Heterogeneous Marrow Uptake on FDG PET/CT is not Always a Sign of Lymphomatous Involvement

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Abstract
Heterogeneous patchy marrow uptake on fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) in a histologically proven case of lymphoma is usually considered a virtually pathognomonic sign of lymphomatous involvement. Here, we present a young male patient of T-cell-rich non-Hodgkin lymphoma (NHL), an uncommon morphologic variant of diffuse large B-cell lymphoma (DLBCL), who had undergone three sequential PET/CT scans at our department during the course of his therapy. These images depict the need for careful direct comparison of the current study with the previous PET/CT studies to avoid erroneous interpretation.

Keywords: Fluorodeoxyglucose, positron emission tomography/computed tomography, T-cell-rich non-Hodgkin lymphoma, bone marrow

Introduction
Marrow involvement in lymphoma is conventionally assessed by bone marrow biopsy. In the recent past, FDG PET/CT evolved in to a complementary tool in the assessment of marrow infiltration.⁰ Various different patterns have been described with the highest specificity ascribed to heterogenous patchy marrow uptake. However, we here describe a case depicting potential erroneous interpretation of post chemotherapy FDG PET/CT studies presenting with this pattern.

Case Report
A 17-year-old male patient presented with bilateral neck swelling (Lt > Rt) with a progressive increase in the size over a duration of 4 months. Fine-needle aspiration biopsy of the swelling revealed lymphomatous involvement and a diagnosis of T-cell-rich diffuse large B-cell lymphoma (DLBCL) was established after lymph nodal biopsy. The patient underwent a baseline positron emission tomography/computed tomography (PET/CT) for initial staging, which showed widespread disease involvement of the lymph nodes [the largest measuring 2.7 × 0.4 cm in the right hilar region; maximum standardized uptake (SUVmax) value 15.6] both above and below the diaphragm [Figure 1a], with splenic and marrow involvement (SUVmax value 12.5). Fused PET/CT [Figure 1b] and PET alone [Figure 1c] sagittal midline sections show heterogeneous marrow involvement of the sternum, multiple vertebrae, and the pubis. Subsequently, the patient received four cycles of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone (R-CHOP) regimen. The interim PET [Figure 1d-f] showed significant resolution in the abnormal fluorodeoxyglucose (FDG) uptake noted in the initial scan. Note can be made of two foci of patchy uptake (SUVmax value 4.0) in the abdominal region localizing to the lumbar vertebrae (arrows in Figure 1d-f). Few faint FDG avid nodes (retroperitoneal, with the largest measuring 1.1 × 1.0 cm) were also noted and the scan was interpreted as minimal metabolically...
Heterogeneous patchy marrow uptake on FDG PET in a histologically proven case of lymphoma is usually considered a virtually pathognomonic sign of lymphomatous involvement. In view of heterogeneous involvement and the disease being an uncommon variant (T-cell rich), FDG avidity in multiple vertebrae was interpreted equivocal for marrow involvement and a marrow biopsy was advised. However, bone marrow biopsy showed normal pattern of cell distribution with no lymphomatous infiltration.

In this case, a careful review of the entire PET/CT study showed an interesting finding. The initial staging PET can be noted to show intense FDG uptake in multiple dorsolumbar vertebrae with relative sparing of the L2 and L4 vertebrae (arrows in Figure 1b and c). It can be observed that the repeatedly noted persistent FDG avidity is actually localizing to the L2 and L4 vertebrae (which were spared of disease involvement in the initial staging scan). This suggests that the heterogeneous uptake is, in fact, due to physiological FDG uptake in the L2 and L4 vertebrae. This flip-flop pattern of uptake with absent uptake in the pathologically involved vertebrae was likely due to chemotheraphy-induced ablation of the entire marrow in those vertebrae, as also described by Lin et al.

A similar pattern of findings can also be noted in the rest of the visualized vertebrae and sternum (arrow heads in Figures 1b and c, e and f, h and i). Thus, we conclude that during chemotherapy, heterogeneous marrow uptake may not always signify pathological involvement and a careful direct comparison with the previous PET studies is strongly advised. T-cell-rich non-Hodgkin lymphoma (NHL) is an uncommon morphologic variant of DLBCL and is pathologically characterized by <10% malignant B cells amid a majority population of reactive T lymphocytes and histiocytes. Clinically, it occurs in younger patients, predominantly affects men, and involves the liver, spleen, and bone marrow with a greater frequency than traditional DLBCL (as also noted in the current case). Although an uncommon variant, T-cell-rich DLBCL is reported to have a natural history similar to that of other DLBCLs and respond similarly to therapy.

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**Figure 1:** PET/CT maximum intensity projection images for initial staging showing widespread disease involvement of lymph nodes both above and below the diaphragm (a) with splenic and marrow involvement. Fused PET/CT (b), and PET alone (c) sagittal midline sections show heterogeneous marrow involvement of the sternum, multiple vertebrae, and the pubis. The interim PET (d-f) showed significant resolution in the abnormal FDG uptake noted in the initial scan, with two foci of patchy uptake in the abdominal region localizing to lumbar vertebrae (arrows in d-f). End of therapy PET/CT (g-i) shows no significant change in tracer distribution except for the persistent heterogeneous FDG uptake (SUVmax value 3.8) in vertebrae.

active residual disease with possibly persistent marrow disease. The patient then underwent another two cycles of R-CHOP regimen and was then referred for assessment at the end of the therapy [Figure 1g-i]. It showed no significant change in tracer distribution except for the persistent heterogeneous FDG uptake (SUVmax value 3.8) in the vertebrae. The bone marrow biopsy from the involved vertebra was negative for any lymphomatous infiltration, suggesting that persistent heterogeneous FDG avidity in the bone marrow after chemotherapy may not always signify pathological involvement.
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How to cite this article: Reddy Gorla AK, Mittal BR, Bhattacharya A, Malhotra P, Varma S. Heterogeneous marrow uptake on FDG PET/CT is not always a sign of lymphomatous involvement. World J Nucl Med 2016;15:59-61.

Source of Support: Nil, Conflict of Interest: None declared