Evaluation of Infiltrative Cardiomyopathies

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Infiltrative cardiomyopathies are a group of disorders characterized by the abnormal deposition of proteins and/or inflammatory cells leading to cardiac dysfunction and electrical disorders. This chapter will illustrate the role of PET/CT in cardiac sarcoidosis and amyloidosis, and the complementary role of PET/MR and 99mTc PYP SPECT.

3.1 Cardiac Sarcoidosis

3.1.1 Background

Sarcoidosis is a multisystem disorder that is characterized histologically by non-caseating, non-necrotic granulomas. Although it most commonly manifests in the lungs or with lymphadenopathy, it can affect any organ. Only 40–50% of patients with cardiac sarcoidosis (CS) diagnosed at autopsy had the diagnosis made during their lifetime.

Areas of active cardiac inflammation demonstrated increased glucose metabolism and therefore increased FDG uptake on PET. On the contrary MPI (by SPECT or PET with perfusion tracers) can show areawes of hypoperfusion due to inflammation and vascular compression due to edema or myocardial fibrosis and scar. Depending on the degree of active inflammation on FDG-PET and resting perfusion defects on MPI, the disease can be staged as no evidence of activity (no inflammation or scar), early stage (active inflammation with mild or no scar), progressive disease (active inflammation with moderate scar), or fibrous disease (minimal or no inflammation with severe scar).

The evaluation of myocardial uptake of ^{18}F-FDG PET in cardiac sarcoidosis is not simple as the metabolic utilization of glucose can be physiological, and ischemia may affect myocardial uptake. Therefore, adequate patient preparation aimed to suppress myocardial utilization is mandatory.

The presence of obstructive coronary disease and myocardial ischemia should be excluded by stress imaging, CT angiography or, when needed, invasive coronary angiography.

Evaluation of myocardial uptake requires an accurate quality control to exclude attenuation artifacts due to misalignment between PET and CT or presence of attenuators (devices, prosthetic valves, coronary calcification). Both attenuation corrected, and uncorrected images should be considered. Semiquantitative measurements can be helpful in serial follow-up after appropriate treatment, as it is in other non-cardiac localizations. Integrated PET/MR or PET/CT and MR fusion imaging could be useful to increasing specificity of MR findings and for follow-up.

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3.1.2 DIAGNOSIS: Examples Illustrating Diagnostic Certainty (Unlikely, Possible, Probable, Highly Probable)

Case 48

History

- 61-year-old female with a remote history of biopsy-proven pulmonary sarcoidosis was referred for FDG cardiac PET due to a new left bundle branch block (Figs. 3.1 and 3.2).

PET/CT Images

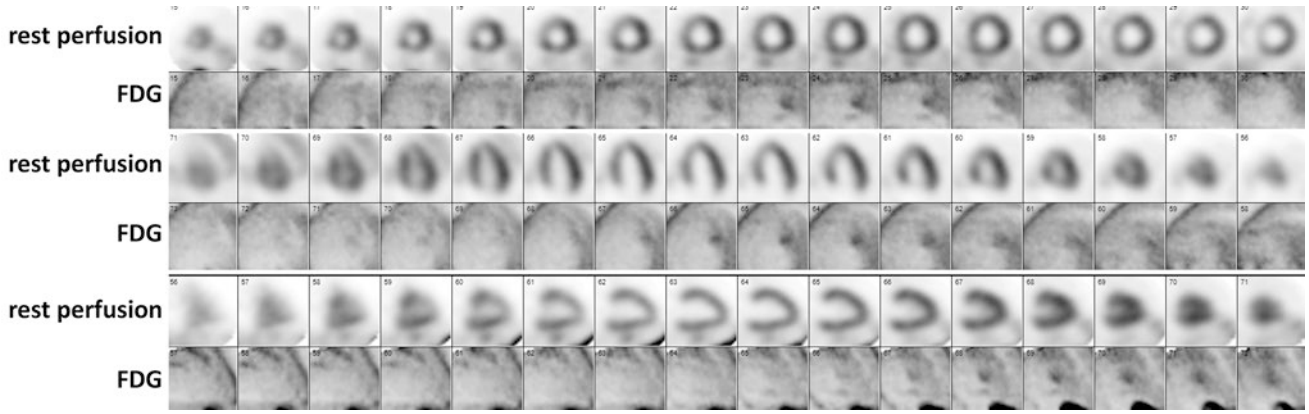

Fig. 3.1 Rest ^{99m}Tc-sestamibi SPECT myocardial perfusion and rest ^{18}F-deoxyglucose (FDG) PET/CT images. There is no evidence of regional perfusion defects. There is adequate suppression of FDG uptake in the normal myocardium. The FDG images demonstrate no evidence of focal glucose uptake in the heart

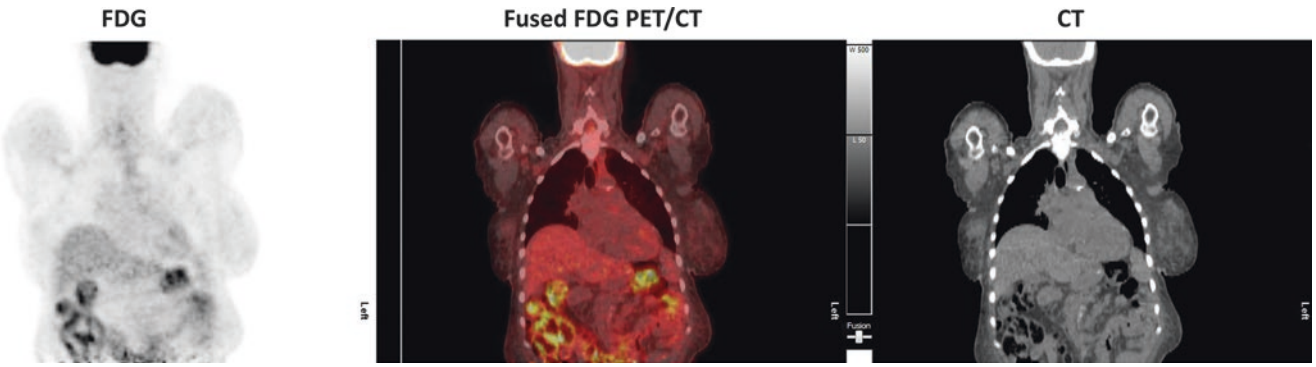

Fig. 3.2 Limited whole-body FDG PET/CT images demonstrate no evidence of metabolically active extracardiac sarcoidosis

Findings

- Rest myocardial perfusion images demonstrate no evidence of regional perfusion defects.
- There is adequate suppression of FDG uptake in the normal myocardium. The FDG images demonstrate no evidence of focal glucose uptake.
- The ECG-gated images demonstrate moderate LV dysfunction with a rest LVEF of 42% and mildly enlarged volumes and paradoxical septal motion consistent with LBBB.
- There is no evidence of metabolically active extracardiac sarcoidosis.

Differential Diagnosis

- None

Correlative Imaging

- Cardiac magnetic resonance imaging (MRI) revealed patchy subepicardial late gadolinium enhancement (LGE) in the basal anteroseptum (Fig. 3.3).
- The cine MRI images demonstrated a left ventricular ejection fraction of 35% with abnormal septal motion in keeping with the known left bundle branch block.

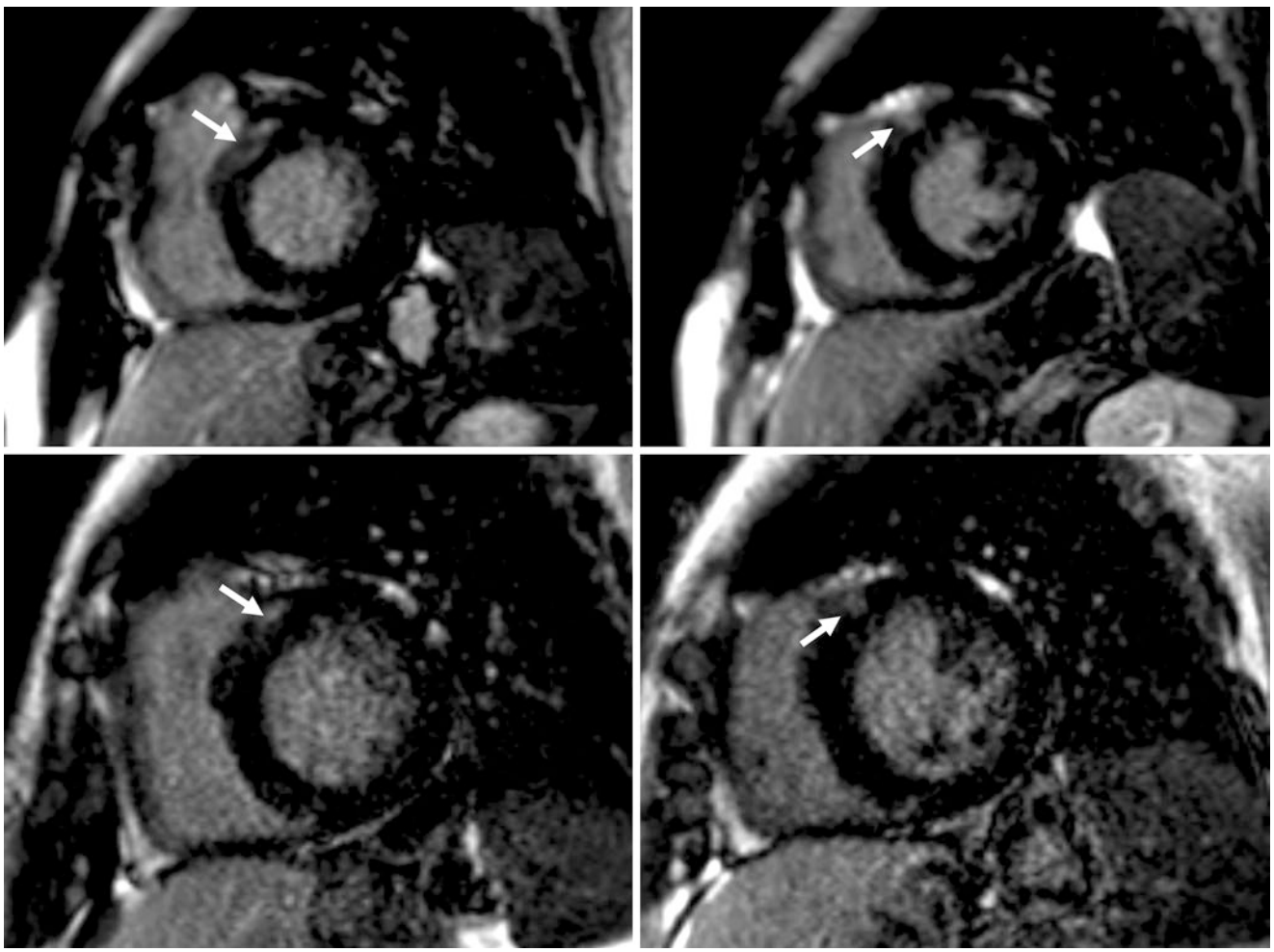

Fig. 3.3 Selective short axis views of her contrast-enhanced cardiac magnetic resonance imaging (MRI) demonstrate patchy subepicardial late gadolinium enhancement (LGE) in the basal anteroseptum (arrows)

Management

- Initiation of immunosuppressive therapy for the patient was deferred as the patient did not have evidence of active inflammation even though there was some suspicion of cardiac involvement given the cardiac MRI findings.
- The patient underwent vasodilator stress myocardial perfusion imaging, which was normal, to explore ischemia as the cause of her left bundle branch block.

Teaching Points

- The cardiac sarcoidosis likelihood by cardiac MRI was deemed possible (10–50%) due to one focal area of late gadolinium enhancement.
- The absence of regional perfusion defects or FDG uptake is consistent with a PET likelihood of active cardiac sarcoidosis categorized as unlikely (<10%).

Further Reading

Vita T, 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: e007030.

Divakaran S, et al. Diagnostic accuracy of advanced imaging in cardiac sarcoidosis: an imaging-histologic correlation study in patients undergoing cardiac transplantation. Circ Cardiovasc Imaging. 2019 Jun;12(6):e008975.

Chareonthaitawee P, et al. Joint SNMMI-ASNC Expert Consensus Document on the Role of ^{18}F-FDG PET/CT in Cardiac Sarcoid Detection and Therapy Monitoring. J Nucl Med. 2017 Aug;58(8):1341–1353.

Case 49

History

- 69-year-old male without obstructive coronary artery disease by angiography was referred for a cardiac PET to evaluate for cardiac sarcoidosis due to recurrent ventricular tachycardia (Figs. 3.4 and 3.5).

PET/CT Images

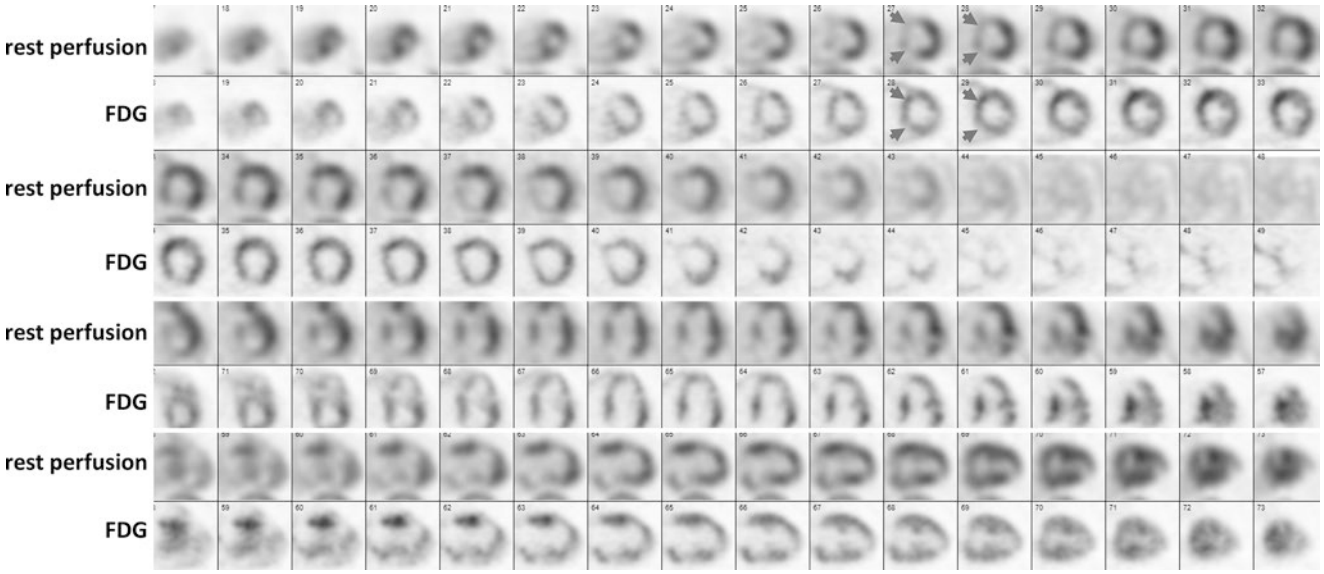

Fig. 3.4 Rest ^{99m}Tc-sestamibi SPECT myocardial perfusion and ^{18}F-deoxyglucose (FDG) PET/CT images. There is no evidence of regional perfusion defects. There is inadequate suppression of FDG uptake in the normal myocardium. The FDG images demonstrate mild-moderate diffuse glucose uptake in the heart

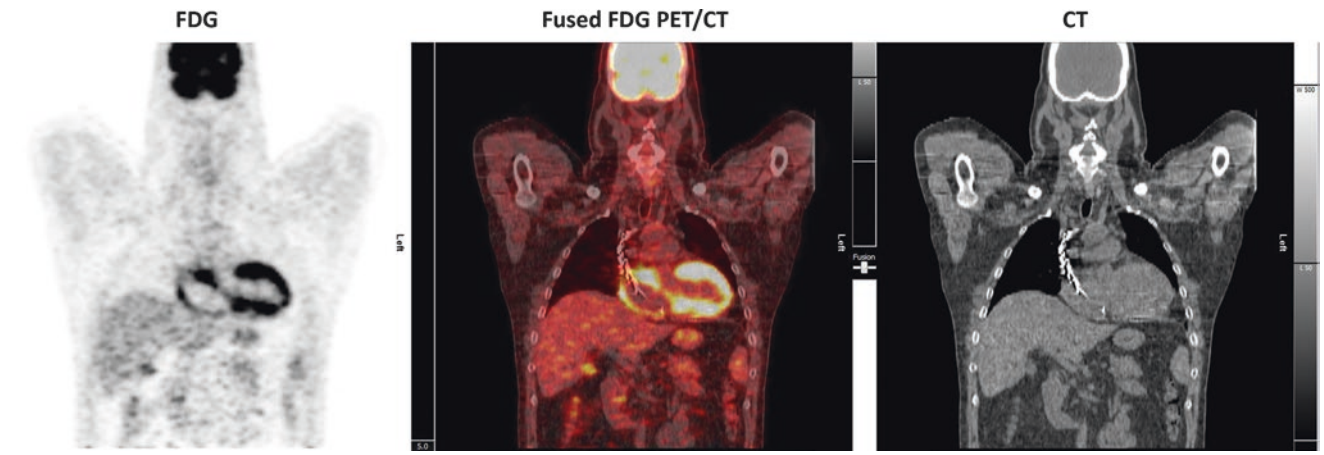

Fig. 3.5 Limited whole-body FDG PET/CT images demonstrate no evidence of metabolically active extracardiac sarcoidosis

Findings

- There is no evidence of regional perfusion defects on the rest images.
- There is inadequate suppression of FDG uptake in the heart. The FDG images demonstrate diffuse myocardial glucose uptake.
- The ECG-gated images demonstrated normal LV function with a rest LVEF of 57% with normal volumes and regional wall motion and thickening.
- The limited whole-body PET/CT images demonstrate no evidence of abnormal extracardiac FDG uptake.

Differential Diagnosis

- Poor diet preparation.
- Heart failure and ventricular tachycardia resulting in myocardial glucose utilization despite adequate diet preparation.
- Diffuse isolated cardiac sarcoidosis.

Correlative Imaging

- None

Management

- The patient underwent an electrophysiology study where three ventricular tachycardia morphologies were identified. Two were ablated, and one was not due to proximity to the conduction system. His ventricular tachycardia has remained controlled since then on antiarrhythmic drug therapy.

Teaching Points

- FDG PET likelihood of cardiac sarcoidosis is possible (10–50%) when there is a single perfusion defect without associated FDG uptake OR no perfusion defects but non-specific FDG uptake (diffuse FDG uptake of the left ventricular myocardium or focal FDG uptake with signal intensity that is only mildly increased when compared with background/blood pool uptake), like in this case.
- The use of FDG PET to detect inflammation may be limited in cases of severe heart failure and/or recurrent ventricular tachycardia due to preferential and physiologic glucose utilization by the myocardium despite adequate diet preparation.
- Severe diffuse isolated cardiac sarcoidosis in this patient is also less likely as LV function was normal.

Further Reading

Vita T, Okada D, Veillet-Chowdhury M, Bravo P, 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. Circulation: Cardiovascular Imaging. 2018;11.

Divakaran S, Stewart G, Lakdawala N, Padera R, Zhou W, Desai A, et al. Diagnostic Accuracy Of Advanced Imaging In Cardiac Sarcoidosis: An Imaging-Histologic Correlation Study In Patients Undergoing Cardiac Transplantation. Journal of the American College of Cardiology. 2019;73:934.

Chareonthaitawee P, Beanlands R, Chen W, Dorbala S, Miller E, Murthy V, et al. Joint SNMMI–ASNC Expert Consensus Document on the Role of ^{18}F-FDG PET/CT in Cardiac Sarcoid Detection and Therapy Monitoring. Journal of Nuclear Medicine. 2017;58: 1341–1353.

Case 50

History

- 45-year-old man with a history of cardiac arrest 1 year prior with no coronary artery disease by angiography (Fig. 3.6), and implantation of an ICD for secondary prevention.
- He was referred for a PET/CT for evaluation for cardiac sarcoidosis due to a recent diagnosis of biopsy-proven reticuloendothelial sarcoidosis (Figs. 3.7 and 3.8).

Coronary angiography

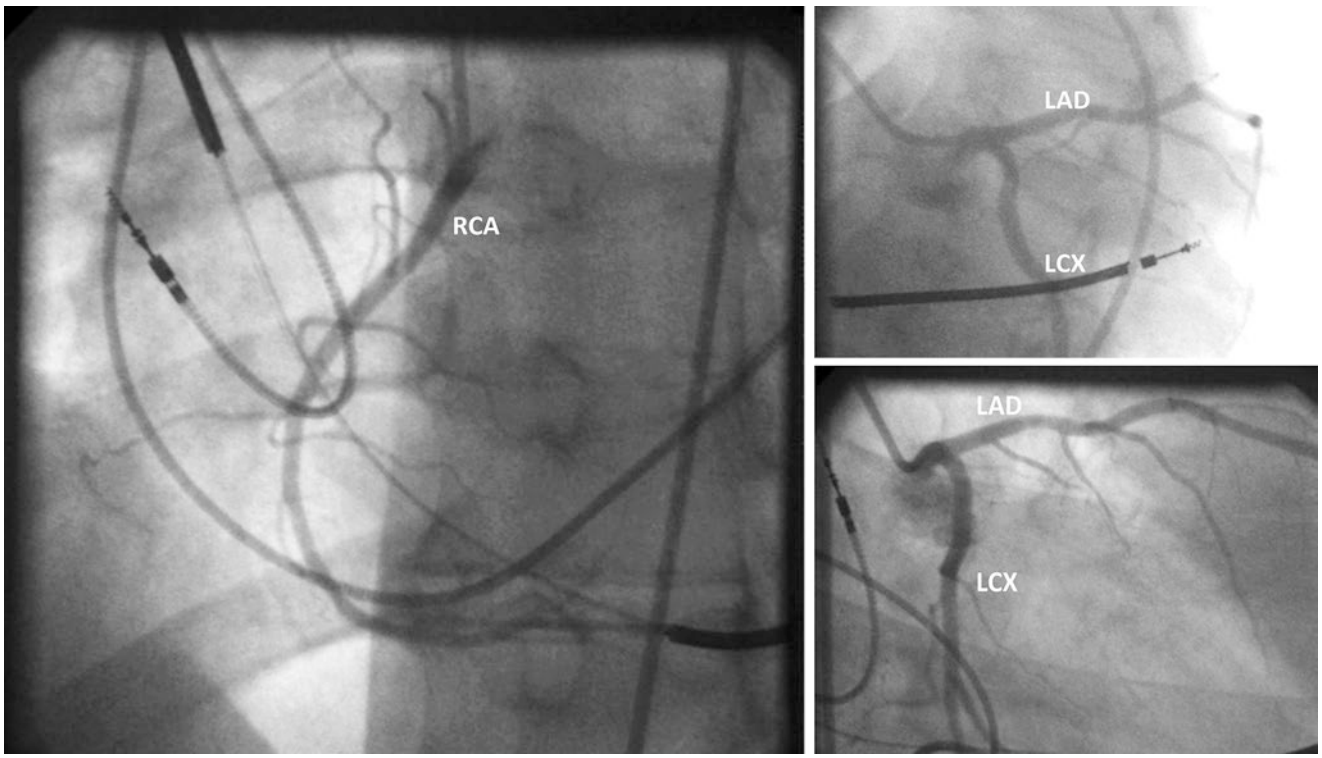

Fig. 3.6 Selective coronary angiographic views demonstrating normal coronary arteries

PET/CT Images

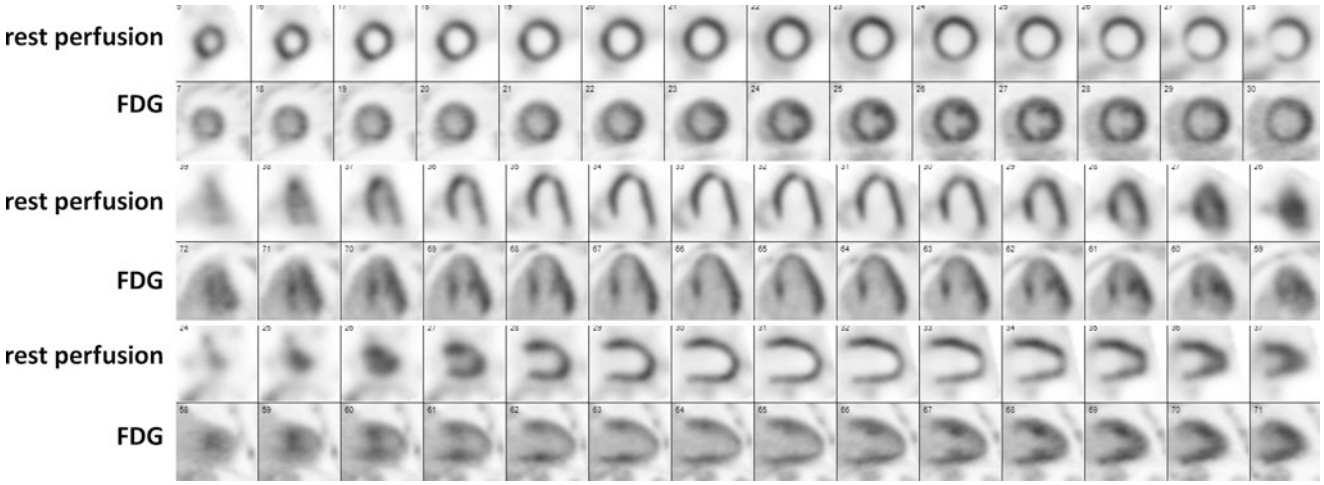

Fig. 3.7 Rest ^{82}Rubidium myocardial perfusion and ^{18}F-deoxyglucose (FDG) PET/CT images. The cardiac FDG images demonstrate adequate suppression of glucose uptake. There is predominantly matched reduction in perfusion and FDG uptake except for the mid and basal anteroseptal wall that shows increased glucose uptake (perfusion-FDG mismatched defect) (arrows)

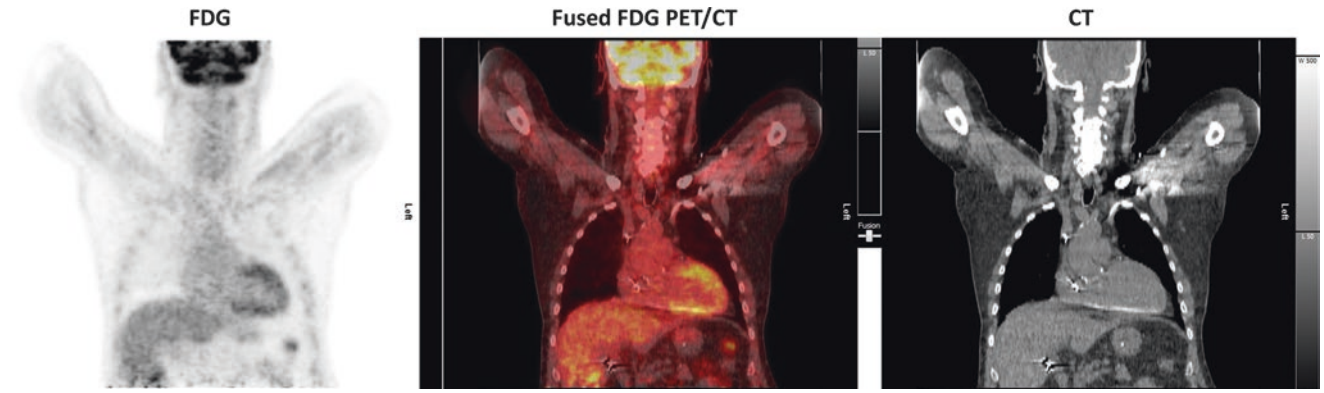

Fig. 3.8 Limited whole-body FDG PET/CT images demonstrate no evidence of metabolically active extracardiac sarcoidosis

Findings

- Rest myocardial perfusion imaging revealed a medium-sized perfusion defect of severe intensity in the mid and basal inferior and the basal inferoseptal walls. In addition, there were patchy areas of perfusion deficit in the mid and apical anterior and anteroseptal walls.
- The cardiac FDG images demonstrate predominantly matched reduction in perfusion and FDG uptake except for the mid and basal anteroseptal wall that shows increased glucose uptake (perfusion-FDG mismatched defect).
- The ECG-gated images demonstrated severely reduced LV function with a rest LVEF of 35% with moderately enlarged volumes and severe global hypokinesis.
- The limited whole images demonstrated no evidence of abnormal extracardiac FDG uptake.

Differential Diagnosis

- Coronary artery disease
- Isolated cardiac sarcoidosis
- Myocarditis
- Arrhythmogenic cardiomyopathy
- Idiopathic dilated cardiomyopathy

Management

- The patient was treated with prednisone for immunosuppression, but without improvement in his heart failure. He eventually underwent successful heart transplantation. Explant histology confirmed the presence of cardiac sarcoidosis.

Teaching Points

- The pattern of multiple patchy perfusion defects not following a normal coronary distribution with evidence of FDG uptake categorize this patient as "probable" for cardiac sarcoidosis.
- FDG PET cardiac sarcoidosis likelihood is probable (50–90%) when there are multiple, noncontiguous perfusion defects without associated FDG uptake OR a single perfusion defect with associated focal or focal on diffuse FDG uptake OR there are no perfusion defects, but focal or focal on diffuse FDG uptake.

Further Reading

Vita T, Okada D, Veillet-Chowdhury M, Bravo P, 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. Circulation: Cardiovascular Imaging. 2018;11.

Divakaran S, Stewart G, Lakdawala N, Padera R, Zhou W, Desai A, et al. Diagnostic Accuracy Of Advanced Imaging In Cardiac Sarcoidosis: An Imaging-Histologic Correlation Study In Patients Undergoing Cardiac Transplantation. Journal of the American College of Cardiology. 2019;73:934.

Case 51

History

- 55-year-old male with a history of biopsy-proven extracardiac sarcoidosis and recent diagnosis of nonischemic cardiomyopathy was referred to evaluate for cardiac sarcoidosis.
- The patient underwent both rest ^{99m}Tc-sestamibi SPECT myocardial perfusion and ^{18}F- FDG PET/CT (Figs. 3.9 and 3.10).

SPECT and PET/CT Images

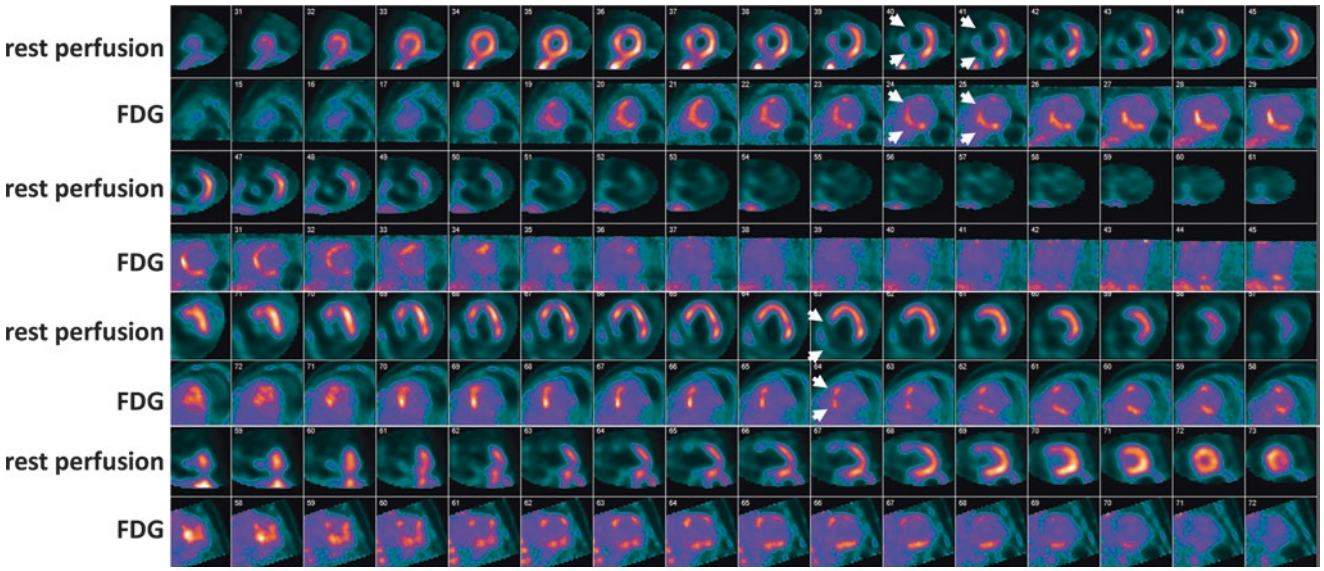

Fig. 3.9 Rest ^{99m}Tc-sestamibi SPECT myocardial perfusion and ^{18}F-deoxyglucose (FDG) PET/CT images

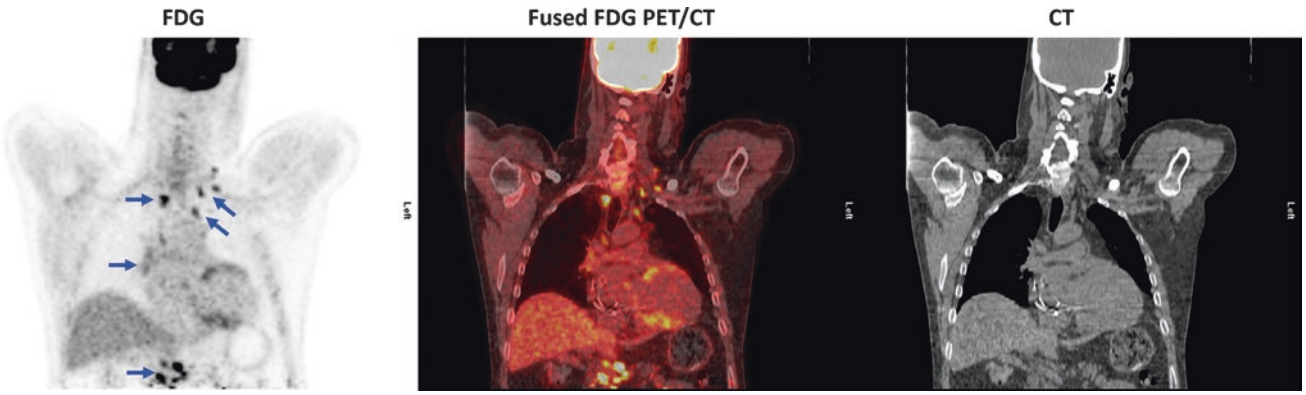

Fig. 3.10 Limited whole-body PET/CT imaging shows multiple FDG-avid bilateral mediastinal, hilar, and upper abdominal lymph nodes (arrows)

Findings

- There is a medium-sized and severe perfusion defect involving the mid and basal anteroseptal, inferoseptal, and inferior walls.
- The cardiac FDG images show increased glucose uptake in almost all hypoperfused regions (perfusion-FDG mismatched defects).
- The limited whole-body PET/CT imaging shows multiple FDG-avid bilateral mediastinal, hilar, and upper abdominal lymph nodes.

Differential Diagnosis

- None

Correlative Imaging (Fig. 3.11)

- Gross photograph of a 4-chamber view of the explanted heart shows diffuse involvement of the myocardium by sarcoid. The right ventricle is extensively involved, as is the interventricular septum, with more patchy involvement of the left ventricle.
- Photomicrograph of hematoxylin and eosin (H&E) stained section showing myocardium with a non-necrotizing granuloma containing abundant giant cells. There is fibrosis and a lymphocytic infiltrate at the periphery of the granuloma (200× original magnification).

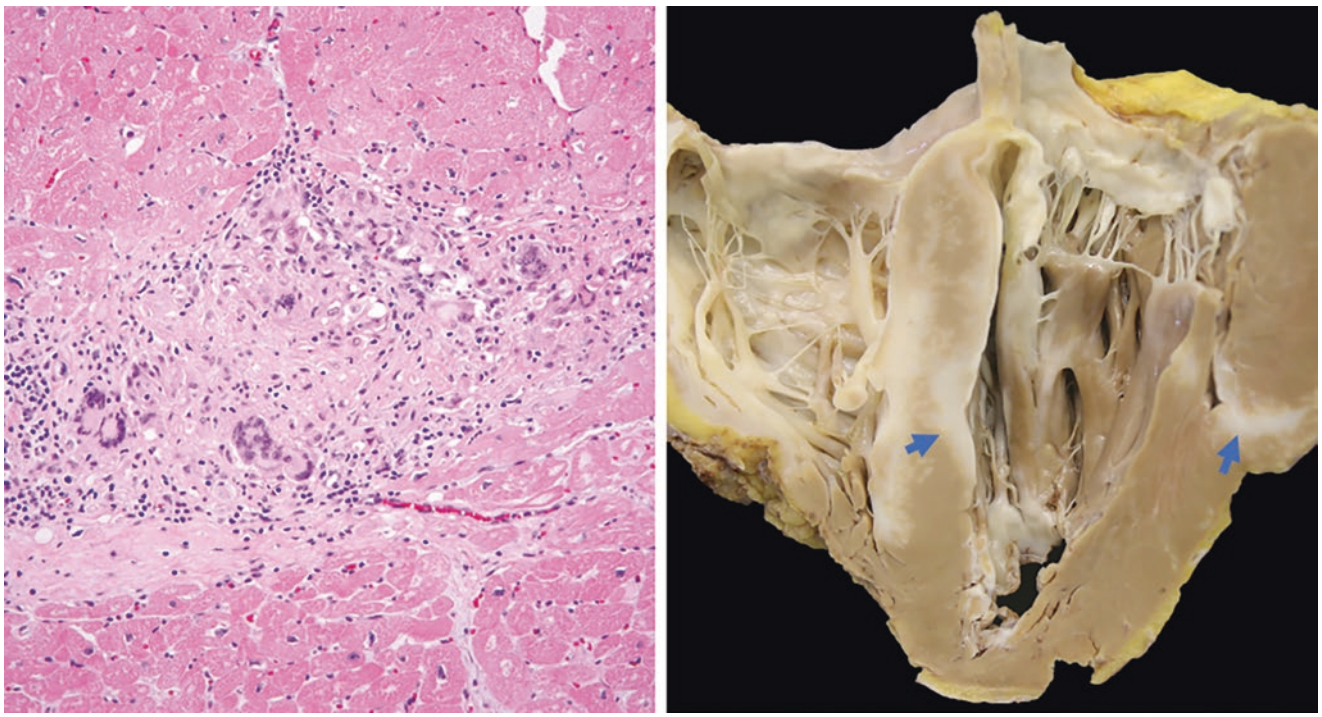

Fig. 3.11 RIGHT panel: Gross photograph of a 4-chamber view of the explanted heart shows diffuse involvement of the myocardium by sarcoidosis (arrows). The right ventricle is extensively involved, as is the interventricular septum, with more patchy involvement of the left ventricle. LEFT panel: Photomicrograph of hematoxylin and eosin (H&E) stained section showing myocardium with a non-necrotizing granuloma containing abundant giant cells. There is fibrosis and a lymphocytic infiltrate at the periphery of the granuloma (200× original magnification)

Management

- The patient eventually underwent left ventricular assist device placement and subsequent successful cardiac transplantation for end-stage sarcoid cardiomyopathy.

Teaching Points

- FDG PET likelihood of cardiac sarcoidosis is highly probable (>90%) when there are multiple, noncontiguous perfusion defects with associated FDG uptake or multiple areas of focal FDG uptake and extracardiac FDG uptake is present.

Further Reading

Vita T, Okada D, Veillet-Chowdhury M, Bravo P, 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. Circulation: Cardiovascular Imaging. 2018;11.

Divakaran S, Stewart G, Lakdawala N, Padera R, Zhou W, Desai A, et al. Diagnostic Accuracy Of Advanced Imaging In Cardiac Sarcoidosis: An Imaging-Histologic Correlation Study In Patients Undergoing Cardiac Transplantation. Journal of the American College of Cardiology. 2019;73:934.

Chareonthaitawee P, Beanlands R, Chen W, Dorbala S, Miller E, Murthy V, et al. Joint SNMMI–ASNC Expert Consensus Document on the Role of ^{18}F-FDG PET/CT in Cardiac Sarcoid Detection and Therapy Monitoring. Journal of Nuclear Medicine. 2017;58:1341–1353.

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3.1.3 Complementary Value of FDG PET and MRI

Case 52

History

- 60-year-old female with biopsy-proven pulmonary sarcoidosis and known CAD with prior remote PCI to the mid LAD, presented with excessive fatigue and found to have episodes of recurrent ventricular tachycardia.
- A coronary angiogram demonstrated a patent LAD stent and minimal luminal irregularities in the other coronary arteries.
- She was referred for advanced imaging to evaluate for cardiac sarcoidosis with cardiac MR (Fig. 3.12) and rest ^{99m}Tc-sestamibi SPECT myocardial perfusion and ^{18}F-deoxyglucose (FDG) PET/CT (Figs. 3.13 and 3.14).

MR Imaging

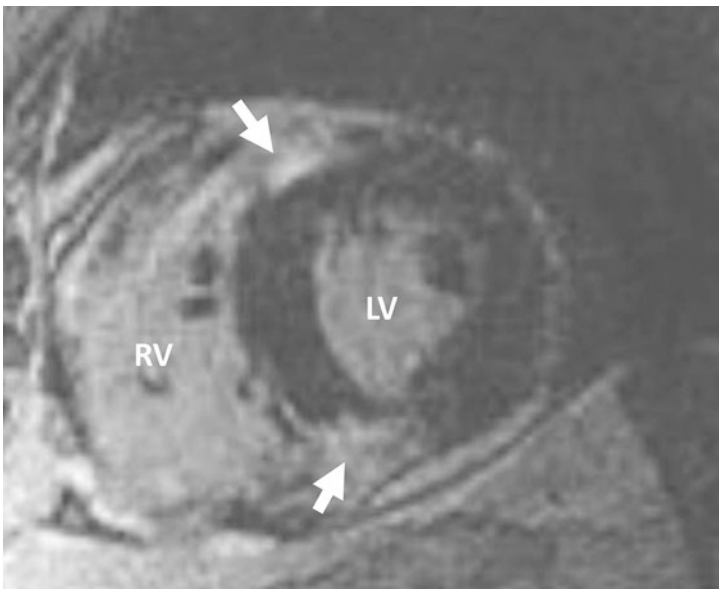

Fig. 3.12 Selected mid short axis slice of the patient's contrast-enhanced cardiac MRI. There is dense subepicardial late gadolinium enhancement involving the basal and mid inferoseptal and to a lesser extent the anterior and anteroseptal walls (arrows). There is additional subepicardial late gadolinium enhancement in the apical inferoseptal segment at the inferior RV insertion site (not shown)

PET/CT Imaging

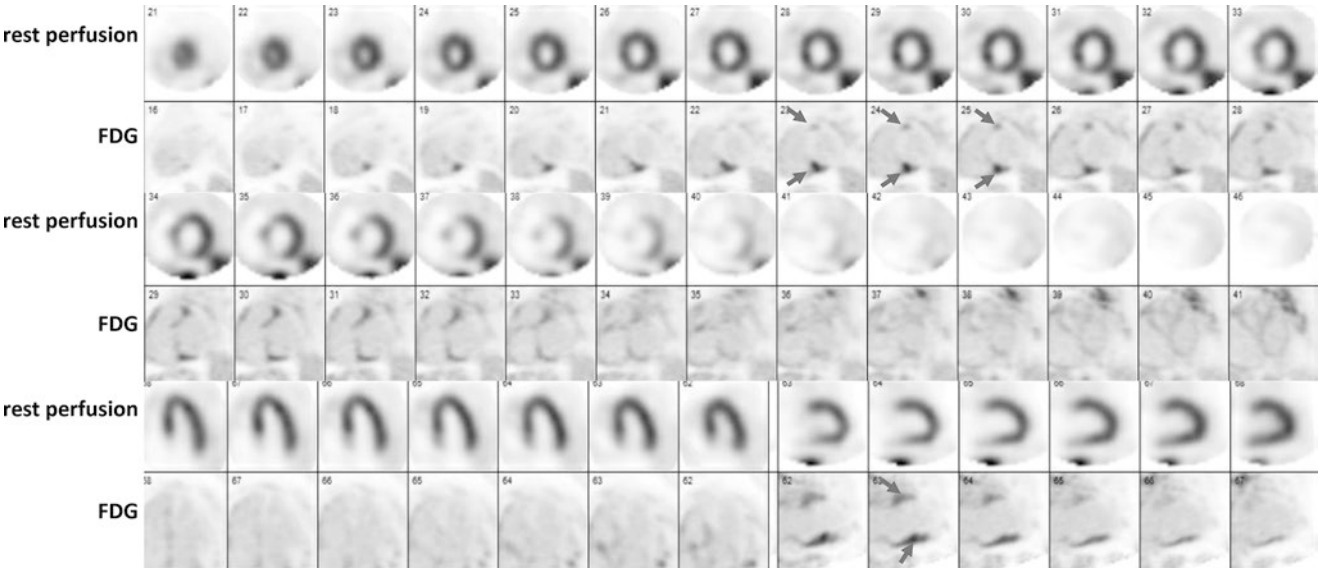

Fig. 3.13 Rest ^{99m}Tc-sestamibi SPECT myocardial perfusion and ^{18}F-deoxyglucose (FDG) PET/CT images. The rest perfusion images showed a small and severe perfusion defect involving the mid and basal inferoseptal and basal anteroseptal LV segments. The FDG images demonstrate adequate suppression of glucose uptake by normal myocardium. There is intense focal FDG uptake in the mid and basal inferoseptal wall and mild uptake in the basal anteroseptal wall (perfusion-FDG mismatched defects, arrows)

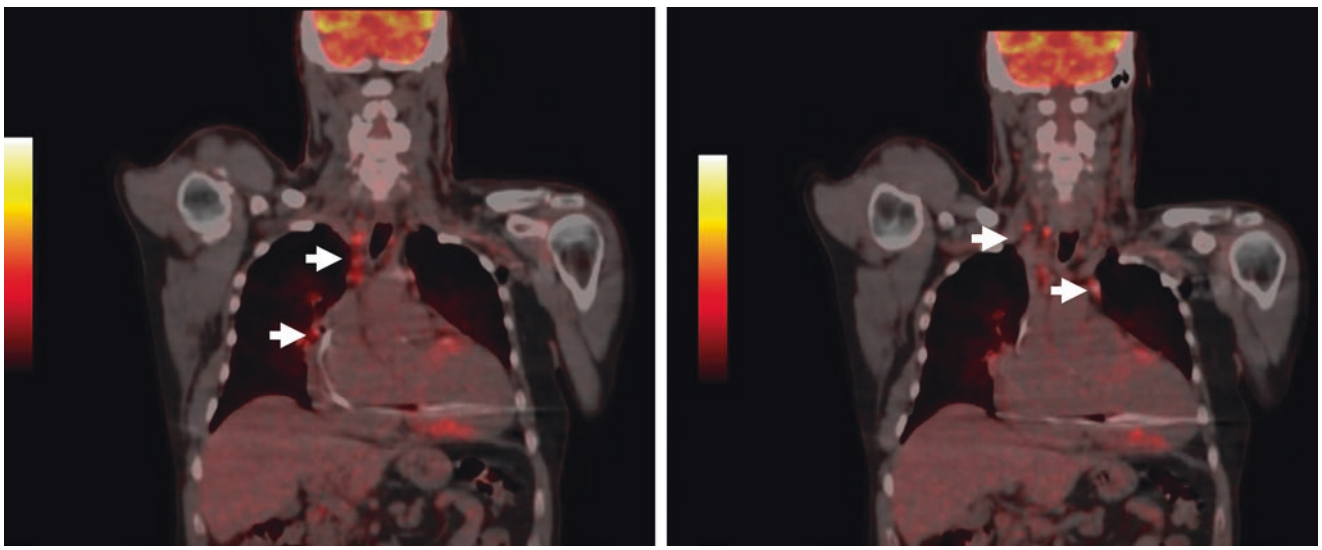

Fig. 3.14 Limited whole PET/CT images demonstrating increased FDG uptake in upper mediastinal and hilar nodes, consistent with active extracardiac sarcoidosis (arrows)

Findings

MR Imaging

- There is dense subepicardial late gadolinium enhancement involving the basal and mid inferoseptal and to a lesser extent the anterior and anteroseptal walls. There is additional subepicardial late gadolinium enhancement in the apical inferoseptal segment at the inferior RV insertion site.
- Global LV function was mildly reduced.
- Based on these findings and recurrent symptomatic episodes of VT, the patient underwent an AICD placement.
- A few months post AICD placement the patient was referred for FDG PET/CT study for evaluation of active cardiac sarcoidosis.

PET/CT Imaging

- There was adequate suppression of FDG uptake by normal myocardium.
- The rest perfusion images showed a small and severe perfusion defect involving the mid and basal inferoseptal and basal anteroseptal LV segments.
- The FDG images demonstrate intense focal glucose uptake in the mid and basal inferoseptal wall and mild uptake in the basal anteroseptal wall (perfusion-FDG mismatched defects).
- The ECG-gated images demonstrated mildly reduced LV function with a rest LVEF of 48% and mild global hypokinesis.
- The limited whole PET/CT images demonstrate increased FDG uptake in upper mediastinal and hilar nodes, consistent with active extracardiac sarcoidosis.

Differential Diagnosis

- Myocarditis: Given clinical presentation and absence of troponin elevation, this diagnosis was considered less likely.

Management

- Given the absence of recurrent ventricular arrhythmias and after detailed discussion with the patient regarding potential benefit vs risk of immunosuppressive therapy, it was decided to perform watchful waiting and eventually repeat the FDG PET scan during follow-up to look for signs of disease progression.

Teaching Points

- FDG PET and MRI have complementary value in the evaluation of patient with suspected cardiac sarcoidosis. Both have very high sensitivity and negative predictive value.
- In the setting of a positive MRI, like in this case vignette, the metabolic signal from FDG PET provides an indication of active inflammation and the potential need to consider immunosuppressive therapy.
- When immunosuppressive therapy is started, FDG PET is then used to monitor treatment response.

Further Reading

Vita T, Okada D, Veillet-Chowdhury M, Bravo P, 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. Circulation: Cardiovascular Imaging. 2018;11.

Chareonthaitawee P, Beanlands R, Chen W, Dorbala S, Miller E, Murthy V, et al. Joint SNMMI–ASNC Expert Consensus Document on the Role of ^{18}F-FDG PET/CT in Cardiac Sarcoid Detection and Therapy Monitoring. Journal of Nuclear Medicine. 2017;58:1341–1353.

3.1.4 Differential Diagnosis

Case 53

History

- 47-year-old male with a history of cardiomyopathy and no evidence of coronary artery disease by angiography was referred to evaluate for cardiac sarcoidosis due to diffuse hypokinesis of a non-dilated left ventricle on echocardiogram.
- The patient underwent rest ^{82}Rubidium myocardial perfusion study and ^{18}F-deoxyglucose (FDG) PET/CT (Figs. 3.15 and 3.16).

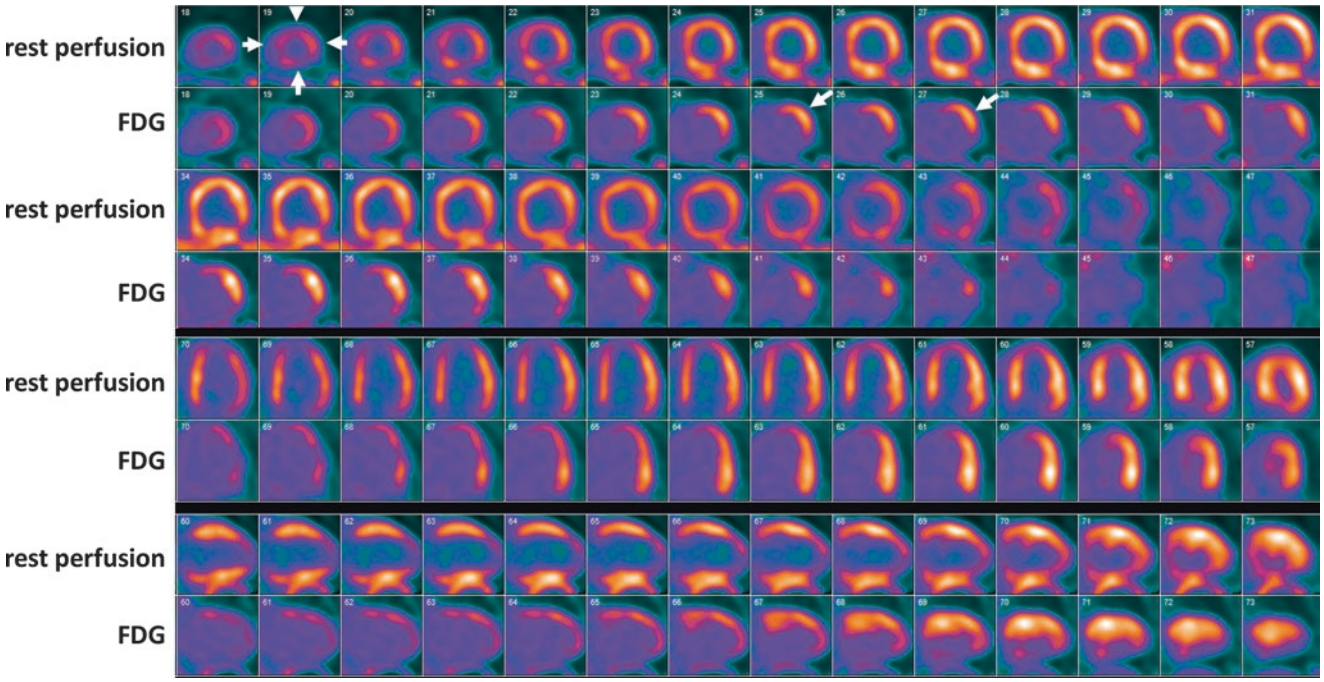

Fig. 3.15 PET/CT images showing a medium-sized perfusion defect in the apical LV segments and apex on rest ^{82}Rubidium myocardial perfusion study. There is intense ^{18}F-deoxyglucose (FDG) uptake in the apical lateral and the mid and basal anterolateral walls

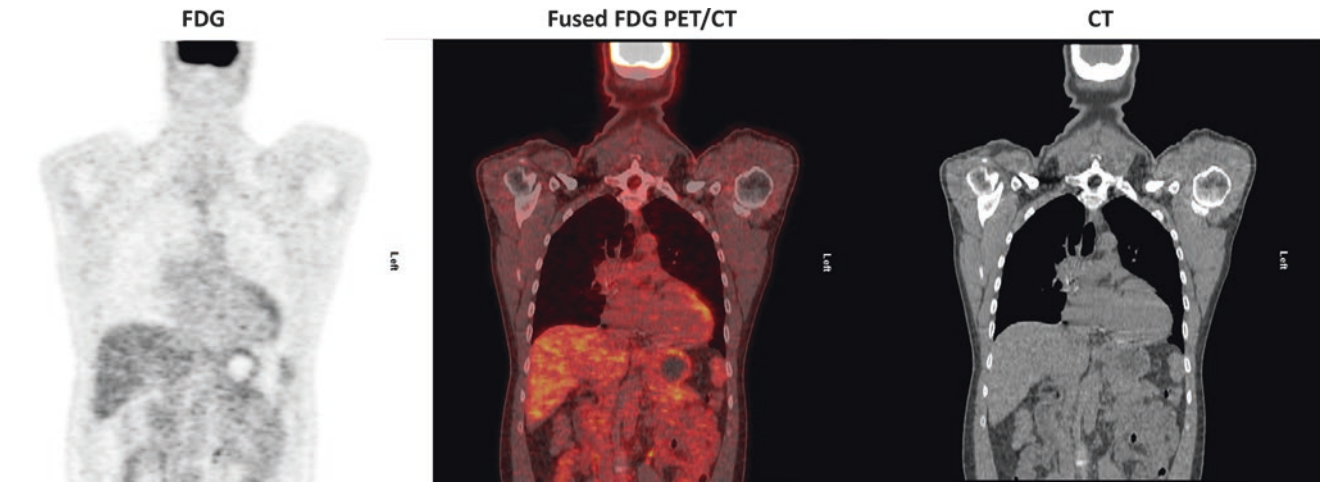

Fig. 3.16 Limited whole-body PET/CT images demonstrating no evidence of abnormal extracardiac FDG uptake

Findings

PET/CT Images

- The rest myocardial perfusion images show a medium-sized perfusion defect in the apical LV segments and apex. There is also a small-sized perfusion defect in the basal inferolateral wall.
- On the FDG images, there is intense FDG uptake in the apical lateral and the mid and basal anterolateral walls.
- The ECG-gated images demonstrated severe LV systolic dysfunction with a rest LVEF of 35% and severe global hypokinesis.
- On the whole-body PET/CT images, there is no evidence of abnormal extracardiac FDG uptake.

Differential Diagnosis

- Coronary artery disease
- Cardiac sarcoidosis
- Myocarditis
- Arrhythmogenic cardiomyopathy
- Idiopathic dilated cardiomyopathy

Management

- The patient underwent genetic testing which revealed a disease-causing mutation in the phospholamban gene (c.40_42delAGA) consistent with the diagnosis of arrhythmogenic cardiomyopathy. His heart failure progressed and required left ventricular assist device placement and he eventually underwent successful cardiac transplantation.

Correlative Imaging (Fig. 3.17)

- Gross photograph of four chamber view of the explanted heart showing fatty replacement of the right ventricular free wall characteristic of AC. An AICD lead is seen in the right heart along with evidence of an apically placed left ventricular assist device (*left panel*).
- Photomicrograph of hematoxylin and eosin (H&E) stained section demonstrating transmural fibrofatty infiltration of the right ventricular free wall without other significant pathology. Occasional islands of viable myocardium remain. (40× original magnification) (*right panel*).

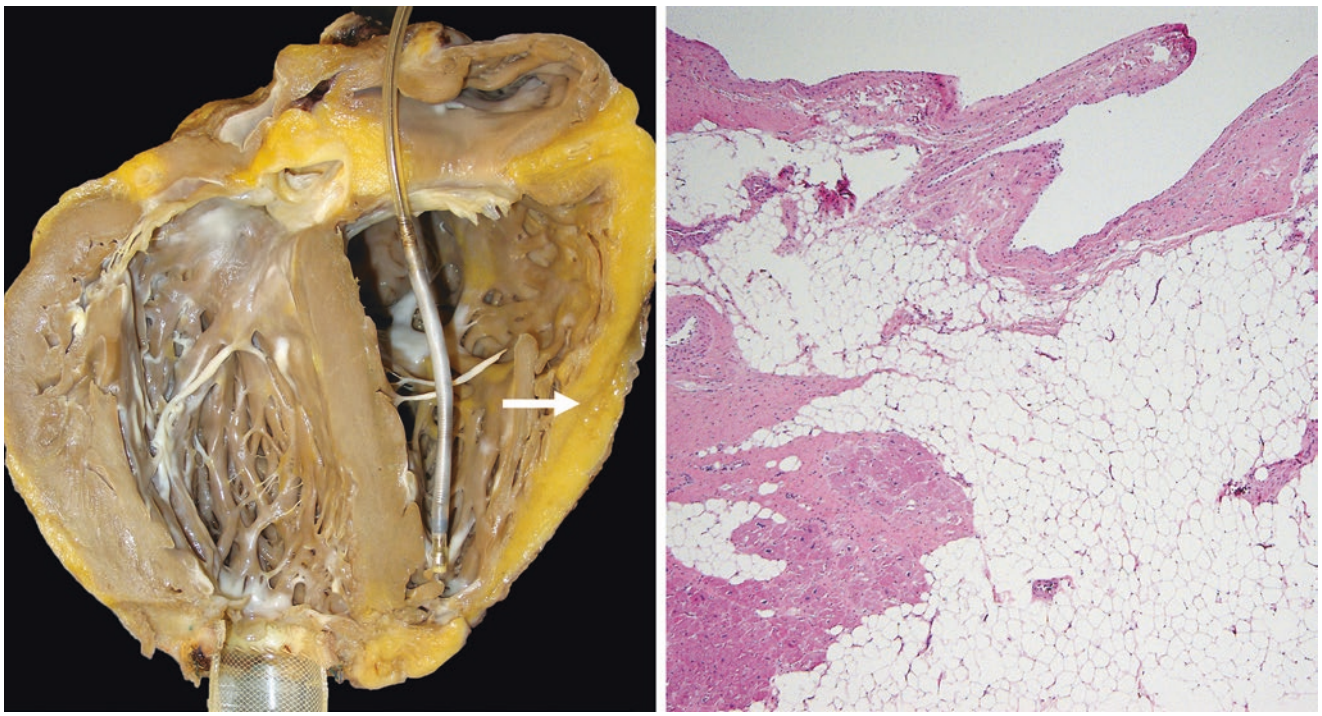

Fig. 3.17 LEFT panel: Gross photograph of four chamber view of the explanted heart showing fatty replacement of the right ventricular free wall characteristic of AC. An AICD lead is seen in the right heart along with evidence of an apically placed left ventricular assist device. RIGHT panel: Photomicrograph of hematoxylin and eosin (H&E) stained section demonstrating transmural fibrofatty infiltration of the right ventricular free wall without other significant pathology. Occasional islands of viable myocardium remain. (40× original magnification)

Teaching Points

- The pattern of perfusion abnormalities and non-matching focal FDG uptake makes this case "probable" for cardiac sarcoidosis. FDG PET cardiac sarcoidosis likelihood is probable (50–90%) when there are multiple, noncontiguous perfusion defects without associated FDG uptake OR a single perfusion defect with associated focal or focal on diffuse FDG uptake OR there are no perfusion defects, but focal or focal on diffuse FDG uptake.

Further Reading

Divakaran S, Stewart G, Lakdawala N, Padera R, Zhou W, Desai A, et al. Diagnostic Accuracy Of Advanced Imaging In Cardiac Sarcoidosis: An Imaging-Histologic Correlation Study In Patients Undergoing Cardiac Transplantation. Journal of the American College of Cardiology. 2019;73:934.

Protonotarios A, Wicks E, Ashworth M, Stephenson E, Guttmann O, Savvatis K, et al. Prevalence of ^{18}F-fluorodeoxyglucose positron emission tomography abnormalities in patients with arrhythmogenic right ventricular cardiomyopathy. International Journal of Cardiology. 2019;284:99–104.

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Case 54

History

- 47-year-old female with a history of lymphocytic myocarditis with restrictive cardiomyopathy and chronotropic incompetence requiring dual chamber pacemaker placement was referred for FDG PET for the evaluation of cardiac sarcoidosis and rest ^{99m}Tc-sestamibi SPECT myocardial perfusion (Figs. 3.18 and 3.19).

PET/CT Images

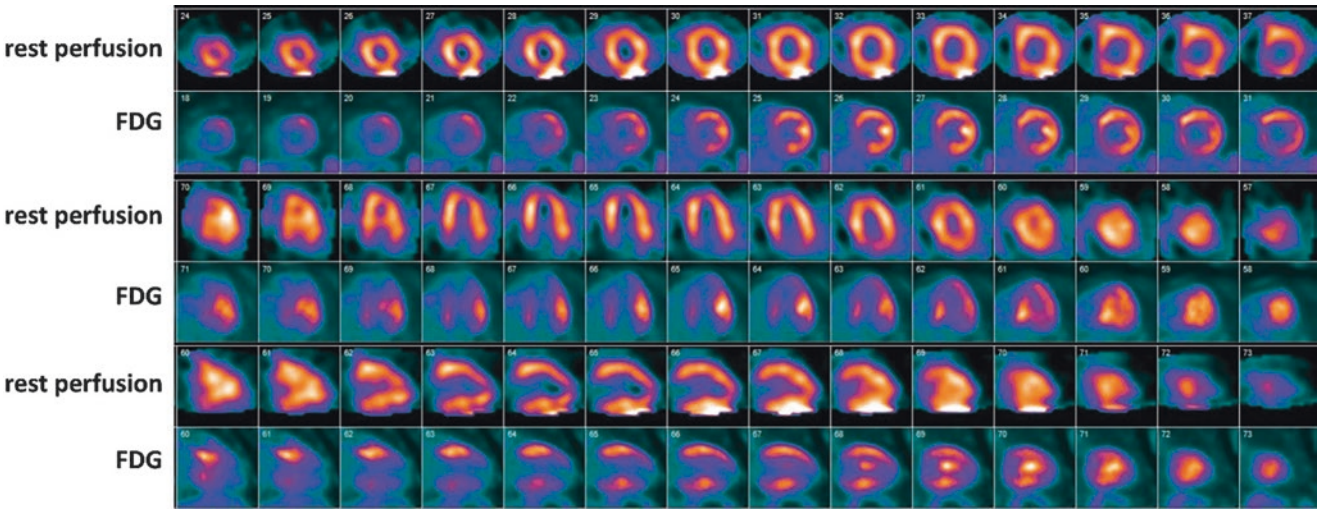


Fig. 3.18 Rest ^{99m}Tc-sestamibi SPECT myocardial perfusion and ^{18}F-deoxyglucose (FDG) PET/CT images

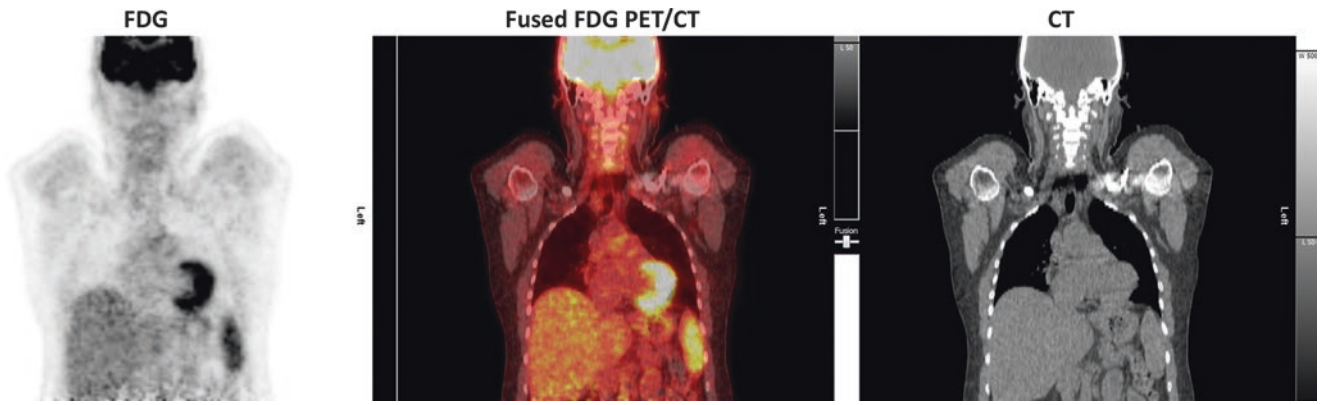


Fig. 3.19 Limited whole-body PET/CT images demonstrating diffuse increased FDG uptake in the spleen

Findings

- The rest myocardial perfusion images demonstrated no regional defects.
- The cardiac FDG images demonstrated intense glucose uptake throughout the anterior and lateral walls of the left ventricular myocardium with less FDG uptake in the inferior wall and the apex.
- The ECG-gated images demonstrated normal LV systolic function with a rest LVEF of 67% and normal regional wall motion and thickening.
- On the whole-body PET/CT images, there was diffuse increased FDG uptake in the spleen, but no other areas of abnormal extracardiac FDG uptake.

Differential Diagnosis

- Myocarditis
- Cardiac sarcoidosis
- Arrhythmogenic cardiomyopathy
- Partial suppression of FDG uptake

Correlative Imaging

- None

Management

- The patient eventually underwent biventricular assist device placement and subsequent successful cardiac transplantation for end-stage restrictive cardiomyopathy. Histology of the explanted heart revealed restrictive cardiomyopathy with biventricular hypertrophy and active myocarditis.

Teaching Points

- The PET pattern in this case is "possible" for cardiac sarcoidosis.
- FDG PET likelihood of cardiac sarcoidosis is possible (10–50%) when there is a single perfusion defect without associated FDG uptake OR no perfusion defects but nonspecific FDG uptake (diffuse FDG uptake of the left ventricular myocardium or focal FDG uptake with signal intensity that is only minimally increased when compared with background/blood pool uptake).
- Myocarditis should almost always be in the differential diagnosis when cardiac sarcoidosis is suspected as both the clinical presentation (heart failure, ventricular tachycardia) and imaging findings can be similar.

Further Reading

Vita T, Okada D, Veillet-Chowdhury M, Bravo P, 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. Circulation: Cardiovascular Imaging. 2018;11.

Divakaran S, Stewart G, Lakdawala N, Padera R, Zhou W, Desai A, et al. Diagnostic Accuracy Of Advanced Imaging In Cardiac Sarcoidosis: An Imaging-Histologic Correlation Study In Patients Undergoing Cardiac Transplantation. Journal of the American College of Cardiology. 2019;73:934.

3.1.5 Risk Stratification by FDG PET

Case 55

History

- 43-year-old male with history of ventricular tachycardia status post ICD implantation was referred for FDG PET to evaluate for possible cardiac sarcoidosis (Figs. 3.20 and 3.21).

SPECT and PET/CT Images

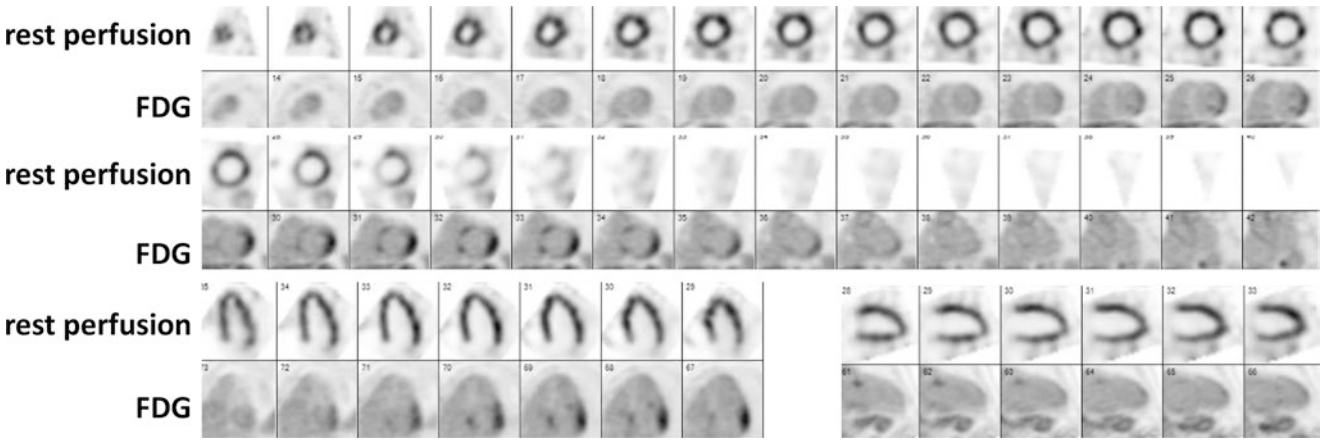


Fig. 3.20 Rest ^{99m}Tc-sestamibi SPECT MPI and ^{18}F-FDG PET scan

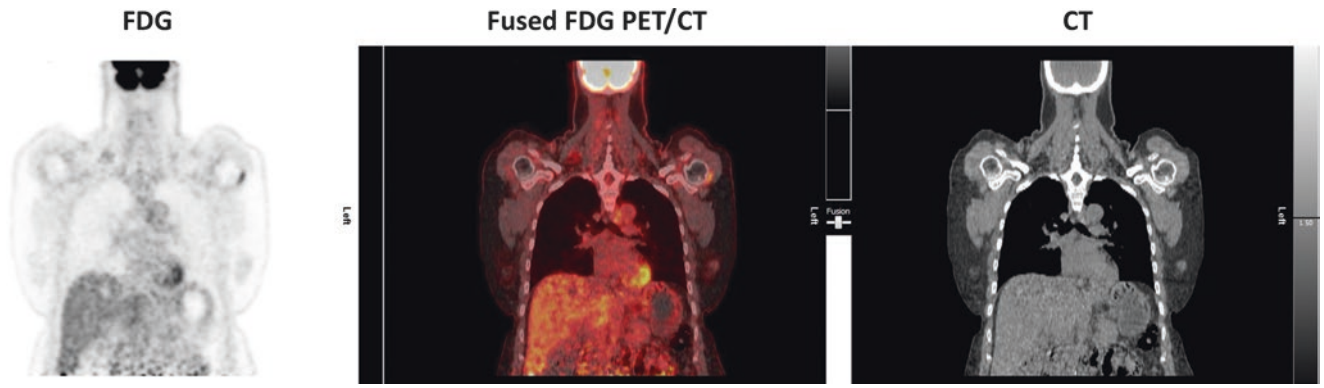


Fig. 3.21 Limited whole-body PET/CT images showing no evidence of metabolically active extracardiac sarcoidosis

Findings

- The rest myocardial perfusion images demonstrated no regional defects.
- The cardiac FDG images demonstrated moderate focal glucose uptake in the basal lateral wall.
- The ECG-gated images demonstrated normal LV systolic function with a rest LVEF of 51% with normal volumes, regional wall motion and thickening.
- On the whole-body PET/CT images, there was no evidence of metabolically active extracardiac sarcoidosis.

Differential Diagnosis

- Partial suppression of FDG uptake
- Cardiac sarcoidosis

Management

- Initiation of immunosuppressive therapy for the patient was deferred as the patient did not have definitive evidence of active inflammation.

Correlative Imaging

- None

Teaching Points

- The focal area of moderate FDG uptake without associated regional perfusion defects and no evidence of abnormal extracardiac FDG uptake is consistent with a PET likelihood of active cardiac sarcoidosis categorized as possible (10–50%).
- However, the presence of moderate focal FDG uptake involving only the lateral wall without any perfusion defects is associated with low risk.
- In patients with equivocal evidence of active myocardial inflammation, follow-up imaging may be helpful to ascertain progression or resolution of scan findings, which would be especially helpful in patients with recurrent symptoms or changes in LV function.

Further Reading

Blankstein R, Osborne M, Naya M, Waller A, Kim C, Murthy V, et al. Cardiac Positron Emission Tomography Enhances Prognostic Assessments of Patients With Suspected Cardiac Sarcoidosis. Journal of the American College of Cardiology. 2014;63:329–336.

Case 56

History

- 75-year-old female with known pulmonary sarcoidosis presented with ventricular tachycardia/cardiac arrest. She received a secondary prevention ICD and was subsequently referred for an FDG PET/CT to evaluate for cardiac sarcoidosis (Fig. 3.22).

SPECT and PET/CT Images

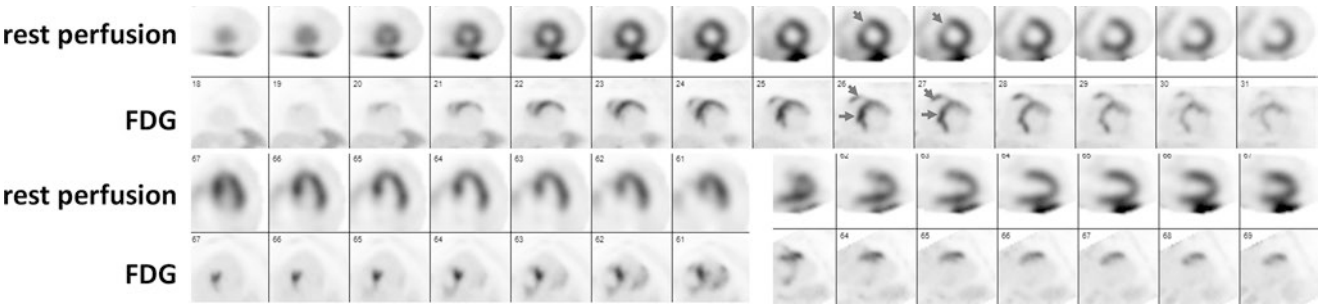


Fig. 3.22 Rest ^{99m}Tc-sestamibi SPECT myocardial perfusion and ^{18}F-deoxyglucose (FDG) PET/CT images

Findings

- Rest myocardial perfusion images demonstrated a small perfusion defect of severe intensity involving the basal anteroseptal wall.
- There was adequate suppression of FDG uptake in the normal myocardium. The FDG images demonstrate intense focal glucose uptake involving the mid and basal anterior and septal walls. There is also focal FDG uptake in the RV free wall.
- The ECG-gated images demonstrated normal LV systolic function with a rest LVEF of 60% and normal volumes, regional wall motion and thickening.
- There was no evidence of metabolically active extracardiac sarcoidosis.

Differential Diagnosis

- None

Correlative Imaging

- None

Management

- The patient was started on anti-inflammatory therapy including corticosteroids.

Teaching Points

- FDG PET likelihood of cardiac sarcoidosis is highly probable (>90%) when there are multiple, noncontiguous perfusion defects with associated FDG uptake or multiple areas of focal FDG uptake and extracardiac FDG uptake present.
- The presence of a perfusion-FDG mismatched defect associated with focal FDG uptake in the RV free wall identifies patients at high risk for ventricular arrhythmias and death.

Further Reading

Blankstein R, Osborne M, Naya M, Waller A, Kim C, Murthy V, et al. Cardiac Positron Emission Tomography Enhances Prognostic Assessments of Patients With Suspected Cardiac Sarcoidosis. Journal of the American College of Cardiology. 2014;63:329–336.

Vita T, Okada D, Veillet-Chowdhury M, Bravo P, 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. Circulation: Cardiovascular Imaging. 2018;11.

Chareonthaitawee P, Beanlands R, Chen W, Dorbala S, Miller E, Murthy V, et al. Joint SNMMI–ASNC Expert Consensus Document on the Role of ^{18}F-FDG PET/CT in Cardiac Sarcoid Detection and Therapy Monitoring. Journal of Nuclear Medicine. 2017;58:1341–1353.

3.1.6 Evaluation of Response to Therapy

Case 57

History

- 68-year-old male with a history of biopsy-proven cardiac sarcoidosis status post anti-inflammatory therapy, was referred for FDG PET/CT to evaluate response to immunosuppressive therapy.
- The patient was studied prior (Fig. 3.23) and after therapy (Fig. 3.24).

SPECT and PET/CT Images

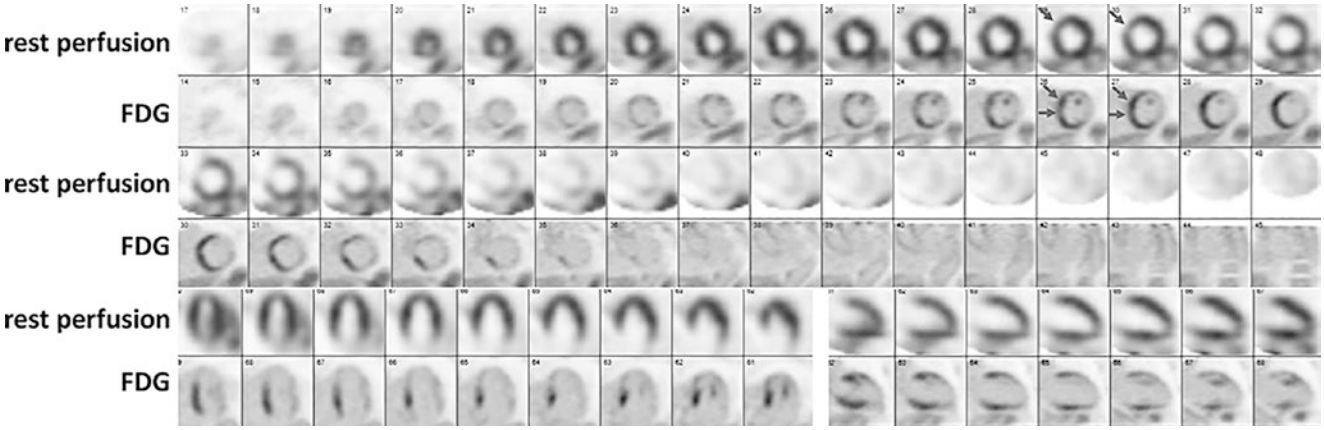


Fig. 3.23 Baseline study. Rest ^{99m}Tc-sestamibi myocardial perfusion and ^{18}F-deoxyglucose (FDG) PET/CT

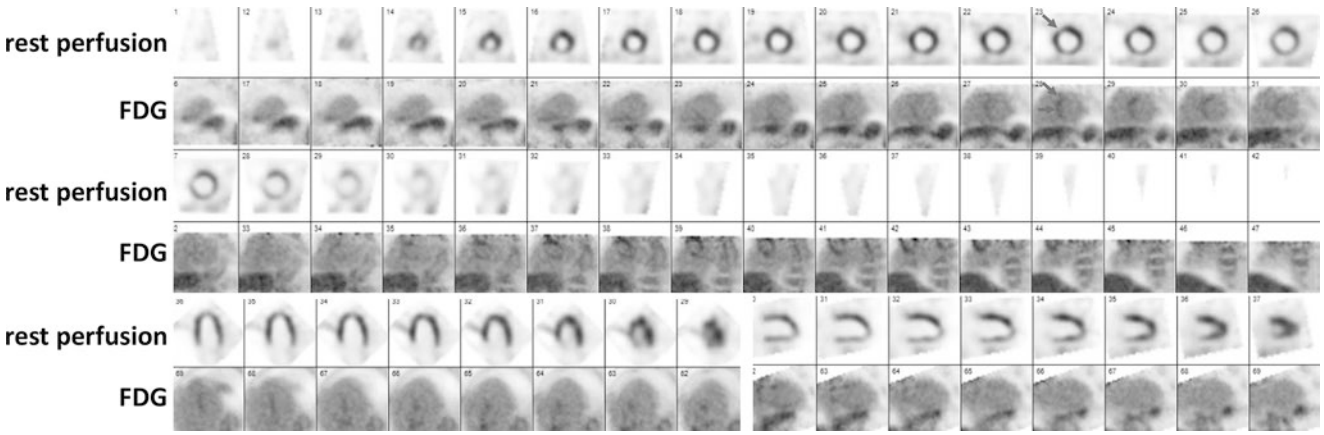


Fig. 3.24 Follow-up study. Rest ^{99m}Tc-sestamibi myocardial perfusion SPECT and ^{18}F-deoxyglucose (FDG) PET/CT

Findings

Baseline study (Fig. 3.23):

- The rest perfusion images demonstrate a small perfusion defect of severe intensity involving the mid and basal anteroseptal wall.
- The FDG PET/CT study demonstrates adequate suppression of glucose uptake in normal myocardium. There is a focus of intense FDG uptake involving the mid and basal interventricular septum (perfusion-FDG mismatched defect).
- The ECG-gated images demonstrated moderate LV systolic dysfunction and a rest LVEF of 42% with mildly enlarged volumes and moderate global hypokinesis.

Follow-up study (7 months after baseline) (Fig. 3.24):

- The rest perfusion images demonstrate a small perfusion defect of mild intensity involving the basal anteroseptal wall, which appears decreased in size and intensity compared to the baseline study.
- The FDG PET/CT study demonstrates adequate suppression of glucose uptake in normal myocardium. There is minimal FDG uptake involving the basal interventricular septum.
- The ECG-gated images demonstrated normal LV systolic function and a rest LVEF of 52% with normal volumes and regional wall motion.

Quantitative analysis of the intensity and extent of FDG uptake shows a decrease of both SUVmax and volume of FDG uptake (Table 3.1).

Correlative Imaging

- None

Table 3.1 Quantitative analysis

Exam sequence	Myocardial SUVmax	Volume of FDG uptake (SUVmax >2.7, mL)
Baseline	5.9	22.63
Follow-up	1.6	0.91

Management

- After the baseline scan, the patient was started on prednisone (20 mg/day) and methotrexate (20 mg/week). Following the results of the second scan, the patient began tapering immunosuppressive therapy.

Differential Diagnosis

- None

Teaching Points

- FDG PET/CT is currently the standard of care for the evaluation of response to anti-inflammatory therapy in patients with cardiac sarcoidosis.
- A decreased burden of inflammation, as shown in this case, helps with decisions regarding tapering/discontinuation of immunosuppressive therapy.
- The decreased burden of inflammation was associated with interval improvement in LV systolic function.
- Adding objective quantitative analysis of the intensity and extent of FDG uptake to the qualitative interpretation is recommended to track response to therapy. The use of maximum standardized uptake value (SUVmax) is recommended to monitor the intensity of inflammation in response to therapy. Additionally, some measure of extent of active inflammation is also recommended.

Further Reading

Chareonthaitawee P, Beanlands R, Chen W, Dorbala S, Miller E, Murthy V, et al. Joint SNMMI–ASNC Expert Consensus Document on the Role of ^{18}F-FDG PET/CT in Cardiac Sarcoid Detection and Therapy Monitoring. Journal of Nuclear Medicine. 2017;58:1341–1353.

Gillmore JD, Maurer MS, Falk RH, Merlini G, Damy T, Dispenzieri A et al. Nonbiopsy Diagnosis of Cardiac Transthyretin Amyloidosis. Circulation 2016;133:2404–12.

Dorbala S, Ando Y, Bokhari S, Dispenzieri A, Falk R, Ferrari V, et al. ASNC/AHA/ASE/EANM/HFSA/ISA/SCMR/SNMMI expert consensus recommendations for multimodality imaging in cardiac amyloidosis: Part 1 of 2—evidence base and standardized methods of imaging. Journal of Nuclear Cardiology. 2019;26:2065–2123.

Case 58

History

- 58-year-old male with a history of ventricular arrhythmias and biopsy-proven cardiac sarcoidosis was referred to assess response to immunosuppressive therapy.
- The patient was studied prior (Fig. 3.25) and after therapy (Fig. 3.26).

SPECT and PET/CT Images

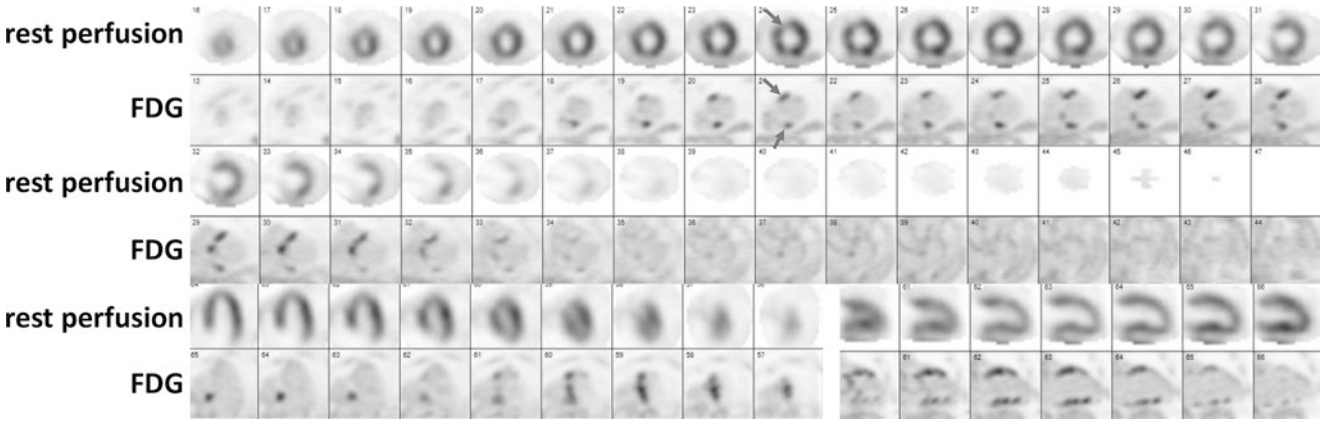


Fig. 3.25 Baseline study. Rest ^{99m}Tc-sestamibi myocardial perfusion SPECT and ^{18}F-deoxyglucose (FDG) PET/CT

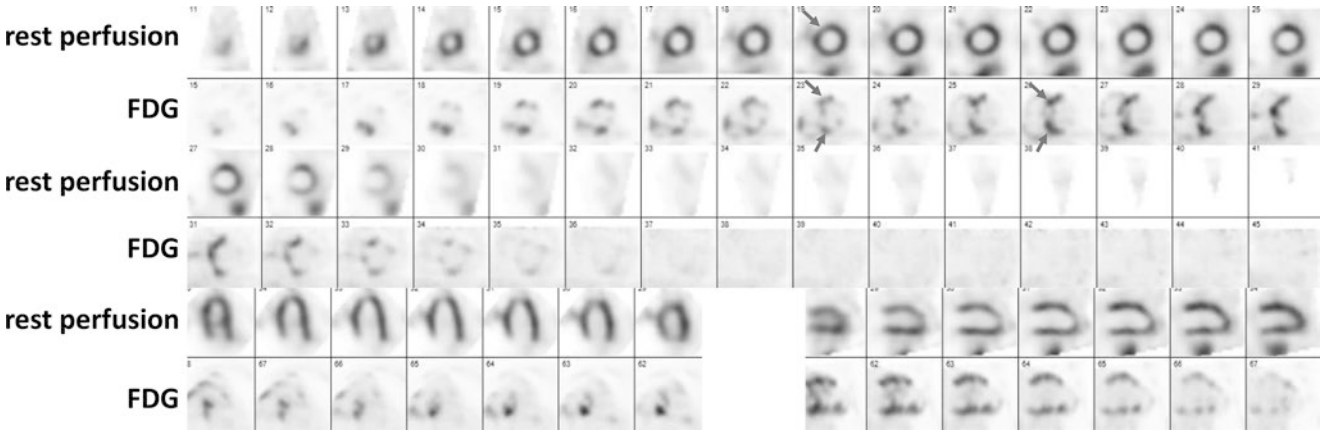


Fig. 3.26 Follow-up study. Rest ^{99m}Tc-sestamibi myocardial perfusion SPECT and ^{18}F-deoxyglucose (FDG) PET/CT

Findings

Baseline study (Fig. 3.25)

- The rest perfusion images show a small perfusion defect of moderate intensity involving the mid and apical anterior wall.
- The FDG images demonstrate adequate suppression of glucose uptake in normal myocardium. There is intense focal glucose uptake in the mid and basal anteroseptal and inferoseptal LV segments.
- The ECG-gated images demonstrated normal LV systolic function and a rest LVEF of 57% with normal volumes and regional wall motion.
- There was mild extracardiac FDG uptake in diaphragmatic and abdominal lymph nodes, scattered bilateral pulmonary nodules and osseous uptake.

Follow-up study (6 months after baseline scan) (Fig. 3.26)

- The rest perfusion images show a small perfusion defect of moderate intensity involving the mid and apical anterior wall, which is essentially unchanged compared to his baseline study.
- The FDG images demonstrate adequate suppression of glucose uptake in normal myocardium. Compared to his baseline scan, there is more intense and extensive focal glucose uptake in the mid and basal anteroseptal and inferoseptal LV segments.
- The ECG-gated images demonstrated mildly reduced LV systolic function and a rest LVEF of 47% with normal volumes and mild global hypokinesis.
- Similar FDG-avid extracardiac sarcoidosis involving lymph nodes, spleen, and bones as compared to his baseline scan.

Quantitative analysis of the intensity and extent of FDG uptake (Table 3.2).

Table 3.2 Quantitative analysis

Exam sequence	Myocardial SUVmax	Volume of FDG uptake (SUVmax >2.7, mL)
Baseline	6.1	10.28
Follow-up	14.0	110

Differential Diagnosis

- None

Correlative Imaging

- None

Management

- After the baseline scan, the patient was started on prednisone (20 mg/day) and methotrexate (15 mg/week). Following the results of the second scan, the patient underwent intensification of immunosuppressive therapy.

Teaching Points

- FDG PET/CT is currently the standard of care for the evaluation of response to anti-inflammatory therapy in patients with cardiac sarcoidosis.
- An increased burden of inflammation, as shown in this case, indicates progression of disease and helps with decisions regarding increasing intensity of immunosuppressive therapy or a change in therapy.
- Increased burden of inflammation was associated with interval worsening in LV systolic function.
- As discussed in case # 55, adding objective quantitative analysis of the intensive and extent of FDG uptake to the qualitative interpretation is recommended to track response to therapy.

Further Reading

Chareonthaitawee P, et al. Joint SNMMI-ASNC Expert Consensus Document on the Role of ^{18}F-FDG PET/CT in Cardiac Sarcoid Detection and Therapy Monitoring. J Nucl Med. 2017 Aug;58(8):1341–1353.

Jamar F., Buscombe J., Chiti A., Christian PE, Delbeke D et al. EANM/SNMMI Guideline for ^{18}F-FDG Use in Inflammation and Infection. Journal of Nuclear Medicine 54: 647–658; 2012.

Osborne MT, et al. Reduction in ^{18}F-fluorodeoxyglucose uptake on serial cardiac positron emission tomography is associated with improved left ventricular ejection fraction in patients with cardiac sarcoidosis. J Nucl Cardiol. 2014;21(1):166–74. PMID: 24307261.

3.2 Cardiac Amyloidosis

3.2.1 Background

Nuclear imaging is particularly useful in characterizing cardiac amyloidosis. Amyloidosis is characterized by loss of natural structure of protein precursors and subsequent aggregation of insoluble fibrillar compound. Fibrils are sustained by a secondary antiparallel β-foils structure. Amyloid deposits are found in the extracellular tissue of many organs and deposits can be either focal or systemic. Cardiac involvement is a leading cause of morbidity and mortality due to systemic amyloidosis. Myocardium, conduction system, and vascular structures can be affected. Typically, it shows characteristics of restrictive cardiomyopathy but both diastolic and systolic function are compromised.

The most frequent types of systemic amyloidosis with cardiac involvement are:

1. acquired monoclonal immunoglobulin light chain amyloidosis (AL) due to plasma cells proliferation producing light chain gamma globulins. Treatment of AL cardiac amyloidosis requires treatment of the underlying plasma cell dyscrasia with chemotherapy and treatment for heart failure.
2. the hereditary, transthyretin-related form (TTR), which can be caused by over 100 mutations of transthyretin (TTR), a transport protein mainly synthesized by the liver. TTR is primarily formed in the liver and orthotopic liver transplantation is a rational and effective treatment for this form of amyloidosis.
3. wild-type (non-mutant) transthyretin-related amyloidosis or systemic "senile" amyloidosis (SSA), which mainly affects the hearts of elderly men. Treatment of SSA is normally restricted to symptomatic relief with conventional heart failure therapy. However, some younger SSA patients may be eligible for heart transplantation.

In all three forms, myocardial involvement is frequent and carries major clinical consequences.

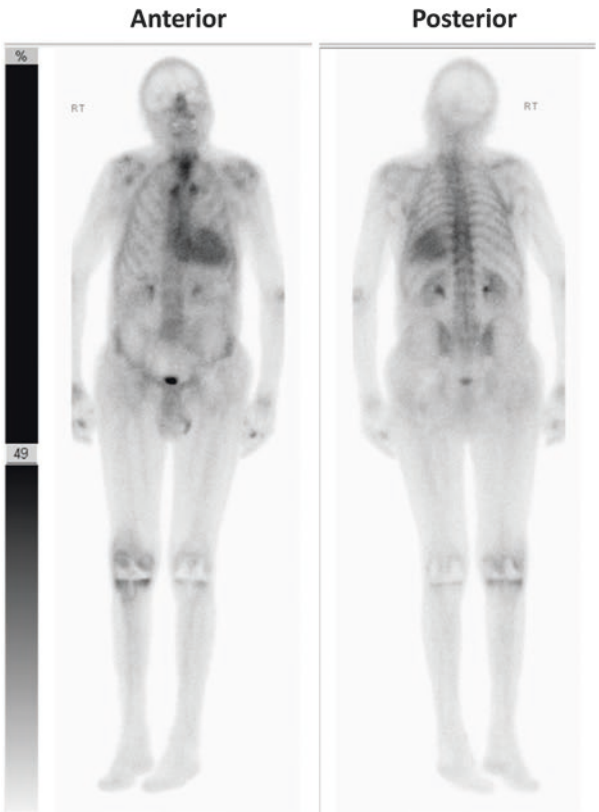
Diagnosis of cardiac amyloidosis is based on (a) biopsy positive Congo red/Thioflavin + polarized light microscopy, (b) genetic analysis/mass spectrometry to identify the protein precursor, (c) contrast MR with gadolinium, showing delayed enhancement of the myocardium in a non-subendocardial distribution.

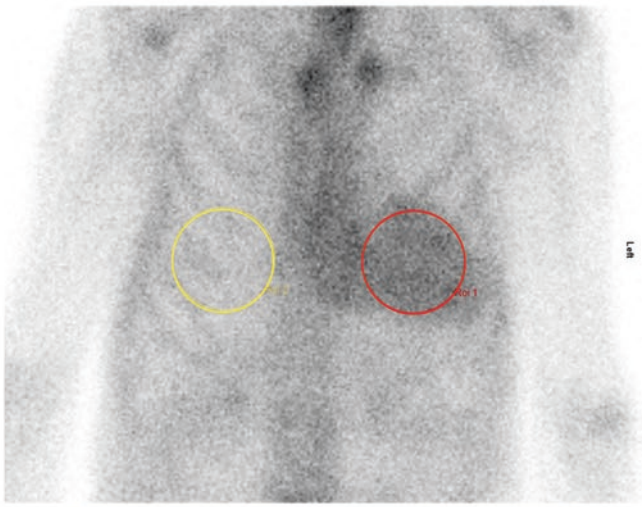
3.2.2 Targeted Amyloid Imaging in ATTR and AL Amyloidosis

Case 59

History

- 72-year-old male with worsening dyspnea on exertion, lower leg swelling and fatigue, and an abnormal echocardiogram was referred for a ^{99m}Tc pyrophosphate (PYP) scan to evaluate for cardiac amyloidosis (Fig. 3.27) and ^{18}F-Florbetapir PET/CT imaging (Fig. 3.28).





Heart ROI mean counts	Contralateral Lung ROI mean counts	H/CL Ratio
44.01	22.24	1.98

Fig. 3.27 Whole-body study using ^{99m}Tc PYP

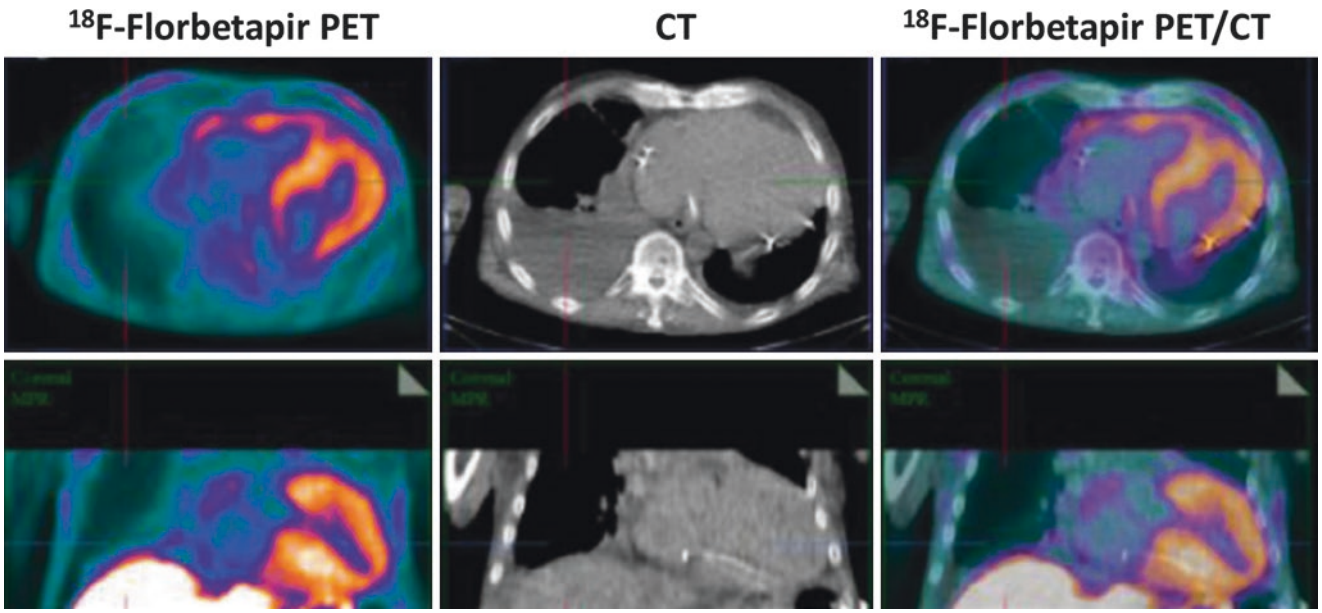


Fig. 3.28 ^{18}F-Florbetapir PET/CT imaging

Findings

- The whole-body and chest planar ^{99m}Tc-pyrophosphate images (Fig. 3.27) demonstrate increased cardiac uptake of the radiotracer. The cardiac uptake was greater than rib uptake (Perugini grade 3).
- The heart to contralateral lung ratio on planar images was 1.98.
- The patient also underwent ^{18}F-Florbetapir PET/CT imaging as part of a research protocol (Fig. 3.28). There is intense cardiac uptake of the radiotracer.
- The apical 4-chamber view on echocardiography (Fig. 3.29) demonstrates thickened left ventricular walls and bi-atrial enlargement. There is also an increased echogenicity of the myocardium.
- The 17-segment polar map of global longitudinal strain (GLS) quantification demonstrates the typical appearance of cardiac amyloidosis with reduced global GLS at the mid and base of the LV with sparing of the apical LV segments.

Differential Diagnosis

- Light chain (AL) cardiac amyloidosis
- Acute myocardial infarction

Teaching Points

- Bone scintigraphy ^{99m}Tc-3,3-diphosphono-1,2-propanodicarboxylic acid (DPD), hydroxymethylene diphosphonate (HMDP), or PYP has high sensitivity and specificity for cardiac transthyretin (ATTR) amyloidosis; and can be used to diagnose cardiac ATTR amyloidosis when a monoclonal gammopathy is excluded.
- Although not common, about 20–25% of patients with AL amyloidosis may demonstrate Perugini grade 2/3 uptake on ^{99m}Tc imaging. In this patient, serum immunofixation and serum free light chain levels were normal, which excluded a monoclonal gammopathy, confirming the presence of ATTR amyloidosis.
- There are two approaches to quantifying myocardial ^{99m}Tc uptake. The semi-quantitative approach is a visual comparison of the myocardial to bone (rib) uptake at 2–3 h (so-called Perugini grade). A quantitative approach involves calculating a heart to contralateral lung ratio (H/CL) by drawing circular regions of interest over the heart and contralateral chest to measure the mean counts in each area. A score greater than 1.5 is considered abnormal.
- ^{18}F-targeted amyloid tracers have high sensitivity for detection of cardiac amyloidosis. However, both AL and ATTR are ^{18}F-beta amyloid tracer avid, making this technique less specific for phenotyping cardiac amyloidosis.

Correlative Imaging

- Echocardiography (Fig. 3.29)

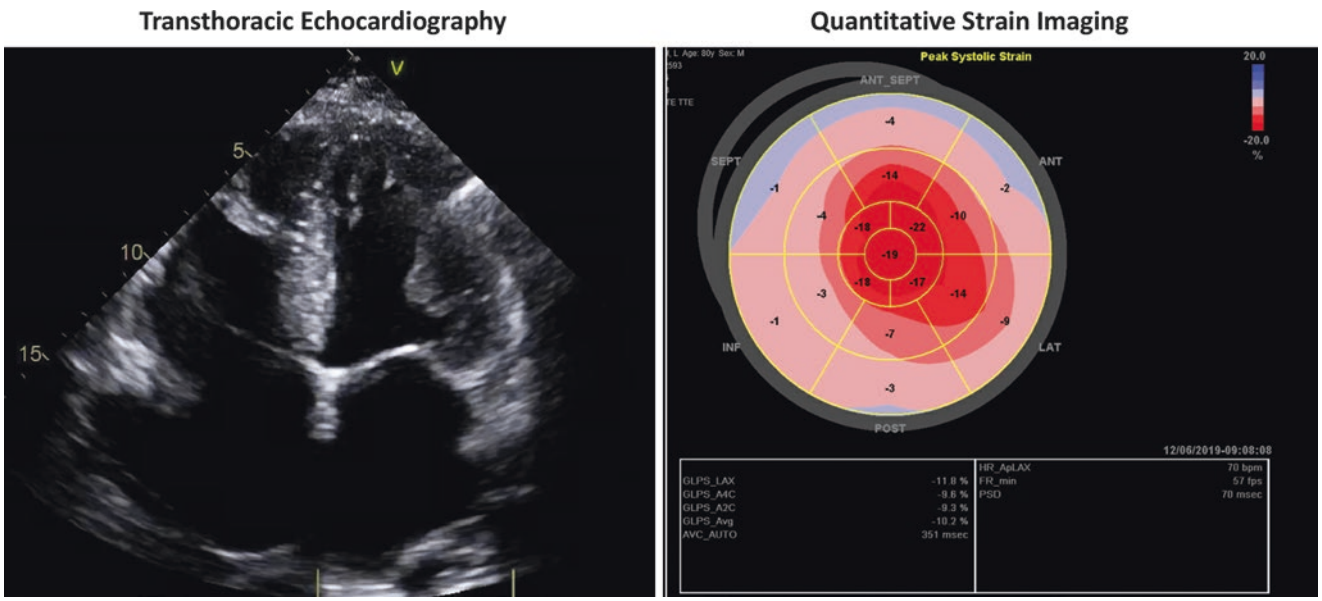


Fig. 3.29 2-D echocardiography images and systolic strain map. The apical 4-chamber view (left panel) on echocardiography demonstrates thickened left ventricular walls and bi-atrial enlargement. There is also an increased echogenicity of the myocardium. A 17-segment polar map (right panel) of global longitudinal strain (GLS) values demonstrates the typical appearance of cardiac amyloidosis with reduced global GLS (−10.2%; normal < −16%), and reduced GLS at the mid and base, and preserved apical GLS

Management

- The patient's heart failure medications were optimized. He was started on a recently approved TTR stabilizer, tafamidis, to slow the progression of the disease.

Further Reading

Chareonthaitawee P, Beanlands R, Chen W, Dorbala S, Miller E, Murthy V, et al. Joint SNMMI–ASNC Expert Consensus Document on the Role of ^{18}F-FDG PET/CT in Cardiac Sarcoid Detection and Therapy Monitoring. Journal of Nuclear Medicine. 2017;58:1341–1353.

Dorbala S, Ando Y, Bokhari S, Dispenzieri A, Falk R, Ferrari V, et al. ASNC/AHA/ASE/EANM/HFSA/ISA/SCMR/SNMMI expert consensus recommendations for multimodality imaging in cardiac amyloidosis: Part 1 of 2—evidence base and standardized methods of imaging. Journal of Nuclear Cardiology. 2019;26:2065–2123.

Case 60

History

- 67-year-old male presented to the emergency department following a syncopal episode, he was noted to have marked orthostatic hypotension. Review of systems revealed months of diarrhea and early satiety.
- An ECG showed low voltage QRS complexes with anterior q waves, an echocardiogram showed concentric left ventricular hypertrophy with an ejection fraction of 50%.
- He was referred for a ^{99m}Technetium pyrophosphate (PYP) scan to evaluate for cardiac amyloidosis (Figs. 3.30 and 3.31).

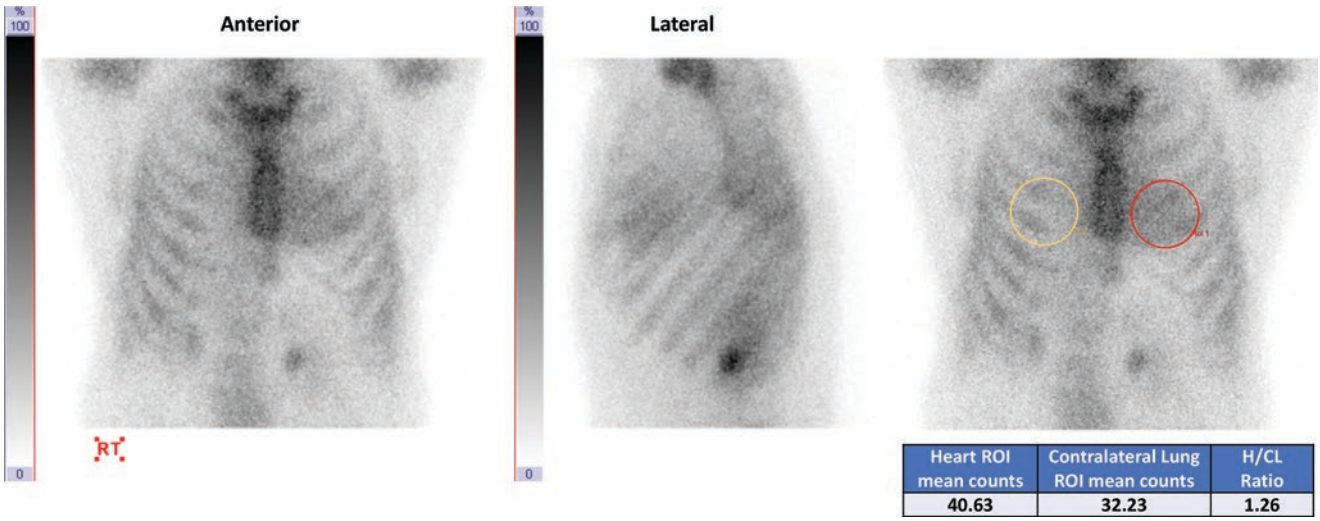


Fig. 3.30 ^{99m}Technetium pyrophosphate (PYP): chest planar views demonstrate mildly increased uptake of the radiotracer in the cardiac region

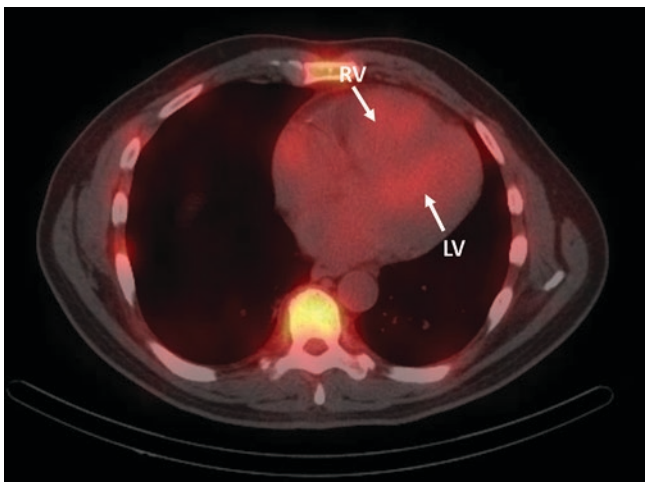


Fig. 3.31 Selected SPECT/CT transaxial section of fused PYP images showing minimal or no radiotracer uptake in the myocardium

This patient also underwent ^{18}F-Florbetapir PET/CT imaging as part of a research protocol (Fig. 3.32).

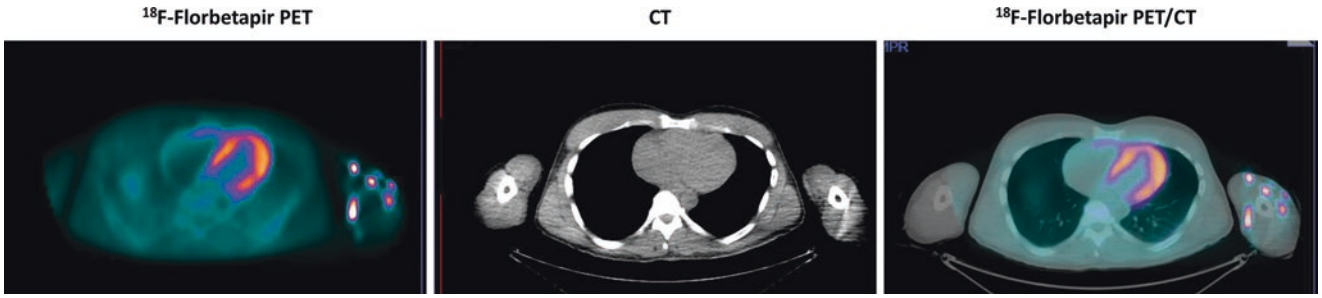


Fig. 3.32 ^{18}F-Florbetapir PET/CT imaging showing intense cardiac uptake of the radiotracer

Findings

- ^{99m}Tc-PYP Imaging
- The chest planar ^{99m}Tc pyrophosphate images demonstrate mildly increased uptake of the radiotracer in the region of the heart, with a retention lower than rib uptake (Perugini grade 1).
- The heart to contralateral lung ratio on planar images was 1.26.
- The fused PYP SPECT/CT images confirmed that there is minimal or no radiotracer uptake in the myocardium and that most of the radiotracer is in the blood pool.

Differential Diagnosis

- Light chain (AL) cardiac amyloidosis

Correlative Imaging (Fig. 3.33)

- Echocardiography
- Contrast-enhanced cardiac MRI

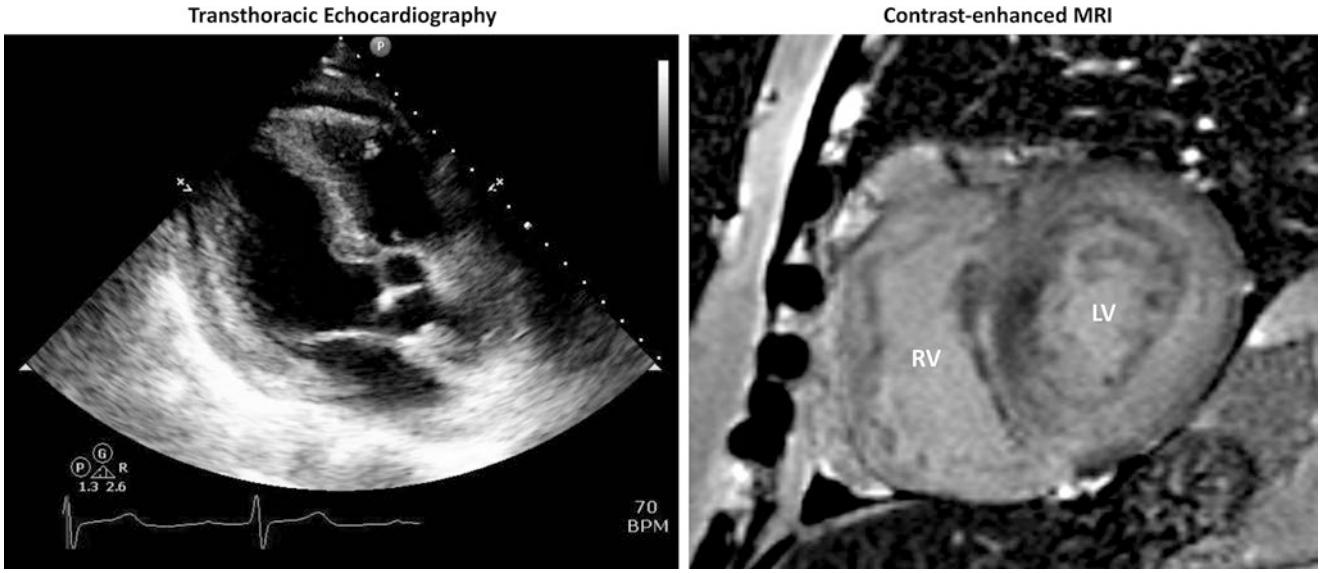


Fig. 3.33 LEFT panel: 2-D echocardiography demonstrates mildly thickened left ventricular walls. There is also a small pericardial effusion seen best along the right ventricular free wall. RIGHT side: Contrast-enhanced MRI images show a typical appearance of diffuse transmural late gadolinium enhancement of the left ventricle and of the right ventricle

Management

- Given the strong clinical and imaging (echocardiography and MRI) evidence of cardiac amyloidosis, serum immunofixation and free light chain levels were performed. They revealed a markedly elevated free Lambda light chain.
- A fat pad biopsy showed amyloid deposition, with a positive Congo red stain, with apple green birefringence under polarized light. Mass spectrometry showed a profile consistent with light chain (lambda) amyloid deposition.
- The patient underwent bone marrow biopsy. He was started on a chemotherapy regimen consisting of Bortezomib, with cyclosporine and dexamethasone. He was also started on midodrine to improve his postural symptoms.

Teaching Points

- Bone scintigraphy ^{99m}Tc- DPD, HMDP, or PYP has high sensitivity and specificity for cardiac transthyretin (ATTR) amyloidosis.
- Diagnosis of cardiac ATTR amyloidosis requires cardiac uptake of the bone seeking radiotracer that is equal or greater than that in the ribs (Perugini grade 2 or 3) or a heart to contralateral lung ratio (H/CL) greater than 1.5 (see case # 59).
- This case shows cardiac uptake that is less than that in the ribs (Perugini grade 1) and a H/CL ratio of 1.26. While this does not exclude ATTR amyloidosis, it makes it less likely.
- SPECT/CT imaging helps localize radiotracer uptake. In this case, it confirmed that tracer activity was mostly confined to the blood pool.
- The presence of a markedly elevated free Lambda light chain in serum points to a plasma cell dyscrasia associated with AL amyloidosis. The demonstration of amyloid deposition on fat pad biopsy and the mass spectrometry showing a profile consistent with light chain (lambda) amyloid deposition confirmed the diagnosis of AL amyloidosis.
- As discussed in Case # 59, ^{18}F-beta amyloid targeted tracers have high sensitivity for detection of cardiac amyloidosis but lacks specificity to differentiate AL from ATTR cardiac amyloidosis.

Further Reading

Gillmore J, Maurer M, Falk R, Merlini G, Damy T, Dispenzieri A, et al. Nonbiopsy Diagnosis of Cardiac Transthyretin Amyloidosis. Circulation. 2016;133:2404–2412.

Dorbala S, Ando Y, Bokhari S, Dispenzieri A, Falk R, Ferrari V, et al. ASNC/AHA/ASE/EANM/HFSA/ISA/SCMR/SNMMI expert consensus recommendations for multimodality imaging in cardiac amyloidosis: Part 1 of 2—evidence base and standardized methods of imaging. Journal of Nuclear Cardiology. 2019;26:2065–2123.