Case Report

Unusual location of recurrent mantle cell lymphoma on fluorodeoxyglucose-positron emission tomography despite complete metabolic resolution of previous sites of disease

ABSTRACT

This case report presents a patient with recurrent pleomorphic mantle cell lymphoma (MCL), which is a relatively rare but aggressive type of lymphoma. A positron emission tomography/computed tomography scan performed to assess treatment response demonstrated a complete metabolic response in the sites of primary disease while also revealing new subcutaneous lesions, which were biopsy-proven recurrent disease. This case illustrates the importance of the different biological behavior of MCL, whereby new sites of metabolically active lesions can represent recurrent disease, even though there is a complete metabolic response at sites of primary disease.

Keywords: Fluorodeoxyglucose-positron emission tomography/computed tomography, mantle cell lymphoma, recurrent lymphoma, treatment response

INTRODUCTION

Mantle cell lymphoma (MCL) is a type of non-Hodgkin's lymphoma which accounts for approximately 6% of all lymphomas and is considered aggressive and incurable.[1,2] The 5-year survival ranges from <15% to 60%.[3] It commonly occurs in the lymph nodes, bone marrow, or spleen. The gastrointestinal tract and Waldeyer ring are other important sites of extranodal involvement.[4] Although considered incurable, a variety of life-prolonging treatments is available or being studied. The most common kind of treatment is immunochemotherapy, e.g., variations of R-CHOP, R-bendamustine, R-BAC, and R-DHAP. BTK inhibitors such as ibrutinib are rather new substances that are used for the treatment of patients with relapsed or refractory MCL.[5] Additional research is being conducted, especially exploring the use of radioimmunotherapy and targeted therapy.

Fluorodeoxyglucose (FDG)-positron emission tomography/computed tomography (PET/CT) is commonly used to diagnose and manage lymphoma patients. The unique value of FDG-PET/CT lies within its ability to differentiate between residual metabolically active tumor and inactive scar tissue or necrosis, which makes it a superior tool in the assessment of treatment response.[6] Interim FDG-PET/CT scans performed after two to three cycles of chemotherapy can be used as an

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independent predictor of overall and progression-free survival of patients with high-grade non-Hodgkin's lymphoma.[7]

This report presents a unique case of MCL with the appearance of FDG-avid, biopsy-proven recurrence in unusual locations despite complete metabolic resolution of previous sites of disease.

CASE REPORT

A 77-year-old woman with a known history of MCL in remission since her last chemotherapy (chlorambucil and rituximab) in 2016 was referred for investigation of possible recurrence. Physical examination revealed palpable splenomegaly, and blood tests showed an elevated white blood cell count at 199.8 × 10^9/L.

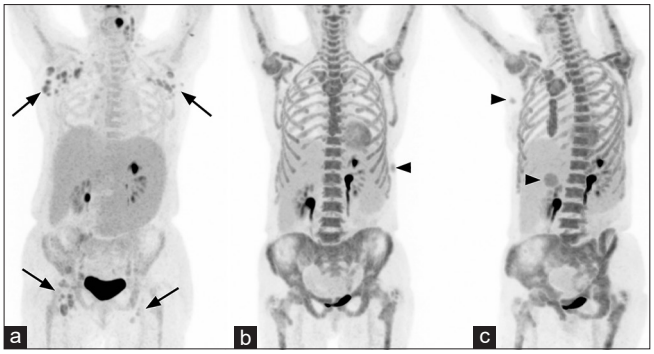

Figure 1: Pretreatment positron emission tomography scan demonstrating primary sites of disease (arrows) on anterior maximum intensity projection (MIP) image (a). Posttreatment positron emission tomography scan anterior (b) and oblique (c) MIP images showing complete metabolic resolution in the sites of primary disease but new fluorodeoxyglucose-avid lesions (arrowheads)

Bone marrow biopsy demonstrated molecular cytogenetic evidence of a relapse of the MCL.

The FDG-PET/CT scan revealed moderately increased FDG uptake greater than the liver in the enlarged spleen. The spleen measured 19.6 cm in the vertical dimension. There were several FDG-avid lymph nodes above and below the diaphragm; measuring up to 2 cm. Diffuse heterogeneous increased bone marrow activity was consistent with lymphomatous involvement. The findings were in keeping with FDG-PET-positive recurrence of MCL, with nodal, splenic, and bone marrow involvement.

The patient received one cycle of R-CHOP followed by ibrutinib and venetoclax, but this was complicated by severe neutropenia; therefore, G-CSF was administered, and rituximab, bendamustine, and cytarabine (R-BAC) treatment were commenced.

After completing one cycle of R-BAC followed by two cycles of R-Bendamustine, the patient presented for restaging FDG-PET/CT. This showed complete metabolic response in previously documented FDG-avid nodal

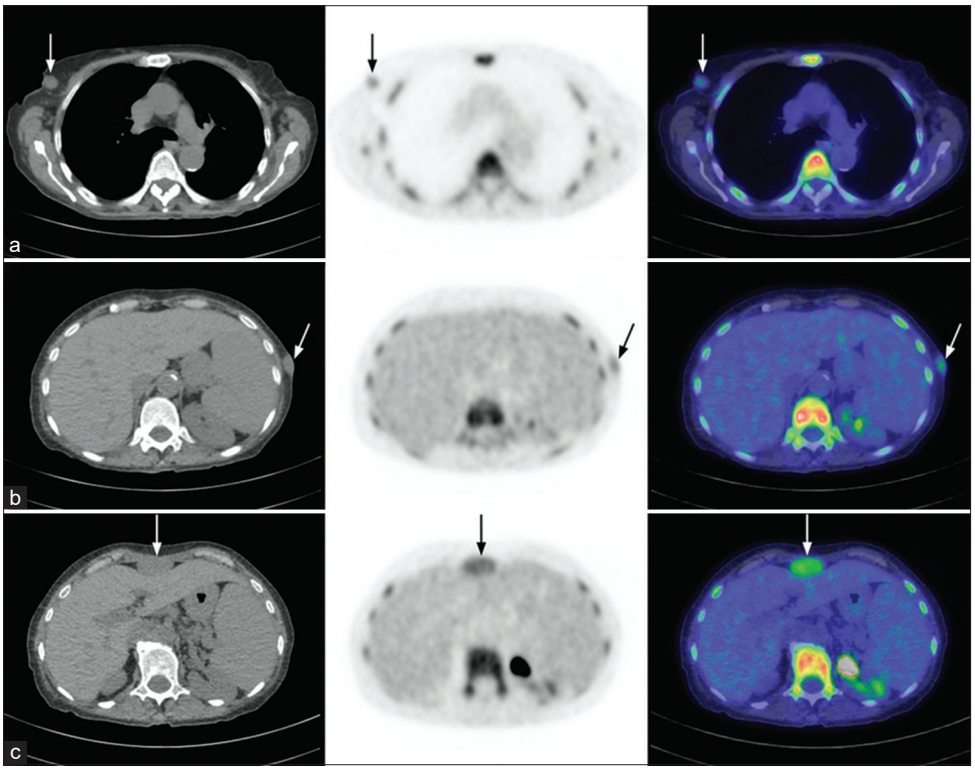

Figure 2: Axial images of the new subcutaneous lesion in the right anterolateral chest wall (row a), left lateral chest wall (row b), and anterior midabdominal wall (row c) demonstrated on computed tomography, positron emission tomography, and fused positron emission tomography/computed tomography

lesions and normalization of splenic uptake associated with significant decrease in size. Diffuse homogenous FDG uptake in the bone marrow was due to posttreatment reactive changes. However, new foci of metabolic activity corresponding to underlying subcutaneous rounded soft-tissue densities had developed in the right anterolateral chest wall, left lateral chest wall adjacent to the 9th rib, and anterior mid-abdominal wall at the level of L1/L2 [Figures 1 and 2].

Based on the FDG-PET/CT findings consistent with a complete metabolic response of previously documented multifocal nodal disease, the new FDG-avid subcutaneous lesions were thought to potentially be inflammatory in etiology, but an ultrasound was suggested for further evaluation.

Targeted ultrasound assessment of the palpable bilateral chest wall lesions demonstrated abnormal lobulated subcutaneous nodules of mixed echogenicity and increased internal vascularity [Figure 3].

Given the atypical ultrasound features in the setting of a complete metabolic response of the nodal disease and spleen, a core biopsy of the right chest wall lesion was performed under ultrasound guidance. The histopathology showed features in keeping with pleomorphic MCL [Figure 4].

DISCUSSION

The usefulness of FDG-PET/CT in patients with MCL has been questioned in the past, due to the disease's incurable nature and often low FDG avidity. Current literature suggests that FDG-PET/CT is still a valuable tool in the management of patients with MCL.[8]

In the presented case, despite the FDG-PET/CT findings being in keeping with a complete metabolic response of the patient's primary disease, new FDG-avid subcutaneous lesions were detected in multiple sites, initially thought to be inflammatory based on the complete metabolic response in all primary sites of disease, but this was biopsy proven to be recurrent disease. Shortly after the scan was performed, the patient's recurrent MCL progressed clinically, with multiple new palpable subcutaneous lesions.

MCL is known to be an aggressive type of lymphoma with a continuously high risk of recurrence. Therefore, suspicion should be directed toward any new FDG-avid lesions, despite being in unusual sites for recurrence, and should be closely followed up. A complete metabolic response of the sites of primary disease does not necessarily lead to the conclusion of new lesions having a different underlying pathology in this type of lymphoma.

According to the Lugano classification, a complete metabolic response is defined as a score of 1 or 2, debatably 3, on the five-point scale based on the Deauville criteria without the occurrence of any new lesions.[9,10] The appearance of new FDG-avid foci is considered progressive disease as long as the lesions are more likely to be lymphoma than another etiology.[10] It is important to be mindful that commonly benign, infectious, or inflammatory processes are the cause of cutaneous or subcutaneous foci of FDG avidity. Most benign tumors demonstrate no or low FDG avidity, yet there are some that have higher FDG uptake. In addition, there is a variety of PET-positive infectious and inflammatory processes, particularly in relation to chemotherapy. The correlation with morphologic features on the CT can be helpful. However, it is most important to consider the biology of the lymphomatous disease being assessed when interpreting new FDG-avid lesions, and further investigation, such as a biopsy, might be required in some cases.[11]

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Conflicts of interest

There are no conflicts of interest.

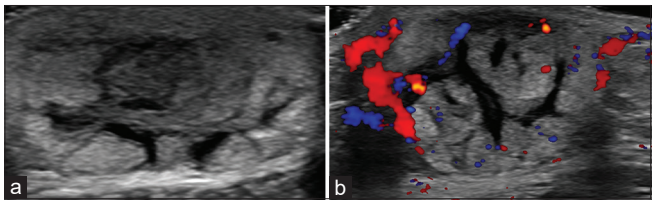

Figure 3: Ultrasound images of the subcutaneous left lateral chest wall lesion (a). Ultrasound images with color Doppler of a newly developed palpable subcutaneous lesion in the right upper chest wall demonstrating the internal vascularity present in all lesions (b)

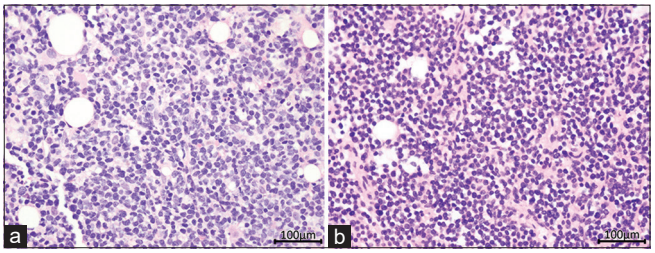

Figure 4: Pleomorphic mantle cell lymphoma demonstrated in the histopathology (hematoxylin and eosin stain) of a pretherapy bone marrow sample (a) and tissue obtained with ultrasound-guided core biopsy of the new posttreatment subcutaneous lesion in the left chest wall (b)

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