

FDG PET scan in a primitive neuroectodermal tumor

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Primitive peripheral neuroectodermal tumor (PNET) is a rare tumor that often arises in soft tissue. Magnetic resonance imaging is a good diagnostic tool that can establish the extent of disease. The utility of positron emission tomography (PET) using F-18-fluoro-2-deoxy-D-glucose (FDG) in the diagnostic work-up and staging of PNET has not been well established. We present a case of PNET of the right upper extremity that did not show FDG uptake despite its large size and aggressive nature.

Key words: primitive peripheral neuroectodermal tumor, FDG PET scan, soft tissue sarcomas

INTRODUCTION

PRIMITIVE PERIPHERAL NEUROECTODERMAL TUMOR (PNET) is one of the tumors in the Ewing's sarcoma family of tumors, which also includes Ewing's sarcoma, extra osseous Ewing's sarcoma, adult neuroblastoma, malignant small-cell tumor of the thoracopulmonary region (Askin's tumor), paravertebral small-cell tumor, and atypical Ewing's sarcoma. They are considered to arise from a common origin, neuroectoderm. Patients with PNET typically present with localized pain or swelling of a few weeks or months duration.

The diagnostic work-up is usually initiated with a plain radiograph. Definition of tumor size and extent is best achieved by magnetic resonance imaging (MRI). The role of positron emission tomography (PET) using F-18-fluoro-2-deoxy-D-glucose (FDG) in the diagnostic work-up has not yet been clearly established.

CASE REPORT

A 36-year-old Caucasian female with a complicated past medical history that included Type 1 diabetes mellitus, idiopathic pancreatitis, cirrhosis, cholangiopathy with

biliary obstruction requiring multiple stent placements, psoriasis, and hypersplenism was seen at our clinic. She had noticed a small nodule on her right lower forearm about 4 years prior to this presentation. At that time, the area around the nodule felt hot and had been treated as cellulitis. However, over the preceding 3 months she noticed a rapidly growing mass in the same area associated with pain. Clinical examination showed a 14 cm mass over the right volar forearm.

Bone scan

A technetium-99m-methylene diphosphonate (Tc-99m MDP) bone scan was performed and the blood pool images showed a large area of photopenia in the right proximal forearm corresponding to the area of mass with some hyperemia near the periphery, mostly seen proximally (Fig. 1A). The delayed images showed heterogeneous areas of increased bone scan activity in the region of the mass (Fig. 1B).

MRI scan

A contrast enhanced MRI scan revealed a 5.1 × 4.2 × 11.0 cm multilobulated forearm mass with prominent peripheral enhancement and a central non-enhancing component (Figs. 2, 3A, and 3B). The mass was centered at the flexor digitorum profundus and did not seem to involve the underlying osseous structures.

Computed tomography (CT) scan

A CT scan of the chest, abdomen, and pelvis revealed five nodules within the right lung. All the nodules were

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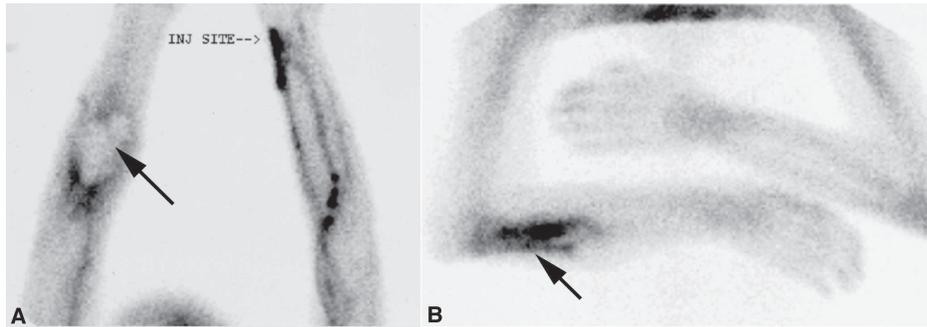


Fig. 1 (A) Tc-99m MDP blood pool image showing a large photopenic area with a peripheral rim of enhancement in the right proximal forearm corresponding to the area of a mass. (B) Delayed images show a heterogeneous pattern of increased activity.

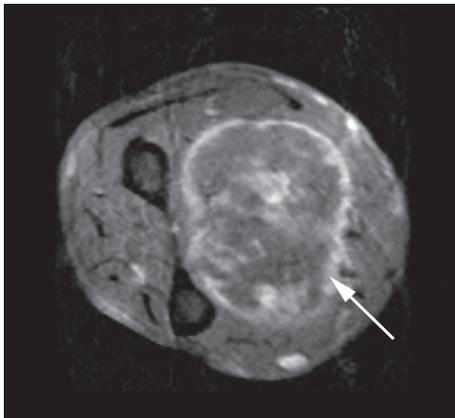


Fig. 2 Axial post gadolinium T1 with fat suppression MRI demonstrates a soft-tissue mass with peripheral and heterogeneous central enhancement.

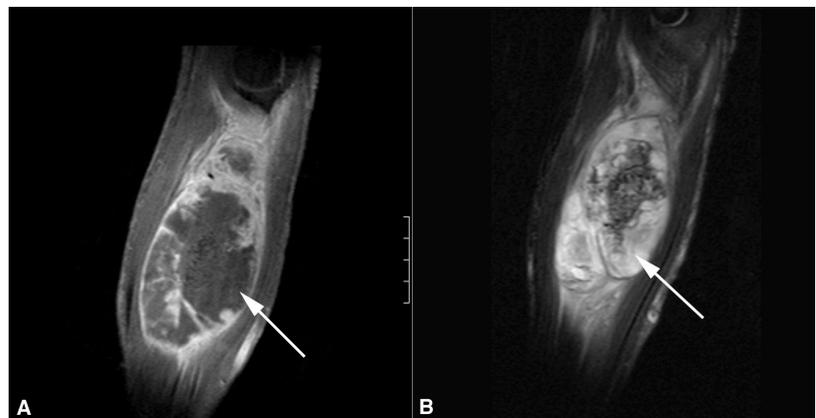


Fig. 3 (A) Sagittal post gadolinium T1 with fat suppression MRI demonstrates a soft-tissue mass with predominantly peripheral enhancement. (B) T2 fat suppressed sequence demonstrates increased signal in the peripheral and a low signal central portion.

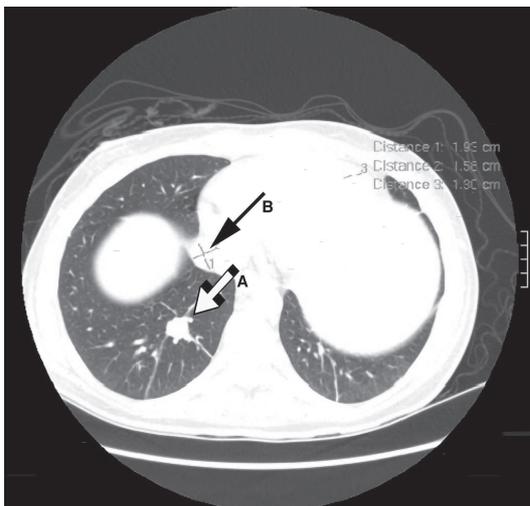


Fig. 4 CT scan of the chest shows a spiculated pulmonary nodule (arrow A) and a pleural-based soft-tissue lesion along the diaphragm (arrow B).

approximately 1–1.5 cm in size. There was no associated lymphadenopathy (Fig. 4).

Core needle biopsy

The biopsy showed undifferentiated small cells arranged in sheets (Fig. 5). There were areas of metaplastic cartilage and bone that was focally calcified (Fig. 6). There was no rosette formation. Immunohistochemical stains for keratin, actin, and desmin were negative within the tumor cells. There was focal staining for S100 and CD57. Most of the tumor in the densely cellular primitive area stained intensely for CD99 (MIC 2) (Fig. 7). These findings were consistent with PNET.

FDG PET imaging

A FDG PET scan was subsequently acquired. There was mild, diffuse, increased activity throughout the muscles secondary to insulin administration (insulin was administered to lower the serum glucose to <250 mg/dl). However, it did not reveal any increased FDG uptake in the

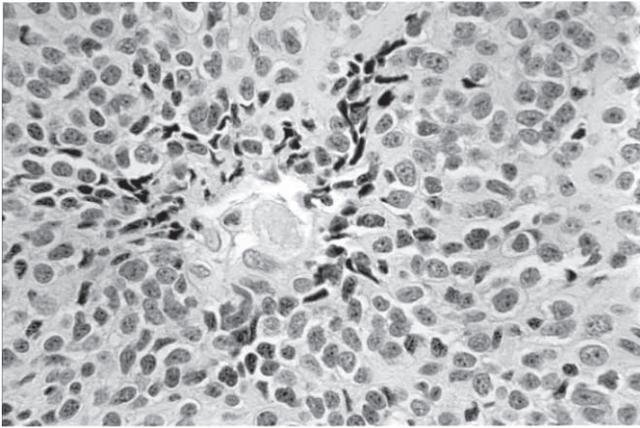


Fig. 5 Histology of biopsy specimen (hematoxylin and eosin staining) shows a tumor consisting of undifferentiated small cells arranged in sheets.

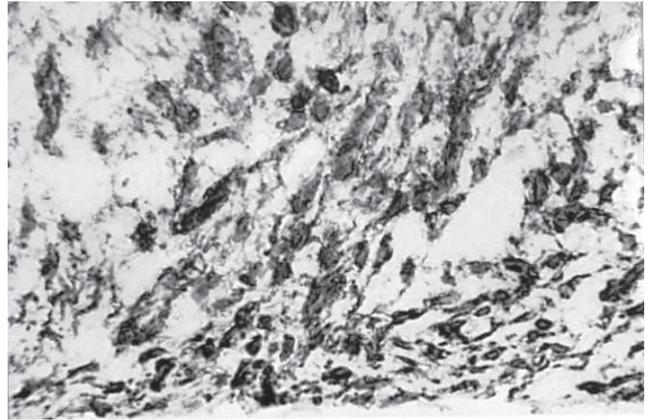


Fig. 7 Immunohistochemical staining revealed strong positive staining for CD99 ($\times 400$).

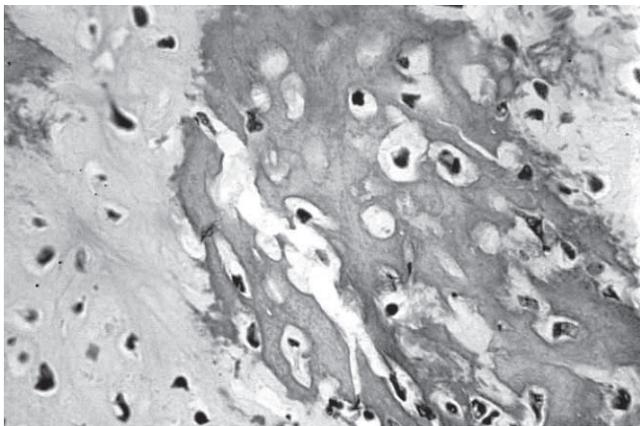


Fig. 6 Metaplastic cartilage and bone, which is focally calcified (hematoxylin and eosin staining $\times 400$).

large right forearm soft tissue mass or within the multiple lung nodules (Fig. 8). The patient was chemoradiotherapy naïve at the time of the PET scan.

Treatment and follow-up

She was started on chemotherapy and radiation treatment to her right arm. A follow-up MRI of upper extremities showed severe spread of tumor by original extension and infiltration into the axilla, scapular musculature, and underlying rib cage, and a CT scan of the chest showed significant worsening of pulmonary and parenchymal metastatic disease. She was enrolled in a hospice and subsequently died.

DISCUSSION

PET scanning of known or suspected malignancy is usually performed after administration of F-18 fluoro-deoxy-glucose, an analog of glucose.¹ Our patient had a rapidly growing mass over a 4-month period that was

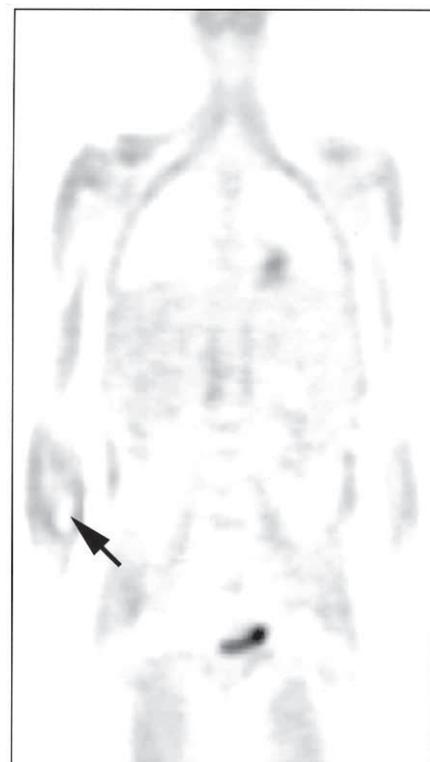


Fig. 8 FDG PET scan shows no increased FDG uptake in the region of the right forearm mass (arrow) or in the lungs.

histologically confirmed to be PNET.

The utility of FDG-PET imaging has not been well established in the diagnosis and staging of soft tissue sarcomas in general and specifically in PNETs. Schwarzbach and colleagues looked at 19 patients with primary sarcomas and 28 patients with 37 suspected recurrences.² The 19 primary tumors included 11 soft tissue sarcomas, 7 benign tumors, and 1 inflammatory mass. However, none of the patients had PNET. The calculated sensitivity of FDG-PET imaging in this group

was 91% and the specificity was 88% for detecting soft tissue sarcomas, while for recurrent tumors FDG-PET had a sensitivity of 88%. The standardized uptake value (SUV) was increased with higher tumor grade but had no correlation to tumor size. SUVs could be used to distinguish between different tumor grades. However, PET did not visualize one low-grade liposarcoma in this series.

Nieweg and colleagues performed FDG-PET scans in 18 patients with soft-tissue sarcoma and 4 patients with a benign soft-tissue lesion. SUVs were calculated. However, no correlation was found between the SUVs and histopathologic malignancy grade.³ They concluded that PET with FDG is an effective technique to visualize soft-tissue sarcomas with a sensitivity of 100%. However, it appeared to be unsuitable for discriminating benign lesions from soft-tissue sarcomas with low or intermediate malignancy grades. Benign lesions could be distinguished from high-grade malignant lesions, but not consistently from lesions with low or intermediate malignancy grades.

Aoki and colleagues⁴ reported a series of 120 soft-tissue sarcomas (85 benign and 35 malignant). A statistically significant difference was observed in SUVs between benign and malignant tumors. However, a considerable overlap in SUV was observed between many benign and malignant lesions. They concluded that SUVs might not accurately reflect the malignant potential of soft-tissue tumors.

Meltzer and colleagues reported a case of a 30-year-old man who had recurrent PNET of the spinal cord.⁵ A FDG PET scan revealed increased uptake in the recurrent tumor. Czekalla and colleagues reported the case of a 14-year-old boy with a PNET of the stomach.⁶ A PET scan demonstrated intense hypermetabolism of the gastric tumor and foci of metastases in the liver. The patient that we report had a peripheral PNET, which despite its aggressive nature, evidenced by rapid growth, contrast enhancement on MRI and its large size, failed to demonstrate any significant FDG uptake. Although the multiple pulmonary nodules were not histologically confirmed, the significant increase in size of the nodules and the appearance of new nodules in the interim on a 5-month follow-up CT scan of the chest implies that the nodules were metastatic in etiology. These multiple metastatic nodules also failed to demonstrate any significant FDG uptake.

The reason for the difference in FDG uptake by a peripheral PNET (ametabolic/hypometabolic observed in our patient) as opposed to the hypermetabolic centrally occurring PNET observed by Meltzer et al. is uncertain, but it may be related to differences in the biological behavior and metabolic profiles of a PNET of a central nervous tissue as compared to that of a PNET arising in the periphery. In addition the PNET in our patient was much better differentiated on histology showing metaplastic bone and cartilage as opposed to the cases reported by Meltzer et al. and Czekalla et al. Well-differentiated tumors are known to be less FDG avid.⁷ The histology of

the PNET in our patient demonstrated components of metaplastic cartilage and bone with focal calcification, suggesting a well-differentiated tumor. This may partly explain its poor FDG uptake. In addition, dispersed and isolated islands of densely cellular tumor were identified on histology, as opposed to large masses of tumor cells. The relatively poor resolution of PET imaging may not be able to optimally detect the increased activity arising from dispersed microscopic islets of tumor cells.

Enhanced glucose (and therefore FDG) uptake and metabolism by cancer cells are postulated to be due to overexpression of glucose transporters, especially Glut-1, resulting in increased glucose transport into cells and overexpression of hexokinase enzymes, such as hexokinase II, that phosphorylate glucose to glucose-6-phosphate.⁸ Both relatively aggressive (e.g., bronchoalveolar carcinoma)⁹ and less aggressive (e.g., prostate carcinoma)¹⁰ tumors have been reported to be falsely negative by FDG-PET, probably due to underexpression of Glut-1 glucose transporter and/or hexokinase II enzyme. Some other tumors known for being less FDG-avid include approximately one-third of hepatocellular carcinomas, carcinoids, primaries arising from the kidneys and bladder, mucus secreting adenocarcinomas, etc. The absence of FDG uptake by the tumor in our patient can be postulated to be due to underexpression of Glut-1 transporter and/or hexokinase II.

CONCLUSION

The use of FDG-PET scanning for the diagnosis and staging of soft-tissue sarcomas has not yet been well established. There are conflicting reports of the accuracy of SUV discrimination between low and high-grade soft-tissue sarcomatous lesions. In our patient, the PNET involving the right forearm, despite being large and aggressive, was falsely negative on the FDG-PET scan. Likewise, the presumed multiple pulmonary metastases were negative. To our knowledge this is the second case report of whole body FDG PET in peripheral PNET and the first reported case of a peripheral PNET arising from muscle.

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