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Research Article

Can 18F-FDG PET/CT Replace Bone Marrow Biopsy in the Rhabdomyosarcoma Patients?

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Abstract

Objectives: To evaluate role of 18F-fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography (18F-FDG PET/CT) in assessing bone marrow involvement in rhabdomyosarcoma (RMS) patients, and whether 18F-FDG PET/CT findings render invasive bone marrow biopsy (BMB) unnecessary.

Materials and Methods: This retrospective study included 20 patients (age < 20 years) with biopsy-proven RMS who underwent 18F-FDG PET/CT and BMB for initial staging between August 2018 to December 2020. The 18F-FDG PET/CT scans were evaluated for bone marrow involvement and compared with the BMB results.

Results: The 18F-FDG PET/CT findings and BMBs excluded bone marrow involvement in 19/20 patients. In the remaining patient, 18F-FDG PET/CT suggested metastatic bone marrow involvement, and BMB detected marrow invasion by malignant cells. Thus, for evaluation of bone marrow involvement, 18F-FDG PET/CT showed a specificity and negative predictive value of 100%, suggesting that BMB may be unnecessary.

Conclusions: 18F-FDG PET/CT showed a high specificity and high negative predictive value for detecting bone marrow metastasis in RMS patients, and its use could preclude the need for invasive BMB. However, further studies are required, as our present work had certain limitations.

Keywords: Rhabdomyosarcoma; FDG PETCT; Bone Marrow Biopsy; Pediatrics

Introduction

Sarcomas include bone and Ewing's sarcomas, peripheral primitive neuroectodermal tumors, and soft-tissue sarcomas. Soft-tissue sarcomas can develop anywhere in the body, but the extremities are the most common sites [1]. Over fifty histological types of soft-tissue sarcomas have been described, including malignant fibrous histiocytoma, leiomyosarcoma, synovial sarcoma, malignant peripheral nerve sheath tumor, and rhabdomyosarcoma (RMS) [2,3]. RMS is most common during childhood but can develop

at any age [4,5]. RMS originates from cells that develop into striated muscles, the most common sites being the head-and-neck region, genitourinary tract, and limbs. However, given its embryonic mesenchymal origin, RMS may develop anywhere. Numerous patients present with localized disease, but approximately 20% present with distant metastases involving the lungs, bone marrow, and bone and distant lymph nodes [6-10]. The cure rate for patients with localized disease is approximately 70%, whereas the prognosis of patients with metastases is poor [11-14]. Accurate staging has both prognostic and therapeutic implications. Newly diagnosed cases are usually evaluated by cross-sectional imaging (magnetic resonance imaging [MRI] or computed tomography [CT]) of the primary tumor, chest CT, radionuclide whole-body bone scanning, and pelvic bone marrow biopsy (BMB) [15]. BMB is an invasive staging procedure required to confirm bone marrow metastasis, which impacts the disease stage. Functional imaging via 18F-fluoro-2-deoxy-D-glucose positron emission tomography/CT (18F-FDG PET/CT) has proven utility for patients with lung carcinoma, lymphoma, and melanoma. PET/CT is used to evaluate the entire body, including the bone marrow. Previous studies found that 18F-FDG PET/CT performed better than conventional imaging in identifying nodal, bone, and bone marrow metastasis from RMS [16,17]. Here, we compared the 18F-FDG PET/CT and BMB findings for bone marrow evaluation in patients with newly diagnosed RMS. We explored whether invasive BMB can be omitted if 18F-FDG PET/CT indicates a lack of bone marrow metastasis.

Materials and Methods

The institutional review board approved this retrospective study. We retrieved the medical records of patients (age < 20 year) with biopsy-proven RMS who underwent PET/CT and BMB, and presented between August 2018 to February 2020. Patients with other synchronous malignancies, a history of cancer treatment, and missing data and patients whose PET/CT and BMB procedures were performed more than thirty days apart were excluded.

PET/CT acquisition and Bone marrow biopsy evaluation

18F-FDG PET/CT acquisition was performed using an integrated PET/CT system (GE Discovery IQ PET/CT, Milwaukee, USA) was used. All patients fasted for 4-6 hour before 18F-FDG (5 MBq/kg body weight) was injected intravenously. PET/CT scanning was performed from cranial vertex to midthigh/toes approximately 60 min after 18F-FDG administration. Low dose CT with 100 kVp and 80-100 mAs was performed for attenuation correction and anatomical correlation. Images were constructed using QCLEAR. 18F-FDG PET/CT scans were evaluated by a qualified nuclear medicine physician. Bone marrow biopsy results were interpreted by pathologist for metastatic bone marrow involvement. 18F-FDG PET/CT scan with no focal FDG uptake other than primary site was considered negative for metastatic bone marrow invasion (Figure 1). The focal FDG uptake exceeding background, in bone marrow without lytic or sclerotic changes on corresponding low-dose CT (Figure 2).

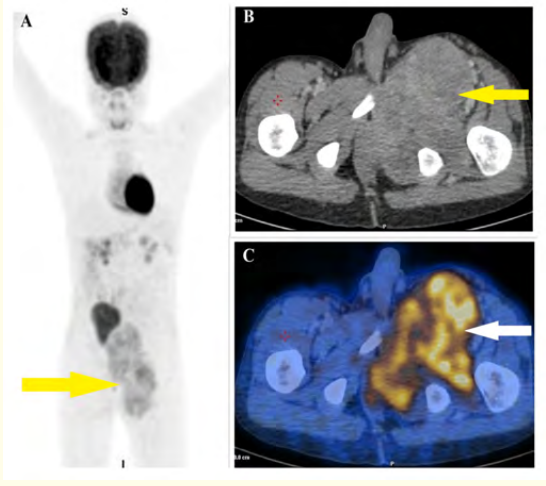

Figure 1: Maximum intensity projection image (A) of 18F-FDG PET/CT showed the primary site of RMS (arrow) with no evidence of distant metastases. The axial CT (B) and fused FDG PET/CT (C) images of primary tumor (arrow).

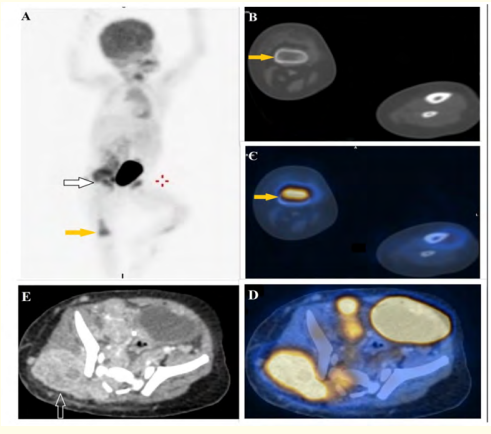

Figure 2: Maximum intensity projection image (A) of FDG PET/CT showed the primary site of RMS (white arrow- A) and bone marrow involvement (colored arrow in B and C) suggestive of metastases. The primary mass in axial PET/CT and CT (D and E respectively) images.

Data analysis

We present descriptive statistics and percentages. We used the standard definitions of negative predictive value and specificity. The negative predictive value of PET/CT for metastatic bone marrow involvement was calculated as the number of true negatives (test-negative patients who did not have the disease) divided by the number of test negatives (patients with negative PET/CT findings). We did not test significance or differences.

Results

A total of twenty patients of age < 20 years (range of 1 to 19 yrs) were eligible for inclusion. The eleven male and nine female patients with RMS involving head neck, thighs and genitourinary region were studied. Both 18F-FDG PET/CT and BMB were negative for bone marrow involvement in nineteen of these patients. In the remaining patient, PET/CT suggested metastatic bone marrow involvement, and BMB confirmed this. The 18F-FDG PET/CT showed specificity of 100 % and negative predictive value of 100 % for evaluation of metastatic bone marrow involvement.

Discussion and Conclusion

Bone marrow involvement is an independent negative prognostic factor in RMS patients [10]. Therefore, assessment of bone marrow involvement is essential. BMB is considered the gold standard. However, BMB is associated with a small but non-negligible risk of hemorrhagic complications [18]. The need for general anesthesia prior to BMB in children adds further complexity. Studies emphasized that bone marrow involvement is unlikely if no metastasis is detected by imaging [19,20]. Newman., *et al*. showed that none of six patients positive on BMB were negative on PET [19]. Kopp., *et al*. reviewed patients who underwent metastatic evaluation by imaging and concluded that, BMAB (Bone marrow aspiration and biopsy) may not be required for initial staging of pediatric and young adult EWS patients deemed non-metastatic by imaging [20].

In our study, the 18F-FDG PET/CT and BMB findings agreed in all cases. The 18F-FDG PET/CT afforded a high specificity and negative predictive value (both 100%) for metastatic bone marrow assessment in RMS cases, consistent with published studies [16,21,22]. Our results support that BMB can be omitted if the 18F-FDG PET/CT findings are negative. In addition, 18F-FDG PET/CT detected additional bone and bone marrow metastases in one of our cases; this has prognostic implications and suggests that other metastases should be sought. Another advantage is that if 18F-FDG PET/CT results are positive, PET/CT can guide biopsy for histological confirmation. The guidelines state that BMB should be considered during workup of sarcoma patients, but the drawbacks of BMB are recognized. The utility of imaging needs to be re-evaluated. The studies on Ewing's sarcoma and osteosarcoma support the omission of BMB [20]. Data comparing the utilities of 18F-FDG PET/CT and BMB in RMS cases remain sparse. Further evaluation is needed to definitively establish 18F-FDG PET/CT as an alternative for BMB.

Our study is not without limitations. First, the sample size was small, and consequently the statistical significance was low. Second, the study was retrospective in nature. Third, PET/CT should preferably precede BMB; we did not explore this topic. However, previous studies have shown that performing BMB before PET/CT did not increase FDG uptake in a manner suggestive of a pathology. Fourth, flow cytometry and reverse-transcription PCR are more sensitive techniques for evaluating minimal bone marrow involvement, but their practical utilities remain unclear. Therefore, currently, 18F-FDG PET/CT remains the primary noninvasive, whole-body staging method.

In conclusion, PET/CT could replace invasive BMB for evaluation of RMS and can be used to exclude the presence of bone marrow metastasis. However, further studies are required to replace BMB conclusively.

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