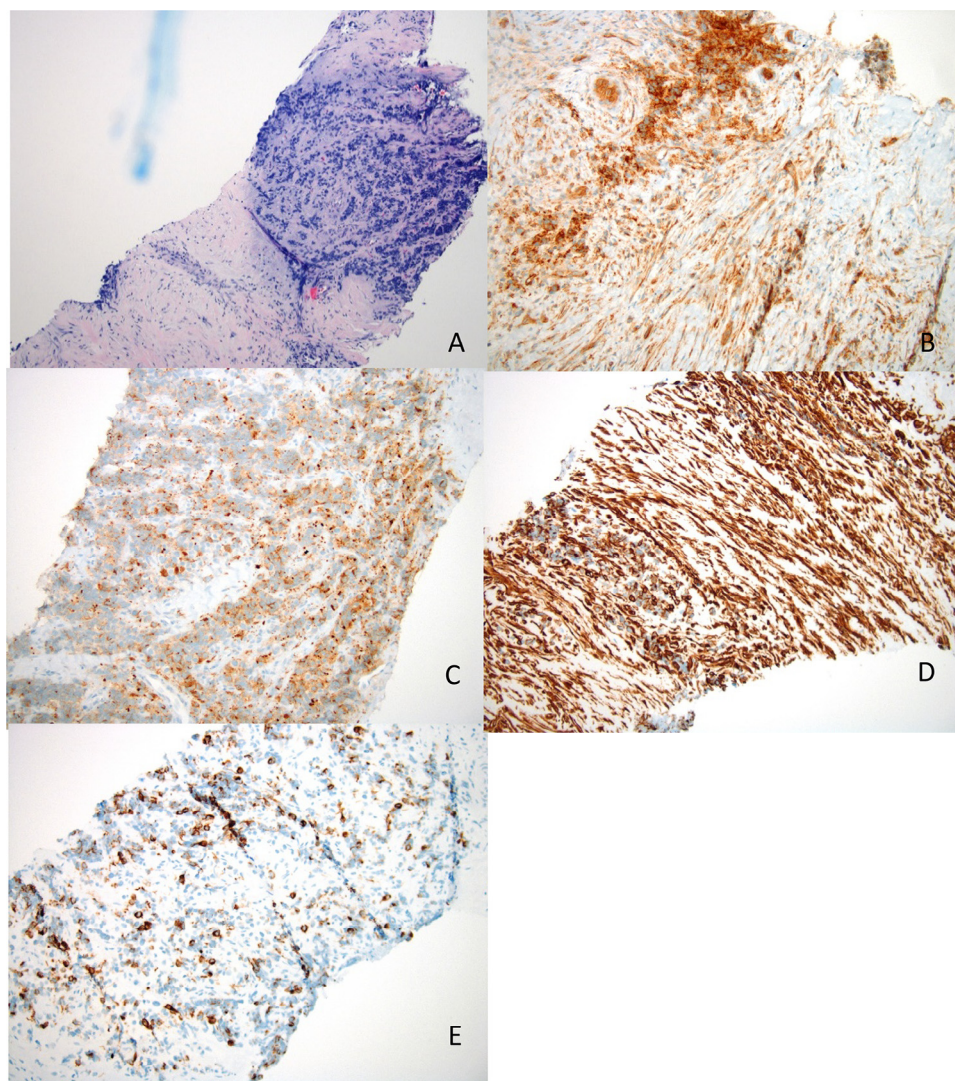
The patient was started on a dose-intensified neoadjuvant therapy regimen of vincristine-doxorubicin-cyclophosphamide alternating with ifosfamide-etoposide, a regimen protocol based on pediatric treatment experience given rarity of the disease in the adult population, with plan for subsequent surgical resection. At the time of this report, status post cycle 2 of neoadjuvant therapy, there was marked response to the chemotherapy regimen. Follow-up CT imaging revealed a decrease in size to 2.8 cm × 1.3 cm × 2.2 cm on April 10, 2017 (Fig. 3). Given dramatic response to chemotherapy, after discussion with patient, surgical resection was waived in lieu of radiation therapy.

## Discussion

Primitive neuroendocrine tumor can be subdivided into central and peripheral variety. EO ES belongs to the latter. The malignancy has primarily been observed in children and young adults, with various studies describing lower extremity and paravertebral soft tissue, or abdomen and pelvic region as the most common locations [22–26]. Thoracic or chest wall



**Fig. 1 – (A, B) Initial CT reveals a lobulated, heterogeneously enhancing mass in the left chest wall musculature without surrounding bony erosion. (C) Images taken at the time of ultrasound-guided biopsy also reveal an oval, lobulated, and well-demarcated mass with heterogeneous hypoechoic echotexture. (D) Staging positron-emission tomography shows a corresponding mass with FDG-avidity up to 7.53 SUV.**



**Fig. 2 – (A) Hematoxylin and eosin stain shows small-blue-round cells, characteristic of Ewing’s sarcoma family tumors. (B-E) Tissue sample was strongly and diffusely immunoreactive for CD99 and synaptophysin, and patchily positive for vimentin and CAM 5.2, respectively.**

involvement in the adult population is extremely rare with a few case reports in the literature. Most common presenting symptoms are an enlarging mass, followed by pain [27].

Radiological appearance of the tumor is largely nonspecific as are most sarcomas. The tumor typically appears as heterogeneously enhancing low-attenuation mass on CT, heterogeneously hypoechoic on ultrasound, and T1 isointense and T2 hyperintense to muscles with heterogenous gadolinium enhancement on MR. The masses are typically noncalcified and appear well-demarcated owing to the presence of a pseudocapsule [28].

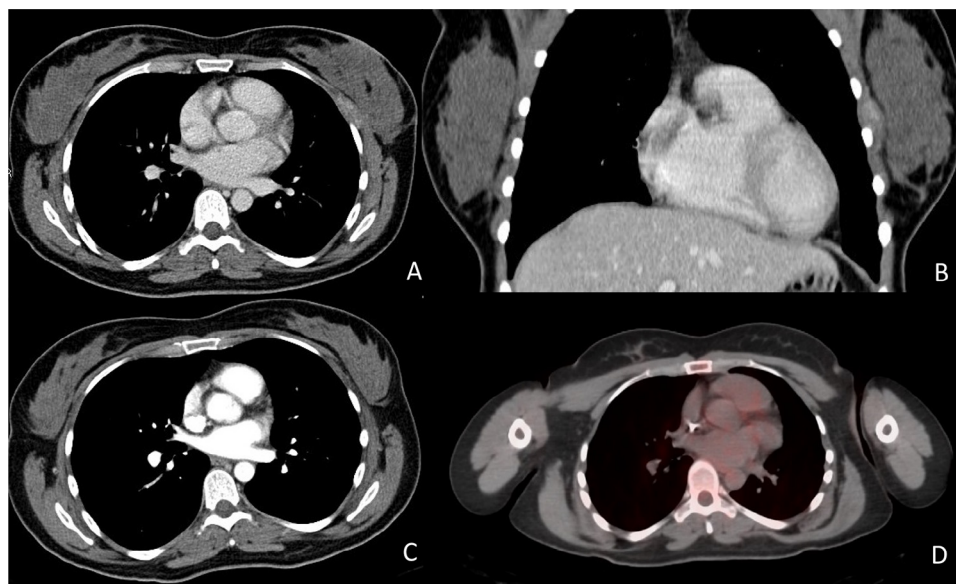
Favorable prognostic factors include localized disease and subcutaneous location of the tumor [27]. Elevated LDH at time of presentation has been shown to be poor prognostic factor in multiple studies, thought to reflect tumor burden [24,25]. One study also showed anemia and leukocytosis as poor prognostic factors [26].

Treatment regimen of EO ES is currently still largely based on pediatric data, with neoadjuvant chemotherapy followed by surgical resection or radiation therapy. Recent study has shown improved survival with a dose-intensified regimen [29].

## Conclusion

Chest wall EO ES is a rare diagnosis, and can be mistaken for breast mass on physical examination alone. Given potential for metastasis with associated markedly poor prognostication, appropriate workup with early diagnosis and treatment is essential. Given rarity in the adult population, current treatment and follow-up care are based on pediatric data.





**Fig. 3 – (A, B) Chest computed tomography (CT) following 2 cycles of chemotherapy shows decrease in size of the chest wall tumor. (C, D) Chest CT and positron-emission tomography-CT following 6 cycles of chemotherapy show complete resolution of the tumor, without residual tumor or local FDG-avidity.**

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