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Case Report

Mesenteric panniculitis mimicking early recurrence at end-of-treatment evaluation in malignant lymphoma: Differentiation by active surveillance with F-18 FDG PET/CT imaging

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ABSTRACT

Mesenteric panniculitis is a relatively rare fibro-inflammatory condition of the mesentery. In acute phase, it demonstrates avid uptake on Fluorine-18 FDG PET/CT (PET/CT). Thorough assessment is needed to differentiate from viable or recurrent disease in patients with malignant lymphoma because it mimics active lymphomatous disease on PET/CT. In this article, 3 illustrative cases of malignant lymphoma are presented. PET/CT demonstrated new FDG-avid mesenteric lesions at the end-of-treatment evaluation while the original disease showed significant response. Early recurrence was initially suspected, but together with clinical course and findings, active surveillance was opted. Sequential follow-up PET/CTs showed various patterns of metabolic activity over time; it can persist for months or more, or metabolic activity can fluctuate over time. Eventually benignity was confirmed in these cases. These cases underscore the importance of interpretation with clinical context and awareness of chronological metabolic changes of mesenteric panniculitis to determine proper management.

Introduction

Mesenteric panniculitis is a relative rare fibro-inflammatory condition of the mesentery with reported prevalence of 0.6% on CT [1]. It comprises several disease entities from self-limiting disease which does not require any treatment to malignant disease, especially malignant lymphoma [1–4]. In most of the cases, imaging has a critical role in evaluating and following up the patients [3–6]. Fluorine-18 FDG PET/CT (PET/CT) is an emerging modality to assess mesenteric panniculitis which has an advantage over the conventional imaging modalities, which enables an assessment of both metabolic and anatomic properties of the disease [5,7]. To date,

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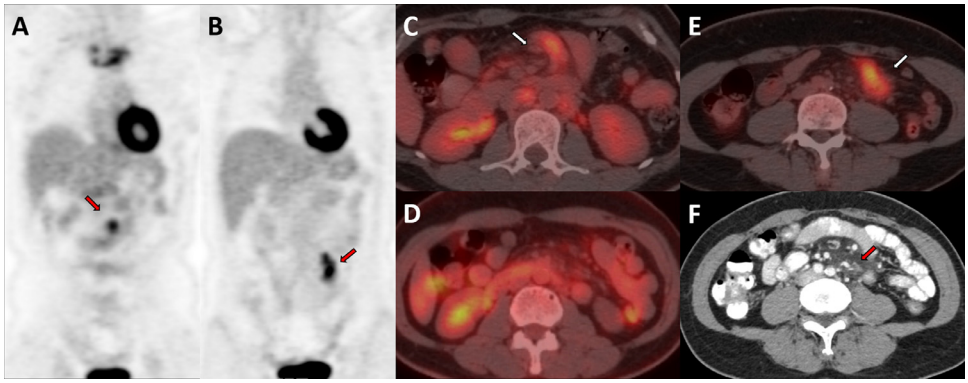

Fig. 1 – Pretherapy FDG PET/CT (A-coronal PET image, C-axial PET/CT fusion image) show FDG-avid lymph nodes in the mediastinum and mid abdomen (arrows). Post-therapy PET/CT (B-coronal PET image, D&E-axial PET/CT fusion images) show complete metabolic response in the pre-existing lesions (D), though there is interval development of an FDG-avid irregular soft tissue in the mesentery with maximum standard uptake value (SUV) of 7.0 (B, E: arrows). Follow-up contrast CT at 1.5 years after completion of the therapy without any specific treatment shows significant interval decrease in conspicuity with residual subtle fat stranding in the corresponding area (F: arrow).

chronological metabolic changes of mesenteric panniculitis developing in the course of malignant lymphoma has not been well described. In this article, 3 illustrative cases of mesenteric panniculitis in the setting of malignant lymphoma are presented. PET/CT demonstrated newly developed FDG-avid mesenteric lesions at the end-of-treatment evaluation in all cases, while the original disease showed significant response. Active surveillance with PET/CT was opted and successfully ruled out recurrence of lymphomatous disease.

Case report

Case 1

Fifty-five years old female who underwent evaluation for initial symptoms of chest discomfort and found to have extensive supra and infra-diaphragmatic lymphadenopathy. Further work-up lead to a diagnosis of stage III follicular lymphoma grade 1-2 (Fig. 1A and C). Given high tumor burden indicated on PET/CT, she underwent 6 cycles of BR therapy (Bendamustine and Rituximab). Post-therapy PET/CT performed 5 weeks after completion of the therapy showed interval complete metabolic response in the pre-existing lesions, while an FDG-avid mass appeared in the mesentery, suspected for a viable lymphoma with maximum standard uptake value (SUV) of 7.0 (Fig. 1B, D, and E). According to the Deauville criteria for therapy response assessment, findings suggested a score of 5 [8]. Though mesenteric panniculitis was felt more likely, early recurrence of lymphoma remained as differential diagnosis. A laparoscopic excisional biopsy was performed, which confirmed mesenteric panniculitis with fat necrosis and histiocyte infiltration. Further follow-up CT (PET/CT was not performed) at 1.5 years without any specific treatment showed interval decreased conspicuity of the mesenteric mass (Fig. 1F).

Case 2

Forty-eight years old female with history of stage IIIB follicular lymphoma, which transformed into “triple-hit” lymphoma, an uncommon aggressive B-cell lymphoma unclassifiable with features intermediate between diffuse large B-cell lymphoma (DLBCL) and Burkitt lymphoma (BL). Pretherapy staging PET/CT showed FDG-avid lymph nodes in the bilateral cervical and supraclavicular regions, which are compatible with high grade lymphoma (Fig. 2A). She underwent 6 cycles of DA-EPOCH-R therapy (dose-adjusted etoposide, doxorubicin, and cyclophosphamide with vincristine, prednisone, and rituximab) and intrathecal methotrexate without any severe complications. Post-therapy PET/CT performed 4 weeks after completion of the therapy showed complete metabolic response in the pre-existing lymph nodes, while new FDG avid, ill-defined nodules appeared in the mesentery with maximum SUV of up to 4.9 (Fig. 2B and C). Findings suggested a Deauville score of 5 [8]. Differential diagnoses included mesenteric panniculitis and early recurrence of lymphoma, though the former was favored. Watchful monitoring was opted instead of biopsy under the assumption of inflammatory etiology. Follow up PET/CT 2 months later showed unchanged appearance (maximum SUV of 4.4) with no signs of progression, thus no further chemotherapy was opted. She underwent consolidative autologous stem cell transplant. PET/CT 2 months post-transplant showed interval mild increase in FDG avidity (maximum SUV of 5.4), but later decreased at 4 months posttransplant (7 months after completion of chemotherapy) without any treatment with maximum SUV of 2.6 (Fig. 2D). A diagnosis of mesenteric panniculitis was made based on the clinical and imaging findings.

Case 3

Fifty-eight years old male with stage IIE (involvement of the pancreas) “double hit” lymphoma, an uncommon aggressive

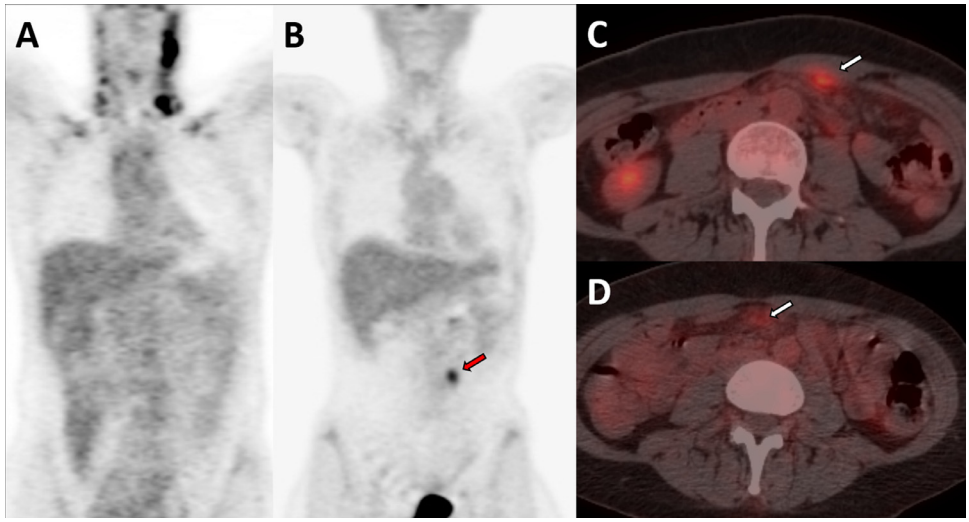

Fig. 2 – Pretherapy PET/CT (A-coronal PET image) shows FDG-avid lymph nodes in the cervical and supraclavicular regions. Post-therapy PET/CT (B-coronal PET image, C-axial PET/CT fusion image) show complete metabolic response in the pre-existing lesions, though there is interval development of FDG-avid irregular nodules in the mesentery with maximum SUV of 4.9 (arrows). There is decrease in FDG avidity 4 months posttransplant (7 months after completion of chemotherapy) with maximum SUV of 2.6 (D-axial PET/CT fusion image: arrow).

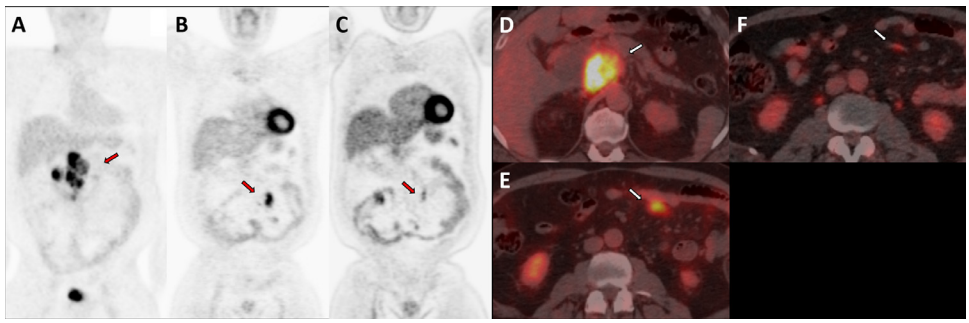

Fig. 3 – Pretherapy PET/CT (A-coronal PET image, D-axial PET/CT fusion image) show FDG-avid conglomerate lymph nodes in the upper abdomen (arrows). Post-chemotherapy FDG PET/CT (B-coronal PET image, E-axial PET/CT fusion image) show complete metabolic response in the pre-existing lesions, though there is interval development of an FDG-avid irregular nodule in the mesentery with maximum SUV of 6.3 (arrows). Follow-up PET/CT 4 months after completion of 1 year of immunotherapy show mildly decreased, but persistent FDG-avid lesion with maximum SUV of 3.3 (C-coronal PET image, F-axial PET/CT fusion image: arrows).

B-cell lymphoma unclassifiable with features intermediate between DLBCL and BL (Fig. 3A and D), who underwent 6 cycles of DA-EPOCH-R therapy. PET/CT performed 5 weeks of the therapy completion showed interval complete metabolic response in the pre-existing lymphomatous lesions, while FDG avid ill-defined nodules appeared in the mesentery with maximum SUV of 6.3 (Fig. 3B and E). Findings suggested a Deauville score of 5 [8]. Mesenteric panniculitis was thought likely, though early recurrence of lymphoma was not ruled out. Biopsy of the new mesenteric ill-defined nodules was attempted, though unsuccessful (inadequate specimen). Subsequently he underwent further immunotherapy for 1 year. Several FDG-PET/CTs were performed during this period, which once showed increase in FDG avidity in mesenteric nodules with maximum SUV of 10.8, though later showed gradual decrease with no other sites of disease recurrence. PET/CT 4 months after completion of the immunotherapy also showed persistent mildly FDG-avid mesenteric nodules with maximum SUV of 3.3 (Fig. 3C and F). Given the overall clinical course, the FDG avid mesenteric nodules were considered to be areas of panniculitis and no further treatment was opted.

Discussion

Recent advancement of imaging techniques allowed to better characterize mesenteric panniculitis, which is occasionally encountered as an incidental finding [1]. It could be just a nonspecific inflammation with various presentations and treatment options [1,2,9], but the association with malignant disease, either direct disease involvement or paraneoplastic

phenomenon especially in malignant lymphoma, has been proposed though there are several recent reports suggesting the contrary [10,11], and still in debate. If it is noted as a solitary abnormality incidentally seen in patients without active malignancy, it would not be difficult to diagnose as a benign finding. However, it would be problematic when mesenteric panniculitis is seen in the context of active malignancy, such as at initial staging or postchemotherapy evaluation, especially in a case of known abdominal involvement. All of the presented cases were widespread malignant lymphoma initially treated with chemotherapy, and mesenteric panniculitis first appeared on the PET/CT at the end-of-treatment evaluation. These findings were immediately discussed with oncologists and decided to be less likely for re-growth or new viable disease of lymphoma given favorable clinical response. However, one might consider that cellular lineages resistant to the current therapy could grow after chemotherapy, especially when PET/CT shows significantly avid uptake in mesenteric lymph nodes or nodules or increase in uptake in the course as seen in the presented cases. Previous researches showed FDG avidity on PET/CT was useful in differentiating malignant from benign conditions in cases of suspicious mesenteric soft tissue density [5,7]. In a study including 71 PET/CT exams, the optimal cutoff of the SUV max was calculated as 3.0 and it yielded the sensitivity of 89% and the specificity of 98% [7]. The sensitivity became even higher if it was combined with the lesion size measured on CT. These researches suggest that PET/CT is both sensitive and specific in diagnosing the etiology of mesenteric panniculitis. However, as seen in the presented cases, it is still uncertain if PET/CT is diagnostic in evaluation of mesenteric panniculitis given FDG is taken up by either inflammatory or malignant cells [12,13] and surely positive PET/CT always needs careful observation and follow up. The clinical decision of mesenteric panniculitis in the latter cases could be biased by preceding cases, but caution should always be taken because malignancy such as early recurrence of lymphoma still remains as a major possibility and not all differential diagnoses can be ruled out clinically [6,14]. Nuclear medicine physicians and radiologists have a pivotal role to raise a possibility of nonspecific inflammation, not to jump into the conclusion of viable malignancy, especially at clinically critical time point as the presented cases.

The exact etiology of mesenteric panniculitis in the presented cases is uncertain, even with surgical biopsy in one of the patients. Given long-standing abnormality in the cases, it is postulated that granulomatous inflammatory pathology could be attributed to this. It has been reported that chemotherapy, steroid therapy, and molecular-targeted therapy for cancers can cause mild to severe complications in the small bowel and colon, such as infectious or noninfectious enteritis/colitis and pneumatosis, probably linked to reduced integration of the intestinal protective layer of the intestine and suppressed immune system activity [15–18]. It would be reasonable that the therapy reduces integrity of the intestinal wall which, in turn, allows bacteria flora or other antigens to move into the intestinal vascular network in the setting of suppressed immune system activity, and subsequently, with rebounding immune system activity after the chemotherapy, it results in accelerated chronic granulomatous formation. In addition, the phenomenon could be associated with sarcoid-like reaction, which is a well-known noncaseating granulomatous disease occurring in association with various malignancies and the treatments [19]. This is theorized that the therapy produces antigenic substances, which are subsequently drained into the downstream regional or nonregional lymph nodes where granulomas are formed [19].

It is unclear if there is specific association between mesenteric panniculitis and the type of lymphoma and chemotherapy regimen. There have been several reports regarding the use of Rituximab-containing chemotherapy and higher incidence of false positive PET/CT results in B-cell lymphoma [20,21]. All of the patients were B-cell lymphoma who were treated with the chemotherapy regimens included Rituximab and alkylating agent, and, in addition, steroid therapy was included in 2 of the cases. Though Rituximab could be a contributing agent, there is no clear evidence to determine the relationship.

In conclusion, mesenteric panniculitis is a relatively rare phenomenon which could be linked to an inflammatory condition or malignant disease. It can occur during the course of treatment of malignant lymphoma and imaging has a pivotal role in evaluation. New or increasing uptake on FDG PET/CT in mesenteric panniculitis may raise a flag for progressive disease, however image interpretation should be performed with clinical context given that treatment associated inflammatory process could occur and mimic viable disease. Sequential follow-up PET/CTs can show various patterns of metabolic activity over time; it can persist for months or more, or metabolic activity can fluctuate over time. Nuclear medicine physicians and radiologist should be familiar with this phenomenon and chronological changes to suggest the proper management.

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