Case report

Disseminated sarcoidosis involving lymph nodes, bone and spleen with progressive cardiac sarcoidosis on $^{18}$F-FDG PET/CT and cardiac MRI

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ABSTRACT

A 63-year-old lady with a background of ischemic heart disease was referred for $^{18}$F-FDG PET/CT for multiple lytic bone lesions which showed disseminated FDG avid lesions in the skeleton, nodal stations as well as spleen simulating advanced malignancy such as diffuse lymphomatous disease. A diagnosis of sarcoidosis was pathologically confirmed with bone biopsy. Following treatment, repeat PET/CT revealed significant regression of FDG avid lesions, however prominent uptake in the lateral ventricular wall was suspicious for active cardiac sarcoidosis, particularly given recurrent chest pain. This was confirmed on cardiac MRI and correlation with PET enabled discrimination between ischemic and non-ischemic fibrosis.

Keywords:
FDG PET/CT
Cardiac sarcoidosis
MRI
CMR

Introduction

Sarcoidosis is a multisystem disease of unknown cause that can affect practically any organ of the body, which is characterized by formation of non-caseating granulomas in affected organs [1]. Cardiac sarcoidosis (CS) is uncommon and can be difficult to detect, and as a result, CS can often be under-recognized in clinical practice [2]. Although isolated CS can occur, CS most often occurs as a manifestation of disseminated sarcoidosis [2,3]. Cardiac magnetic resonance (CMR) and positron emission tomographic (PET) imaging have both emerged as useful modalities to detect CS. However, each of these techniques has unique advantages. For instance, CMR is useful in detecting presence of myocardial fibrosis and PET is useful for visualizing active inflammation [4]. We herein report a case

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of CS in a patient with ischemic heart disease and highlight the complementary value of CMR and 18F-FDG PET/CT which enabled discrimination between ischemic and non-ischemic fibrosis.

**Case presentation**

A 63-year-old lady with a background of hypertension, type 2 diabetes mellitus, chronic kidney disease and ischemic heart disease with previous coronary artery bypass grafting had a cervical spine MRI for occipital pain which incidentally discovered multiple bony lesions within her cervicothoracic spine suspicious of metastatic disease.

She was referred for a18F-FDG PET/CT scan which showed disseminated FDG uptake in large confluent hypodense splenic lesions (Fig. 1, block arrows), numerous nodal stations on both sides of the diaphragm and innumerable lytic lesions in the axial and appendicular skeleton (Fig. 1, thin arrows) simulating advanced malignancy such as diffuse lymphomatous disease with splenic and bony involvement. Physiological uptake of the left ventricle was noted on the initial 18F-FDG-PET/CT with routine patient preparation and diet (Fig. 1, curved arrows). She was referred for further work-up under the care of hematology. Bone biopsy 1 month after presentation showed numerous large granulomas with no abnormal B- or T-cell populations or any malignant cells. Her serum angiotensin converting enzyme was elevated at 94 U/L (<70 U/L).

A diagnosis of sarcoidosis was made and steroids and methotrexate was commenced. Following this, the patient had recurrent myocardial infarction with non-obstructive coronary arteries suspicious of CS. 18F-FDG PET/CT 8 months following presentation to assess for sarcoid disease activity and possible CS was performed with high fat/low carbohydrate dietary preparation. The scan showed significant metabolic response in previous avid sites in the spleen (Fig. 2, block arrows), bones (Fig. 2, thin arrows), and lymph nodes, however prominent focal uptake in the lateral ventricular wall confirmed suspicion of active CS (Fig. 2, curved arrows). Prednisone and methotrexate regimen was up titrated.

Follow up 18F-FDG PET/CT 15 months after presentation with high fat/low carbohydrate diet showed markedly increased FDG uptake in the basal and mid lateral wall of the left ventricle (Fig. 3, black arrows) with complete metabolic response elsewhere including the spleen, bones and lymph nodes. CMR was performed 16 months following presentation which showed patchy nodular myocardial late gadolinium enhancement in a non-ischemic pattern involving the basal and mid lateral/inferior walls localizing to the FDG avid regions on 18F-FDG PET/CT (Fig. 3, white arrows). There was also evidence of curvilinear subendocardial late gadolinium enhancement in the anterior wall localizing to non-FDG avid regions on 18F-FDG PET/CT consistent with previous ischemic infarction (Fig. 3, thin arrows). She was subsequently started on in-
Fig. 2 – (A) $^{18}$F-FDG PET/CT 8 months following presentation with high fat/low carbohydrate diet revealed significant metabolic response in previous avid sites in the spleen (B, C, block arrows) bone (D, E, thin arrows), and lymph nodes, however prominent focal uptake in the lateral ventricular wall is suggestive of active cardiac sarcoidosis (F, G, curved arrows).

Fig. 3 – (A) $^{18}$F-FDG PET/CT 15 months following presentation with high fat/low carbohydrate diet showed markedly increased FDG uptake in the basal and mid lateral wall of the left ventricle (B-E, black arrows) with complete metabolic response elsewhere. Cardiac sarcoidosis (CS) was confirmed on CMR performed 16 months following presentation which showed patchy nodular myocardial late gadolinium enhancement (LGE) in a non-ischemic pattern involving the basal and mid lateral/inferior walls localizing to the FDG avid regions (F, white arrows). There was also evidence of curvilinear subendocardial LGE in the anterior wall consistent with previous ischemic infarction (G, thin arrows).
fliximab, given $^{18}$F-FDG PET/CT evidence of active inflammation despite on prednisone and methotrexate.

**Discussion**

Sarcoidosis is a granulomatous disease that can affect practically any organ of the body. Bone and splenic manifestations occur less commonly in up to 13% and approximately 10% of patients with sarcoidosis, respectively [5,6]. CS is evident in only 5% of patients with sarcoidosis and most often occurs as a manifestation of disseminated sarcoidosis, although isolated CS can also occur [2,3].

$^{18}$F-FDG PET/CT has emerged as a sensitive modality to detect active CS lesions if performed with inhibition of the physiological myocardial uptake with heparin injection or high fat/low carbohydrate diet [7,8]. However, CS, a potentially life-threatening manifestation, is challenging to diagnose due to imperfect diagnostic accuracy as well as lack of validation of existing diagnostic criteria [9]. The Japanese Ministry of Health and Welfare Criteria for Diagnosis of Cardiac Sarcoidosis (Revised 2006) does not include PET/CT as a diagnostic criterion and only includes cardiac MRI abnormalities as a minor criterion, both of which have been shown to be highly sensitive modalities for diagnosis and monitoring [10].

Both CMR and $^{18}$F-FDG PET/CT imaging have unique features that make them useful imaging modalities in CS as they evaluate different aspects of the pathobiology of CS. For instance, CMR is useful for the assessment of regional scar formation and myocardial fibrosis which can occur in various pathological processes including myocardial infarction, myocarditis or CS [11]. $^{18}$F-FDG PET/CT is useful in localising and quantifying active inflammation [4].

Of the few studies that have compared the diagnostic accuracy of PET/CT with CMR, these have shown good agreement, with the advantage of PET being more sensitive than CMR in the assessment of therapeutic response [12,13]. As shown in our case, combining CMR and PET provides complementary value and enhance the diagnostic certainty and PET is able to identify active inflammation and guiding immunosuppressive therapy. A recent study by Vita and colleagues evaluating the utility in combining CMR and PET in 107 patients with possible CS, found that by combining PET and CMR, most patients were correctly reclassified as having a higher or lower likelihood of CS [4].

**Conclusion**

Sarcoidosis is a multisystem disease of unknown cause that can affect practically any organ of the body. CS, an uncommon but potentially life-threatening manifestation, is challenging to diagnose. In this case report, $^{18}$F-FDG PET/CT combined with CMR were able to discriminate between ischemic fibrosis due to coronary artery disease and non-ischemic fibrosis due to sarcoidosis, highlighting the importance of correlation between different imaging modalities.

**Patient consent**

Patient Informed consent and permission obtained.

**REFERENCES**

[1] Valeyre D, Prasse A, Nunes H, Uzunhan Y, Brilley PY, Müller-Quernheim J. Sarcoidosis. Lancet 2014;383(9923):1155–67.

[2] Okada DR, Bravo PE, Vita T, Agarwal V, Osborne MT, Taqueti VR, et al. Isolated cardiac sarcoidosis: a focused review of an under-recognised entity. J Nucl Cardiol 2018;25(4):1136–46.

[3] Patel MR, Cawley PJ, Heitner JF, Klem I, Parker MA, Jaroudi WA, et al. Detection of myocardial damage in patients with sarcoidosis. Circulation 2009;120(20):1969–77.

[4] Vita T, Okada DR, Veillet-Chowdhury M, Bravo PE, Mullins E, Hulten E, et al. Complementary value of cardiac magnetic resonance imaging and positron emission tomography/computed tomography in the assessment of cardiac sarcoidosis. Circ Cardiovasc Imaging 2018;11(1):e007030.

[5] Judson MA. Extrapulmonary sarcoidosis. Semin Respir Crit Care Med 2007;28(1):83–101.

[6] Wilcox A, Bharadwaj P, Sharma OP. Bone sarcoidosis. Curr Opin Rheumatol 2000;12(4):321–30.

[7] Youssif G, Leung E, Mylonas I, Nery P, Williams K, Wisenberg G, et al. The use of $^{18}$F-FDG PET in the diagnosis of cardiac sarcoidosis: a systematic review and metaanalysis including the Ontario experience. J Nucl Med 2012;53:241–8.

[8] Soussan M, Brilley PY, Nunes H, Pop G, Ouvrier MJ, Nagarra N, et al. Clinical value of a high-fat and low-carbohydrate diet before FDG-PET/CT for evaluation of patients with suspected cardiac sarcoidosis. J Nucl Cardiol 2013;20:120–7.

[9] Blankstein R, Waller AH. Evaluation of known or suspected cardiac sarcoidosis. Circ Cardiovasc Imaging 2016;9(3):e000867.

[10] Aggarwal NR, Snipeliski D, Young PM, Gersh BJ, Cooper LT, Chareonthaitawee P. Advances in imaging for diagnosis and management of cardiac sarcoidosis. Eur Heart J Cardiovasc Imaging 2015;16:949–58.

[11] Satoh H, Sano M, Suwa K, Saitoh T, Nobuhara M, Sato M, et al. Distribution of late gadolinium enhancement in various types of cardiomyopathies: significance in differential diagnosis, clinical features and prognosis. World J Cardiol 2014;6(7):585–601.

[12] Ohira H, Tsujino I, Ishimaru S, Oyama N, Takei T, Tsukamoto E, et al. Myocardial imaging with $^{18}$F-fluoro-2-deoxyglucose positron emission tomography and magnetic resonance imaging in sarcoidosis. Eur J Nucl Med Mol Imaging 2008;35:933–41.

[13] Sgard B, Brilley PY, Bouvry D, Djelbani S, Nunes H, Meune C, et al. Evaluation of FDG PET combined with cardiac MRI for the diagnosis and therapeutic monitoring of cardiac sarcoidosis. Clin Radiol 2019;74(1):81.e9-81.e18.