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Flashy lungs and sarcoidosis: Not always a sign of disease activity

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Abstract. This is the case of a 68-year-old man with known cardiac sarcoidosis undergoing treatment with methotrexate who presented with new onset of dyspnea and lipothymia. FDG-PET/CT revealed pathological uptake within lung parenchyma which resolved following discontinuation of methotrexate, compatible with methotrexate-induced pneumonitis. This is the first case of methotrexate-induced pneumonitis documented by FDG-PET/CT.

Key words: methotrexate, pneumonitis, sarcoidosis, PET, FDG, fluorodeoxyglucose

Introduction

Methotrexate (MTX) lung toxicity can result in pneumonitis, which typically presents as progressive dyspnea, cough, and fever. As prognosis is excellent with appropriate clinical management, it is important to recognize methotrexate-induced pneumonitis (MtxIP), especially in patients treated for sarcoidosis. In the presence of known sarcoidosis, new fluorodeoxyglucose (FDG) lung uptake is not necessarily related to pulmonary sarcoidosis (PS). We herein describe the first case of MtxIP documented by FDG positron emission tomography (PET)/computed tomography (CT).

Case report

A 68-year-old man presented with shortness of breath and syncope. Rhythm strips revealed advanced atrioventricular block (Figure 1A). Despite being limited by breathing artefact, cardiovascular magnetic resonance (Figure 1B) showed subendocardial late gadolinium enhancement within the basal interventricular septum and laterobasal wall in a pattern compatible with an ischemic etiology. Epicardial fat infiltration was absent. As coronary angiography only showed minimal non-obstructive coronary artery disease, an alternative diagnosis such as CS was suspected.

Whole body FDG-PET/CT (Figure 2A) was performed following a myocardial suppression protocol to exclude CS. Pathological FDG uptake (SUVmax=15.4) was noted within the myocardium (Figure 2B) involving the left ventricular free wall and septal wall. Increased uptake (SUVmax=14.9) was present within multiple intrathoracic lymph nodes (LN) (Figure 2C). Lung parenchymal involvement was absent. Hilar LN biopsy confirmed the presence of non-caseating granulomas, compatible with sarcoidosis. A clinical diagnosis of CS based on the modified Japanese Circulation Society criteria and the Heart Rhythm Society criteria was retained with extra-cardiac involvement of intrathoracic LN (1,2). A pacemaker was implanted, and treatment was initiated with oral prednisone 50 mg once per day and oral MTX 20 mg once a week.

The patient's shortness of breath resolved and syncope did not recur. A follow-up FDG-PET/CT (Figure 3A) was performed after three months of treatment. Overall, there was complete

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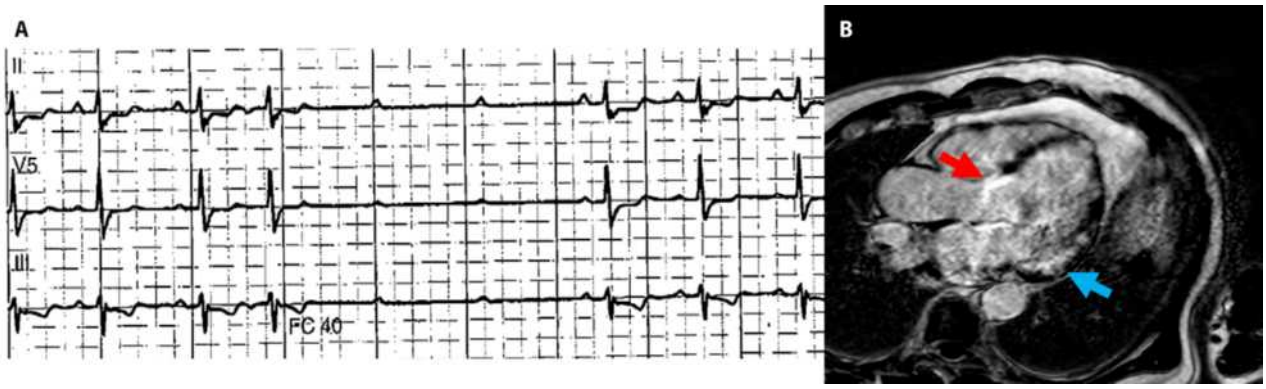

Figure 1. (A) Rhythm strip showing advanced atrioventricular block. (B) Cardiovascular magnetic resonance evidenced subendocardial late gadolinium enhancement within the basal interventricular septum (red arrow) and laterobasal wall (blue arrow) without increased T2-weighted signal.

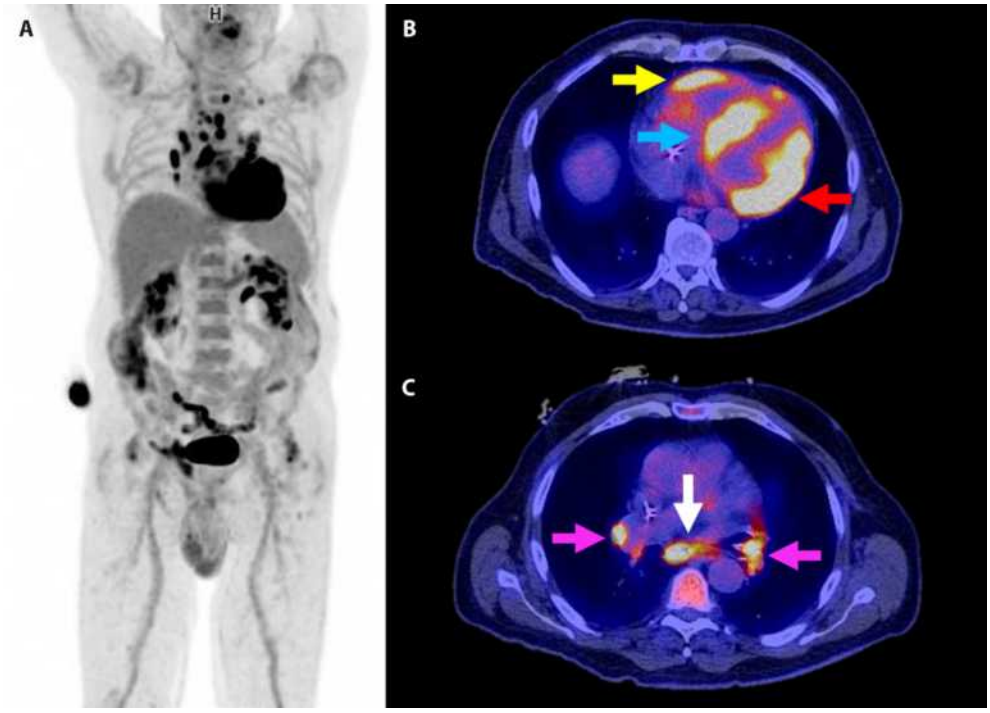

Figure 2. (A) Whole body FDG-PET/CT performed following myocardial suppression protocol (24h high-fat, low-carbohydrate diet, 12h fasting, intravenous heparin). (B) Intense patchy FDG uptake (SUVmax=15.4) was present within the myocardium at the levels of the left ventricular free wall (red arrow), interventricular septum (blue arrow) and right ventricle (yellow arrow). (C) Increased FDG uptake (SUVmax=14.9) was present within multiple intrathoracic LN, notably in the hilar (pink arrows) and subcarinal (white arrow) regions.

resolution of pathological FDG uptake within both the myocardium (Figure 3B) and intrathoracic LN (Figure 3C). Treatment regimen was maintained without modification.

Three months later, the patient was hospitalized for new onset dyspnea and lipothymia. The electrocardiogram showed normal sinus rhythm with ventricular pacing. Cardiac implantable electronic device interrogation data did not report any arrhythmic events. Orthostatic hypotension was evidenced on physical examination and attributed to the patient's antihypertensive medications. FDG-PET/CT (Figure 4A) was repeated to exclude reactivation of sarcoidosis. Pathological FDG uptake remained

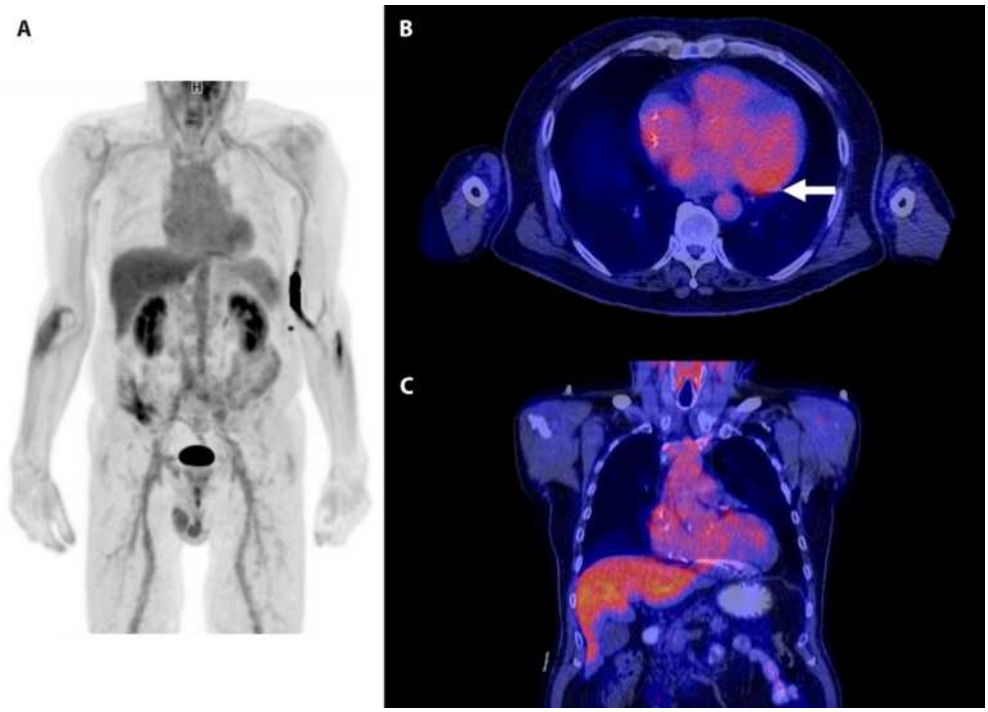

Figure 3. (A) Follow-up whole body FDG-PET/CT was performed following myocardial suppression protocol. (B) Overall, there was complete resolution of the multiple foci of intense FDG uptake in the myocardium with the exception of a low-grade area of uptake (SUVmax=3.5) within the basal anterolateral segment (white arrow), representing non-specific activity probably related to sub-optimal suppression. (C) Uptake within intrathoracic LN also completely resolved.

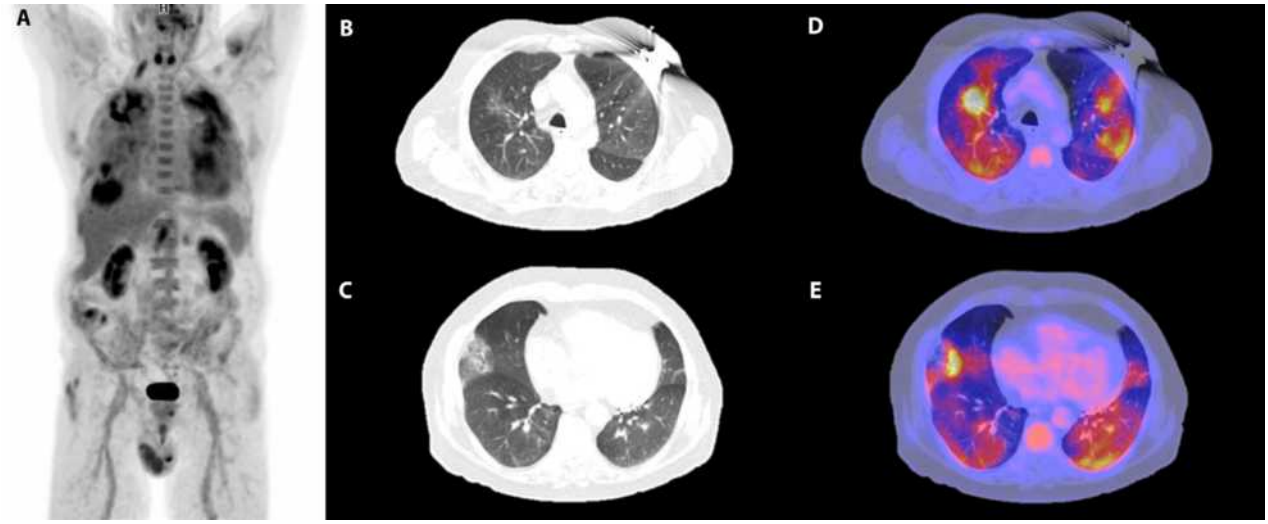

Figure 4. (A) Repeat FDG-PET/CT was performed following myocardial suppression protocol to exclude reactivation of CS. (B, C) Chest CT axial images showed multiple ground glass opacities and reticulations within both lungs. (D, E) These changes were associated with intense hypermetabolism on FDG-PET/CT images (SUVmax=8.1).

absent within the myocardium and intrathoracic LN. Multiple ground glass opacities and reticulations appeared within both lung fields (Figures 4B and 4C) associated with areas of intense FDG uptake (SUVmax=8.1) (Figures 4D and 4E). Differential diagnosis included PS, infectious disease, and MtxIP. Cultures obtained from bronchoalveolar lavage were negative. MtxIP was deemed more likely, but PS could not be completely excluded. MTX was discontinued while oral prednisone was maintained at the same dose of 50 mg per day. Dosage of the patient's antihypertensive agents was reduced.

The patient's dyspnea improved and lipothymia did not recur. Follow-up FDG-PET/CT (Figure 5A) was repeated two months following MTX discontinuation. The previously noted pulmonary lesions improved greatly both radiologically and metabolically (Figure 5B and 5C). Remaining lesions consisted mostly of fibrotic changes and were associated with absent or low FDG uptake (SUVmax=3.4). Pathological FDG uptake remained absent within the myocardium and intrathoracic LN. MtxIP was retained as the final diagnosis.

Discussion

MTX is an antimetabolite with proven benefits as an anti-inflammatory agent in various inflammatory conditions including sarcoidosis, inflammatory bowel diseases and rheumatoid arthritis (3). MTX can result in several manifestations of lung disease, including pneumonitis, pulmonary infection, and pulmonary lymphoproliferative disease. Pneumonitis is a serious complication of MTX treatment with a reported incidence of 3.3-5.5% (4,5). As eosinophils are frequently found within the lung interstitium, it is thought to be a hypersensitivity reaction (6). MtxIP typically presents subacutely with progressive dyspnea, cough and fever (4,7). Importantly, its incidence appears to have no correlation with the duration of therapy or total cumulative dose (8). While most patients recover after withdrawal of MTX alongside corticosteroid administration, irreversible interstitial pneumonia and subsequent death have been reported (9). Radiological features are variable and include diffuse parenchymal opacification, reticular opacities,

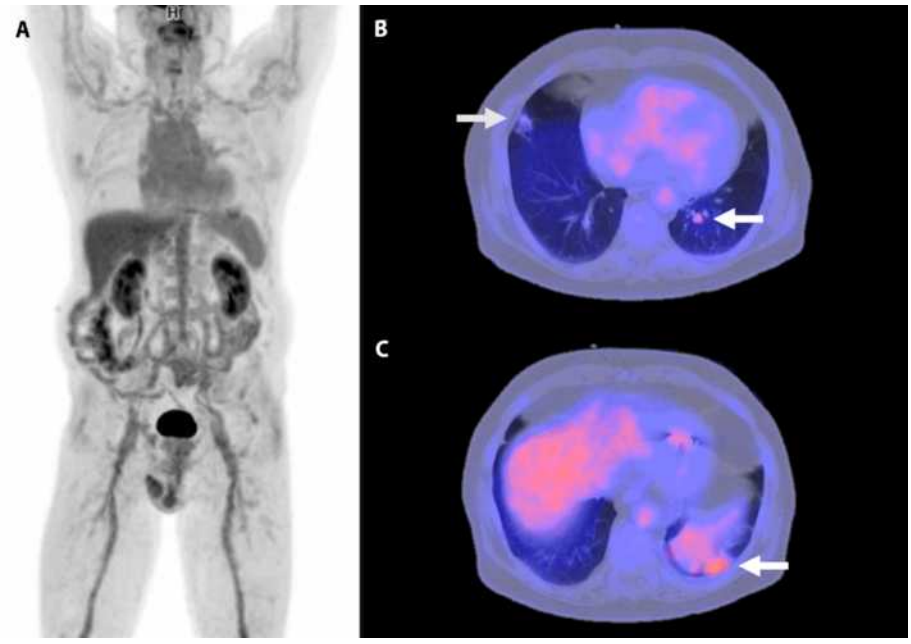

Figure 5. FDG-PET/CT (A) with myocardial suppression protocol was repeated two months following MTX discontinuation. (B, C) Fibrotic changes were seen within both lung fields and were associated with absent or low FDG uptake (SUVmax=3.4) (white arrows).

centrilobular nodules and most commonly a non-specific interstitial pneumonia pattern (8,10). Hilar lymphadenopathy and pleural effusions have also been reported (10,11). To the best of our knowledge, this is the first case of MtxIP documented by FDG-PET, demonstrating it to be an FDG avid disease process. It is important for physicians to recognize that not all foci of increased uptake in a patient with known sarcoidosis is related to this pathology. Although PS may present similarly both radiologically and metabolically, differentiation of both entities requires a thorough clinical history and careful review of previous imaging studies (12,13). As management of MtxIP and PS differ significantly, appropriate and timely diagnosis may have prognostic implications.

Conclusion

To our knowledge, this is the first literature case report of MtxIP documented by FDG-PET. Clinicians should be aware of this entity in sarcoidosis patients treated with MTX. Given the scarcity of data, additional studies are required to establish patterns of FDG uptake in MtxIP.

Conflict of Interest: All authors declare that he or she has no commercial associations that might pose a conflict of interest in connection with the submitted article.

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