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Ewing's Sarcoma Omental Odyssey: Unraveling Rare Metastasis and Unforeseen Treatment Outcome on FDG PET/CT: Case Report with Review of Literature

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Abstract

Ewing's sarcoma is an uncommon and highly metastatic form of sarcoma affecting children and young adults, occurring in approximately 1 in 1.5 million individuals, with a predominance in males. We present an exceptionally unique case highlighting Ewing's sarcoma metastasis to the peritoneum and omentum, identified through an ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) scan and its unforeseen treatment response. In contrast to previously published literature concerning primary peritoneal primitive neuroectodermal tumors, this exceedingly notable instance illuminates the occurrence of metastatic Ewing's sarcoma within the peritoneum, as opposed to originating as a primary tumor within the peritoneum, revealing diagnostic intricacies. This case accentuates several pivotal learning points that enhance our understanding of Ewing's sarcoma. Also, the noteworthy high sensitivity and specificity of ^{18}F-FDG PET/CT allow for early detection of recurrence and treatment response, substantially improving prognosis in Ewing's sarcoma patients, aiding in timely therapeutic interventions and optimizing patient outcomes.

Keywords
- FDG PET/CT
- Ewing's sarcoma
- omentum
- metastasis
- case report

Introduction

Ewing's sarcoma is an uncommon and aggressive malignancy in children and young adults, occurring in approximately 1 in 1.5 million individuals and is predominant in males.[1,2] ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) is the emerging imaging modality utilized for pretreatment staging, therapy response assessment, and evaluation for recurrence.[3,4] Previous studies have analyzed the effectiveness of ^{18}F-FDG PET/CT for initial staging with critical results.[5–9] PET imaging is more sensitive than conventional bone scans for detecting bone metastases.[7,9] Integrated PET/CT outperforms thoracic CT for lung metastases rather than PET alone.[7,8,10]

Here, we present an exceptionally unique case highlighting Ewing's sarcoma of the right tibia that metastasized to the peritoneum and omentum. This is exceedingly uncommon and was identified through an ^{18}F-FDG PET/CT scan and its unforeseen treatment response.

Case Report

A 9-year-old boy presented with a painful and progressively increasing swelling of the right lower leg for 3 months. He had constitutional symptoms, loss of appetite, weight loss, and fever (39.5°C). He was diagnosed with tibial osteomyelitis, and antibiotics were prescribed. He showed no response

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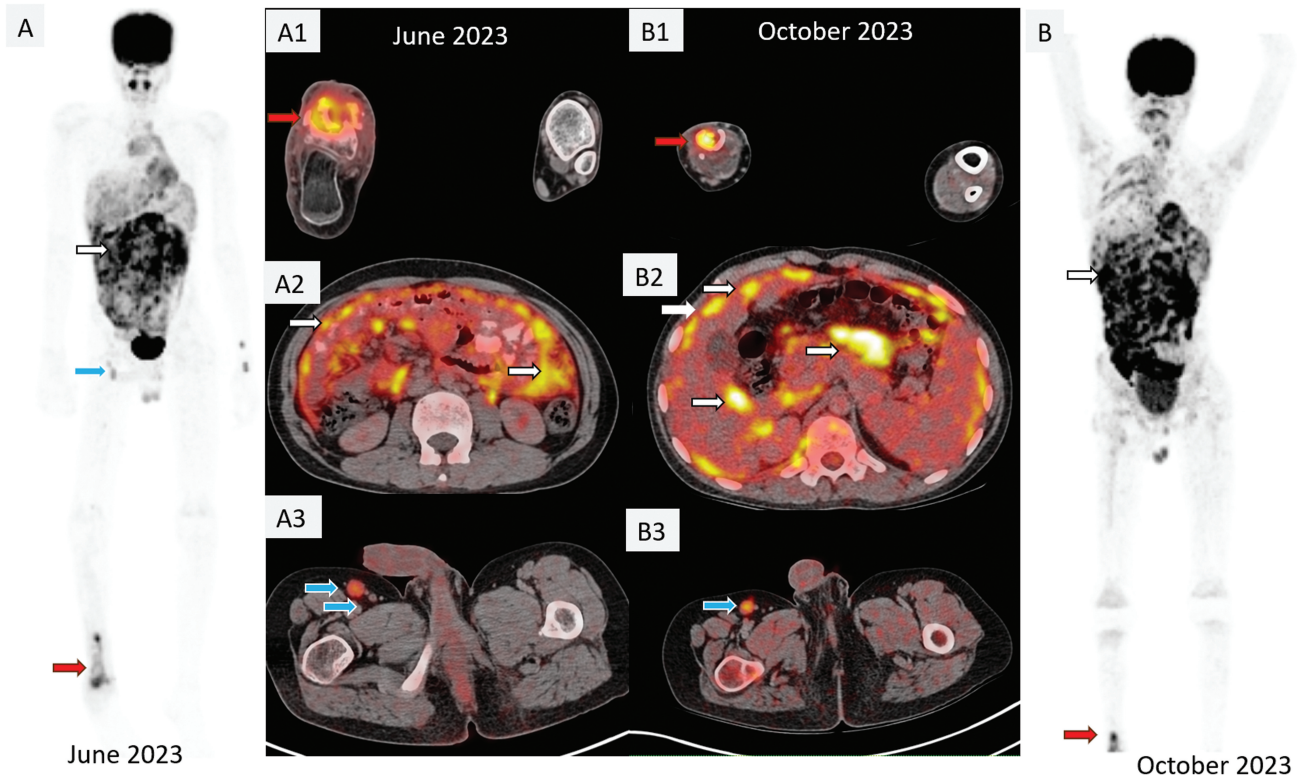

Fig. 1 (A) Baseline whole-body maximum intensity projection image shows a lesion involving the distal right tibia (red arrow), diffuse abdominal uptake (white arrow), and right inguinal lymph nodes (blue arrow). Corresponding fused positron emission tomography/computed tomography (PET/CT) images show A1: fluorodeoxyglucose (FDG)-avid (standardized uptake value maximum [SUV max] 3.0) large lytic lesion involving distal right tibial metaphysis with soft tissue component involvement. It is associated with extraosseous component involvement (red arrow). A2: FDG-avid (SUV max 4.5) multiple variable-sized omental and peritoneal deposits (white arrow). A3: FDG-avid right inguinofemoral lymph node (blue arrow). Follow-up PET/CT MIP images (**B**) and B1 show residual lesions in the lower one-third of the right tibia (red arrow). Fused PET/CT in the abdomen region (B2) shows extensive FDG-avid variable-sized omental and mesenteric deposits (white arrow). B3: FDG-avid right inguinofemoral lymph node (blue arrow).

to the administered antibiotics. A magnetic resonance imaging (MRI) scan of the leg demonstrated cortical destruction with marrow edema in the lateral posterior aspect of the right distal tibial metaphysis. Soft tissue thickening and perilesional edema were observed. Biopsy and immunohistochemistry were performed for diagnosis. These techniques indicated the presence of the biomarkers CD99, NKX2.2, and FLI-1, while being negative for the biomarkers PanCK and LCA, consistent with Ewing's sarcoma.

The patient underwent three uneventful cycles of chemotherapy (vincristine, cyclophosphamide, doxorubicin, and ifosfamide), followed by wide local excision with extracorporeal radiation and reimplantation. A follow-up MRI revealed heterogeneously enhancing soft tissue in the distal tibial epiphysis and tibiotalar joints with the involvement of adjacent muscles and tendons. These sites are prone to recurrence. Hyperintensity was present in the posterior compartment of the leg muscles with no evidence of cortical destruction. An ^{18}F-FDG PET/CT scan was performed to evaluate possible recurrence and restaging. It revealed a heterogeneous FDG-avid large lytic expansile lesion in the right distal tibial metaphysis. An intramedullary soft tissue component is noted with a permeative lesion of the medial cortex. FDG-avid extensive variable-sized omental and peritoneal soft tissue lesions were observed, which raised suspicion of metastasis in the patient's body (►**Fig. 1**). Histopathology confirmed omentoperitoneal involvement in the tumor.

Subsequently, he underwent gemcitabine and docetaxel-based chemotherapy. Follow-up PET/CT scan revealed a metabolically active, destructive, expansile, and lytic lesion with a soft tissue component in the right tibia. Multiple novel metabolically active mediastinal, abdominopelvic, and right inguinal lymph nodes, along with extensive FDG-avid up to centimeter-sized bilateral lung nodules were observed. Omental and mesenteric deposits showed an increase in avidity. The overall scan showed disease progression (►**Fig. 1**).

The patient underwent periosteal scraping followed by targeted therapy, that.is, pazopanib. The patient eventually exhibited clinical improvement. A follow-up ^{18}F-FDG PET/CT scan revealed postsurgery changes with thickening in the postoperative region of the right distal tibia, suggestive of residual primary tumor. Peritoneal deposits showed a partial treatment response (►**Fig. 2**). However, compared to the previous PET/CT scan, there was an observed increase in number and size of the previously observed lymph nodes and lung lesions. Lung lesions showed areas of consolidation and cavitation that raised a possibility of coexisting infection. On further evaluation, the patient was found to have increased levels of β-galactomannan, serum immunoglobulin G levels against *Aspergillus*, and his sputum showed fungal hyphae. The

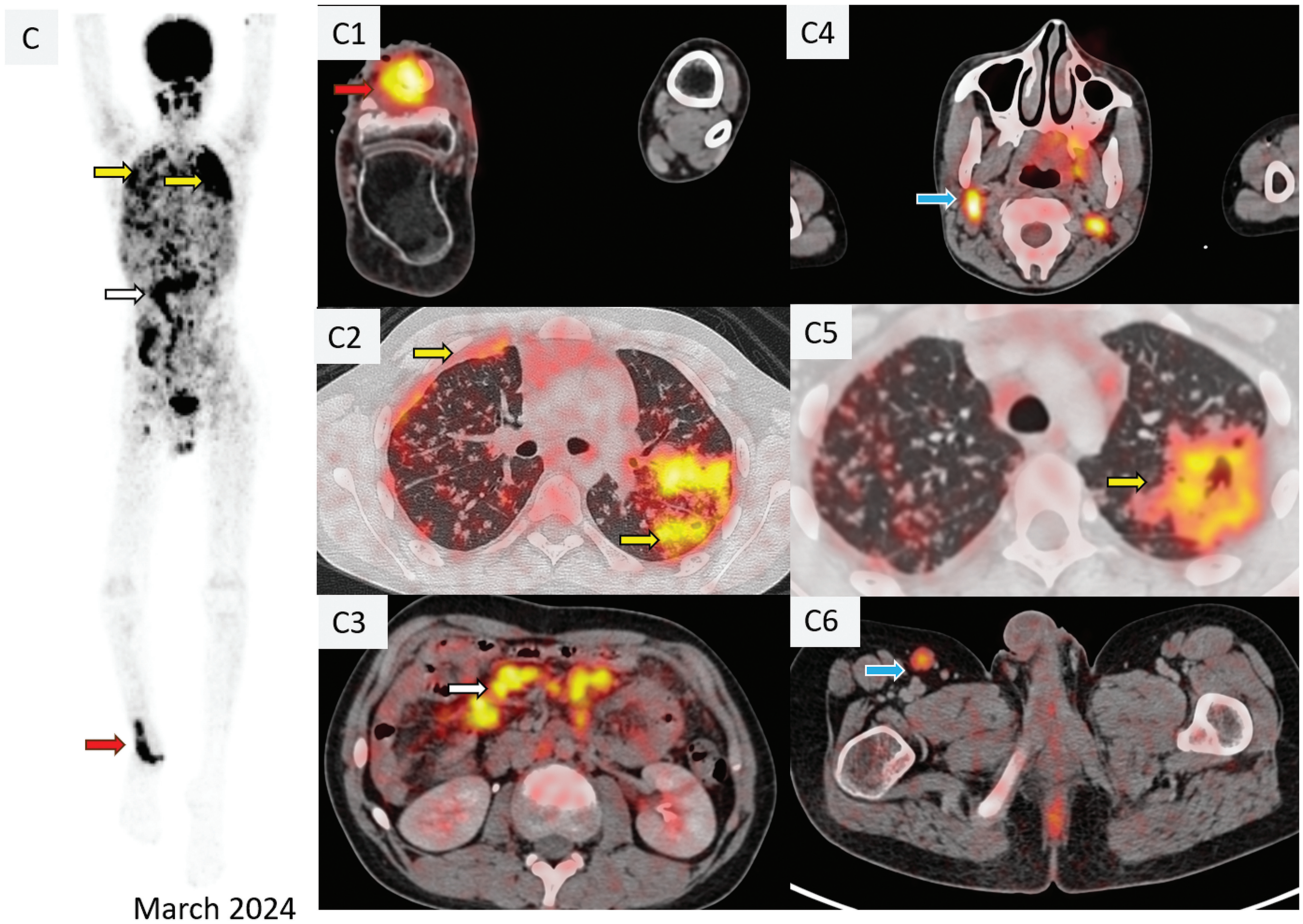

Fig. 2 End of treatment maximum intensity projection image of ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) (**C**) shows the lesion in the right leg (red arrow), extensive lung lesions (yellow arrow). C1: FDG-avid lytic lesion with marrow infiltration and soft tissue component is noted involving the distal shaft of the right tibia. C2: FDG-avid pleural thickening (yellow arrow). C3: FDG-avid omental and peritoneal deposits (white arrow). C4: FDG-avid enlarged cervical lymph nodes (blue arrow). C5: FDG-avid multiple soft tissue nodules in the random distribution in bilateral lung fields with thick-walled cavitary lesions (yellow arrow). C4: FDG-avid right inguinofemoral lymph node (blue arrow).

bronchoalveolar lavage revealed a pulmonary fungal infection, and antifungal treatment, caspofungin, was initiated.

Discussion

Ewing's sarcoma usually initiates in long bones, primarily affecting the femur, tibia, fibula, and humerus.[11,12] Ewing's sarcoma tends to relapse locally and at distant metastasis. Distant metastases involve the lung, bone, and bone marrow.[13] Other sites include lymph nodes, pleura, peritoneum, viscera, and brain.

Here in our case, a 9-year-old boy had a local recurrence postwide local excision and CT. He had extensive metastases to the omentum and peritoneum without lung and bone metastases. Extra-osseous omental Ewing's sarcomas like in this case are sparingly reported.[14] Our case is a first-of-its-kind case elucidating Ewing's sarcoma metastasis to omentum and peritoneum, diagnosed with the help of ^{18}F-FDG PET/CT scan.

Huh et al evaluated the metastatic pattern in 70 patients with Ewing's sarcomas and revealed a 13.8% occurrence of peritoneal metastasis.[15] Sharma et al analyzed the role of ^{18}F-FDG PET/CT scan in 71 patients with Ewing's sarcoma and found recurrence in 42 (59.1%) patients. The most common finding was local recurrence (38 patients), followed by bone (9 patients), lymph nodes (2 patients), and lung metastasis (2 patients).[16]

Our patient presented with extensive asymptomatic peritoneal and omental involvement, which was picked up by an ^{18}F-FDG PET/CT scan. Albano et al have demonstrated higher diagnostic accuracy in ^{18}F-FDG PET/CT than CT for pediatric Ewing's sarcoma.[17] Another study evaluated treatment response, predicted outcomes, and supported decisions on modifying therapy.[18] In the follow-up, there was partial treatment response in the peritoneal lesion with the appearance of multiple lung lesions and nonregional lymph nodes accompanied by metabolically active thickening of the right-sided pleura, which later turned out to be fungal etiology. False-positive results of PET/CT were noted in the inflammation and infection sites, as inflammatory cells may exhibit heightened FDG uptake. This mechanism of FDG uptake in inflammatory cells closely resembles that in tumors despite the differing circumstances.[19,20] However, this false-positive PET for malignancy significantly impacts the treatment. Most

of the patients receiving chemotherapy are immunocompromised, with changes in rapid dissemination of the infectious process. Symptomatology of primary malignancy and chemotherapeutical side effects may conceal an underlying infection that is unveiled by PET/CT. This case illustrates that correlating with clinical data, along with utilizing PET/CT with more specific biochemical tests, is imperative for distinguishing malignancy from benign conditions such as fungal/granulomatous infection. This case highlights rare metastases in Ewing's sarcoma, emphasizing FDG PET/CT's role. Limited by single-case data, future studies should explore underlying mechanisms, prognostic implications, and therapeutic strategies for broader applicability.

Conclusion

Ewing's sarcoma may have asymptomatic extensive metastases, and a whole-body functional imaging FDG PET/CT is imperative for pretreatment staging. A follow-up PET/CT for response evaluation after initial treatment evaluates the residual disease burden and possible progressive disease. It may also disclose several underlying inflammatory and infective pathologies. Understanding these insights can undoubtedly guide future clinical approaches, leading to more effective management and contributing to amplified clinical decision-making and improved patient care.

Authors' Contributions

P.S. conceptualized and designed the study, Y.K. edited the manuscript editing, M.O. edited and revised the manuscript, and S.S. performed research and collected the literature.

Ethical Approval

This study received ethical approval from the Institutional Ethics Committee (IEC).

Patient's Consent

The authors confirm that all necessary patient consent forms have been obtained. The patient has provided written permission for their medical images and clinical details to be included in this publication. They have been informed that their identity will be protected by withholding their name and initials.

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None.

Conflict of Interest

None declared.

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