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CASE REPORT

INTERMEDIATE

CLINICAL CASE

^{18}F-Fluorodeoxyglucose Positron Emission Tomography in Cardiac Inflammation

An Educational Case Series

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ABSTRACT

We present an illustrative educational case series focused on the use of nuclear imaging in the diagnosis and follow-up of cardiac inflammation. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2022;4:101661)
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Nuclear imaging is invaluable not only for the assessment of coronary artery disease and myocardial viability, but also for the noninvasive diagnosis of infectious, inflammatory, and infiltrative cardiovascular disorders.[1] Position emission tomography/computed tomography (PET/CT) accomplishes this via detection of radiopharmaceutical avidity in tissues and precise quantification of their local concentration. The most common radiotracer used for detection of inflammation, ^{18}F-fluorodeoxyglucose (FDG), accumulates proportionally to the degree of cellular glucose metabolism, which is increased in metabolically active white blood cells in sarcoidosis, endocarditis, myocarditis, and pericarditis.[2] Anatomic and morphologic information derived from combination with CT further improves localization, extent, and characterization of lesions detected. Imaging with rubidium-82 (Rb82) offers insight into myocardial perfusion, and may demonstrate scarred myocardium late in the inflammatory process. Unlike imaging for hibernating myocardium, imaging for cardiac inflammation requires preinjection patient preparation intended to suppress normal glucose uptake in cardiac myocytes, which would otherwise overshadow inflammatory foci. We present selected cases illustrating the multimodality assessment of myocardial inflammation.

LEARNING OBJECTIVES

- To accurately assess the burden of cardiac inflammation with the use of ^{18}F-fluorodeoxyglucose PET
- To synthesize a patient's clinical presentation with multimodality imaging findings in the diagnosis of cardiac inflammation

CASE 1

A 60-year-old woman with a long history of complete heart block status-post implantation of a dual chamber permanent pacemaker presented for evaluation of worsening dyspnea. Electrocardiography showed an atrial and ventricular sequentially paced rhythm (**Figure 1**). Echocardiography demonstrated a drop in

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ABBREVIATIONS AND ACRONYMS

FDG = ^{18}F-fluorodeoxyglucose

ICD = implanted cardioverter-defibrillator

LVEF = left ventricular ejection fraction

PET/CT = positron emission tomography/computed tomography

Rb82 = rubidium-82

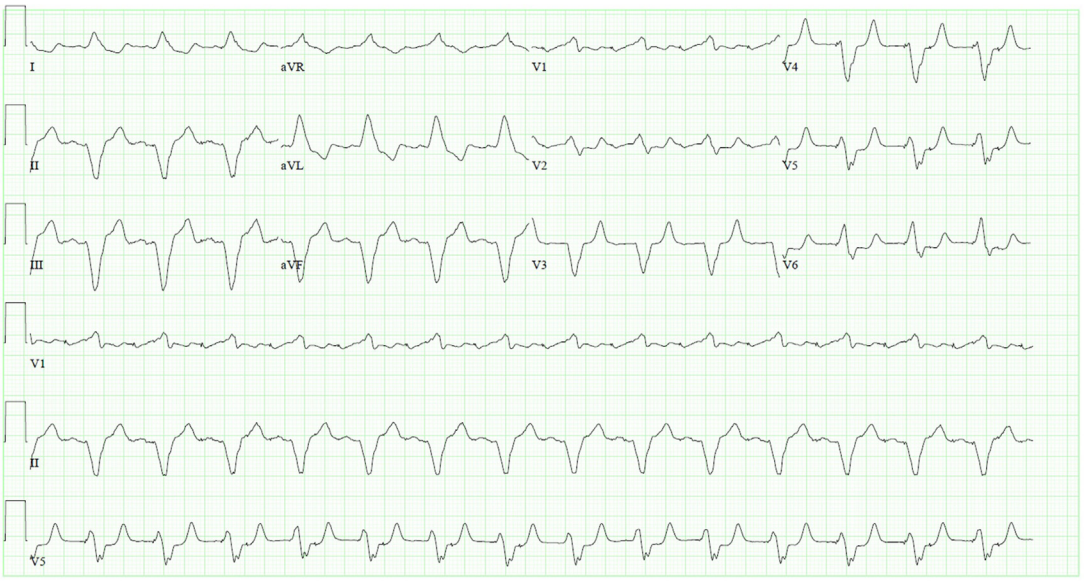
left ventricular ejection fraction (LVEF) from 55% previously to 25% (Videos 1 to 4). LVEF did not improve despite treatment with guideline-directed medical therapy including sacubitril/valsartan and metoprolol. Coronary angiography revealed nonobstructive atherosclerosis. She had a greater than 90% right ventricular pacing burden on device interrogation and therefore was referred to an electrophysiologist for consideration of cardiac resynchronization therapy. However, in light of the young age of onset of complete heart block, chest CT was done to investigate for intrathoracic evidence of sarcoidosis. This revealed scattered nonspecific pulmonary nodules (Supplemental Figure 1). This finding raised the possibility of pulmonary sarcoidosis with cardiac involvement, so resting perfusion and metabolic PET/CT was ordered.

Patient preparation and imaging protocoling were conducted according to the American Society of Nuclear Cardiology guidelines.[1] In brief, the patient was advised to follow a ketogenic diet. Fifteen minutes before injection of 9.8 mCi FDG she received an injection of 50 U/kg heparin intravenously. Resting Rb82 perfusion images after injection of 34.7 mCi Rb82 revealed multiple scattered resting perfusion defects (**Figure 2**). FDG uptake localized to these perfusion defects accounting for inflammation in approximately 20% of the myocardium, including uptake in the right ventricular free wall. In summary, her extracardiac findings of pulmonary nodules, evidence of premature conduction disease, and evidence of inflammation on cardiac PET/CT findings satisfied the Heart Rhythm Society and Japanese Ministry of Health criteria for systemic sarcoid with cardiac involvement.[3,4] She underwent device upgrade with implantation of a cardiac resynchronization therapy defibrillator. In addition to her heart failure medication she was prescribed a steroid taper, methotrexate, and prophylactic trimethoprim/sulfamethoxazole. With these measures she improved clinically. Repeated echocardiography remained stable with no change in LVEF (Video 5).

CASE 2

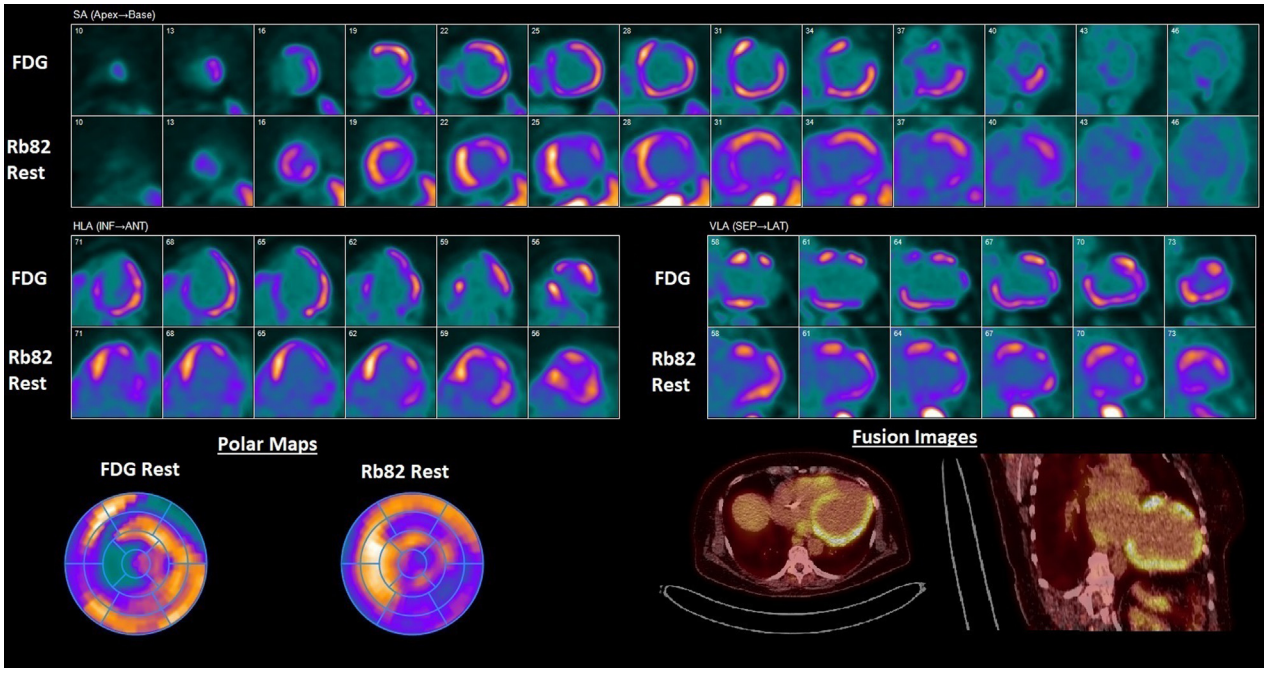
A 41-year-old man presented to the emergency department with generalized malaise. He was found to be hypotensive, and electrocardiography revealed ventricular tachycardia (**Figure 3**). Acute kidney and liver injury were evident on laboratory investigation. Despite cardioversion he remained hypotensive, so

FIGURE 1 Case 1: Electrocardiography



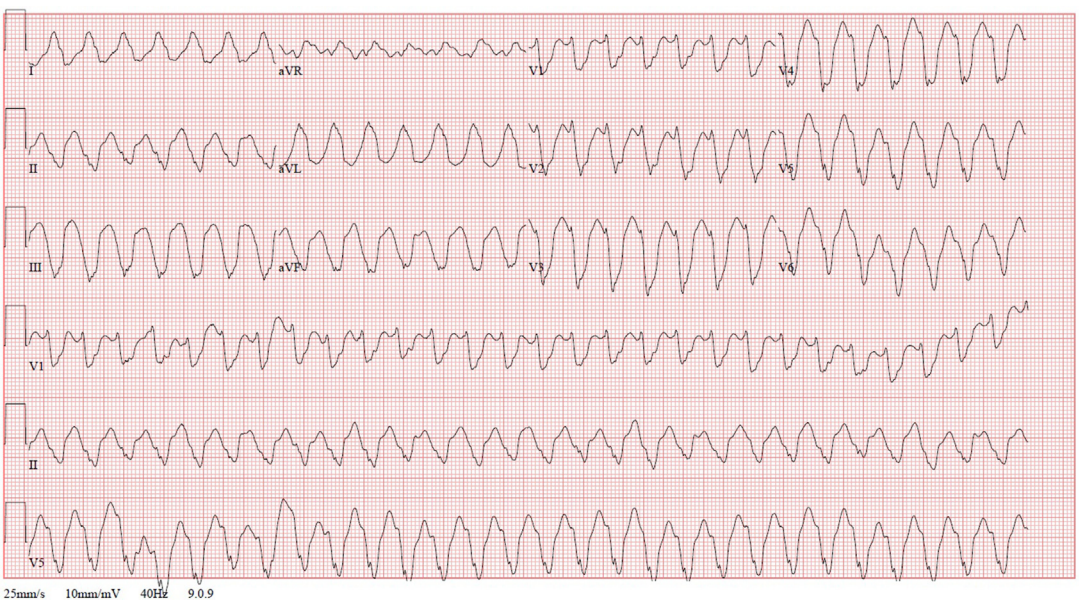
Electrocardiogram demonstrating atrial and ventricular sequential pacing.

FIGURE 2 **Case 1: Positron Emission Tomography**



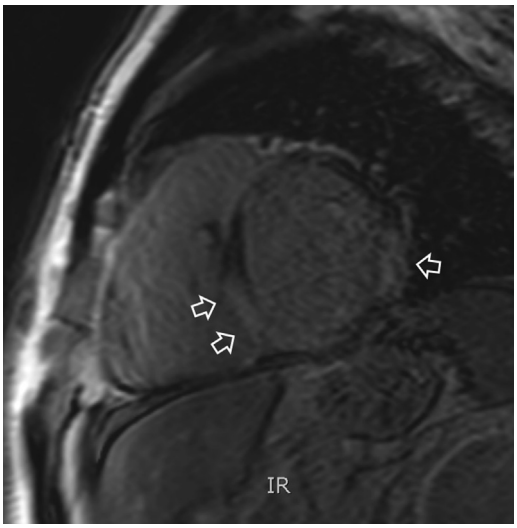
Rubidium-82 (Rb82) and ^{18}F-fluorodeoxyglucose (FDG) images demonstrating active cardiac inflammation. Short-axis (SA), horizontal long-axis (HLA), and vertical long-axis (VLA) images shown. Resting Rb82 images reveal multiple scattered perfusion defects involving the mid-anterior wall, basal and mid-inferolateral wall extending into the basal and mid-inferior wall, and lateral apex. FDG images demonstrate tracer uptake in the corresponding segments, as well as uptake in the right ventricular free wall and the basal anterior segment. **(Bottom left)** Polar maps. **(Bottom right)** Representative co-localized computed tomographic and nuclear images. The correlation between Rb82 perfusion defects and FDG uptake in the absence of ischemic disease is suggestive of active inflammation. ANT = anterior; INF = inferior; LAT =lateral; SEP = septal.

FIGURE 3 **Case 2: Electrocardiography**



Electrocardiogram demonstrating sustained ventricular tachycardia.

FIGURE 4 Case 2: Cardiac Magnetic Resonance Imaging

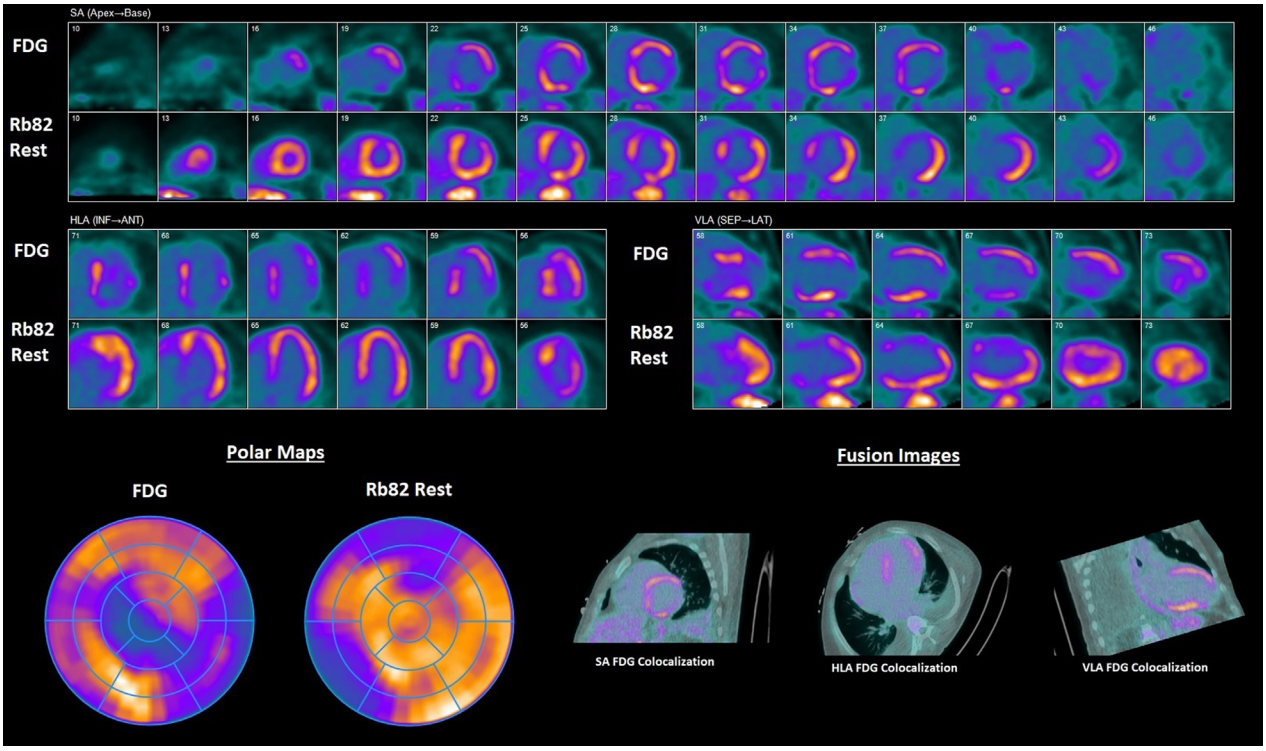


Delayed gadolinium-enhancement cardiac magnetic resonance imaging sequence in the short-axis view at the mid-ventricular cavity. There is patchy late enhancement in the subepicardial inferoseptum and the subendocardial lateral wall in a noncoronary distribution **(arrows)**, suggestive of an infiltrative cardiomyopathy. T2-STIR imaging did not reveal evidence of myocardial edema. IR = inversion recovery sequence.

he was transferred to the cardiac intensive care unit for management of shock. Echocardiography revealed an LVEF of 20% (Videos 6 to 9). Coronary angiography revealed nonobstructive coronary disease (images not shown). The patient underwent cardiac magnetic resonance imaging once stabilized in the intensive care unit, which re-demonstrated reduced ventricular systolic function and showed patchy delayed gadolinium enhancement consistent with nonischemic cardiomyopathy (**Figure 4**). The patient then underwent resting perfusion and metabolic PET/CT to evaluate for active inflammation.

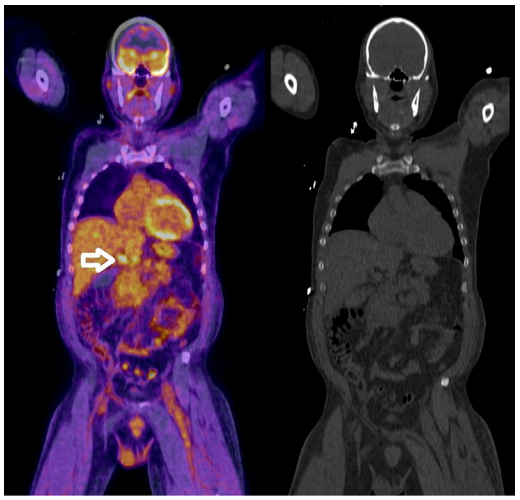
Resting perfusion images after injection of 30 mCi Rb82 showed focal defects in the anterior and inferior walls (**Figure 5**). FDG images after injection of 11 mCi FDG demonstrated patchy uptake in the entire anterior wall, anterior septum, inferior wall, mid-inferoseptal segment, and basal inferoseptal segment; this pattern of uptake matched the perfusion defects seen on perfusion images. In addition, whole-body FDG PET revealed FDG-avid portal adenopathy (**Figure 6**); a biopsy via esophagogastroduodenoscopy of a lymph node in the gastrohepatic ligament revealed noncaseating granulomas consistent with sarcoidosis. The patient

FIGURE 5 Case 2: Cardiac Positron Emission Tomography



Resting Rb82 and FDG demonstrating active cardiac inflammation. Polar maps shown on the bottom left and fusion images with FDG and low-dose computed tomography (CT) on the bottom right. Rb82 imaging demonstrates perfusion defects in the anterior wall extending from the anterior periapical segment to the base, as well as in the basal and mid inferoseptal segments. FDG uptake in these segments represents active inflammation. Abbreviations as in **Figure 2**.

FIGURE 6 **Case 2: Whole-Body PET**

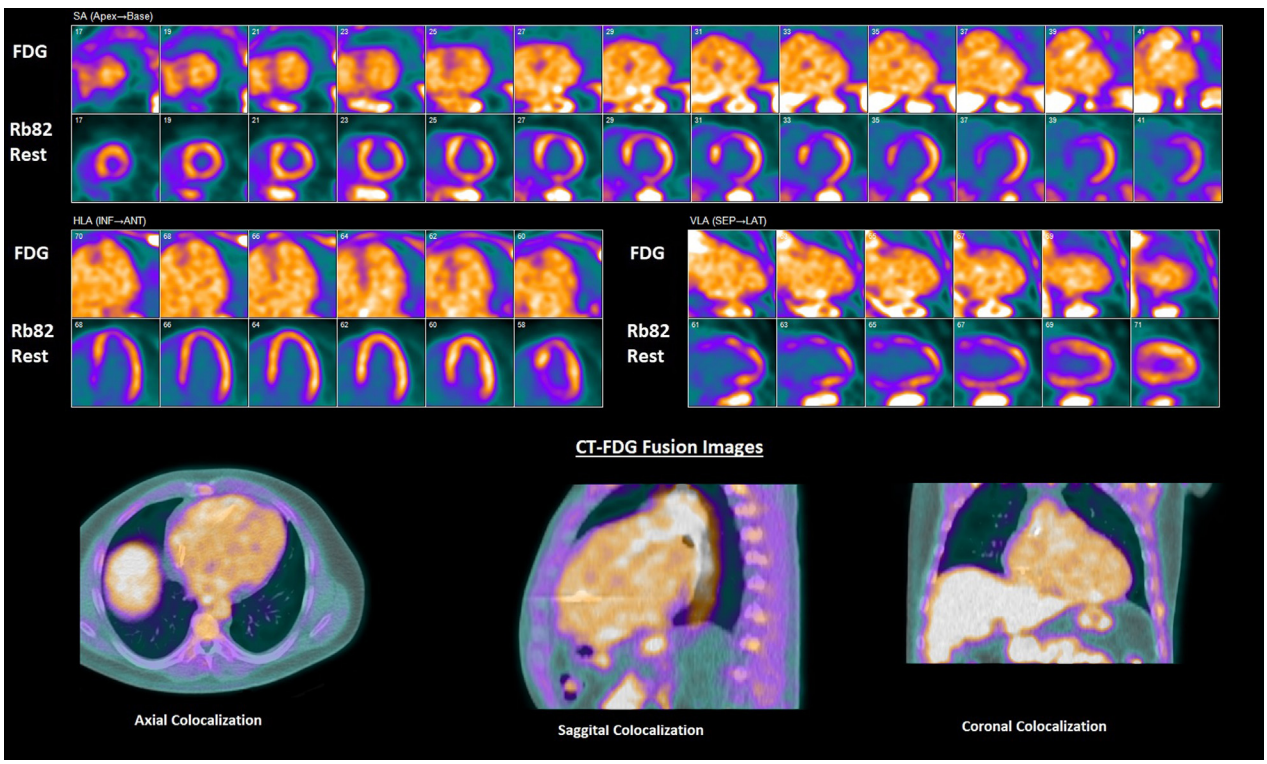


Whole-Body FDG PET/CT images revealing a focus of increased uptake in a periportal lymph node **(arrow)**, suggesting extracardiac involvement of the inflammatory process. Abbreviations as in Figures 2 and 5.

was started on carvedilol, hydralazine, isosorbide dinitrate, prednisone, trimethoprim-sulfamethoxazole for prophylaxis, and valsartan. An implanted cardioverter-defibrillator (ICD) was placed for secondary prevention of ventricular tachycardia.

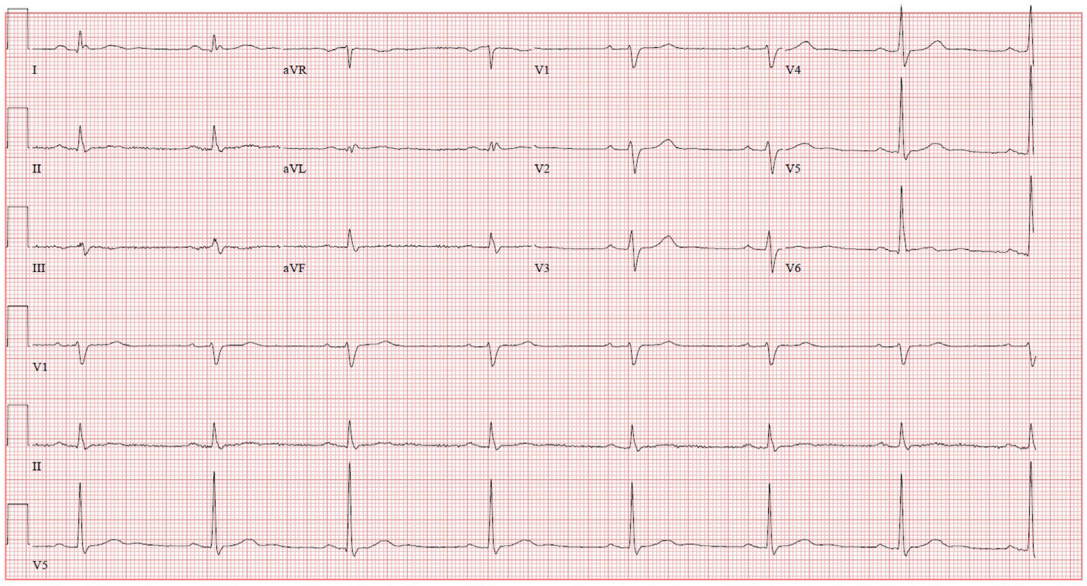
Despite treatment, the patient suffered appropriate ICD discharges requiring initiation of amiodarone, and repeated imaging showed a worsening burden of inflammation. Immunosuppression was intensified with the addition of methotrexate. His renal function had improved and he was changed from valsartan to sacubitril/valsartan with discontinuation of hydralazine and isosorbide. Four months later, repeated PET was done with injection of 30 mCi Rb82 and 12.4 mCi FDG (Figure 7). This revealed a large perfusion defect in the anterior wall and basal inferoseptum with no residual active inflammation; FDG uptake was limited to the cardiac blood pool. Repeated echocardiography showed a modest improvement in LVEF to 29%. Immunosuppression was weaned over the course of 6 months and the patient has remained stable.

FIGURE 7 **Case 2: Repeated PET**



Follow-Up Rb82 and FDG PET on a patient undergoing treatment for cardiac sarcoidosis. Previous study is shown in Figure 6. There are persistent resting perfusion defects in the anterior wall and basal inferoseptum. However, FDG PET demonstrates uptake in the cardiac blood pool but no uptake in the myocardium. FDG co-localization with low-dose CT, shown in the bottom 3 images, corroborates blood pool uptake and absent myocardial uptake. Normalization of the tracer counts to background renders the blood pool signal similar in intensity to the signal from liver uptake. Abbreviations as in Figures 2, 5, and 6.

FIGURE 8 **Case 3: Electrocardiography**

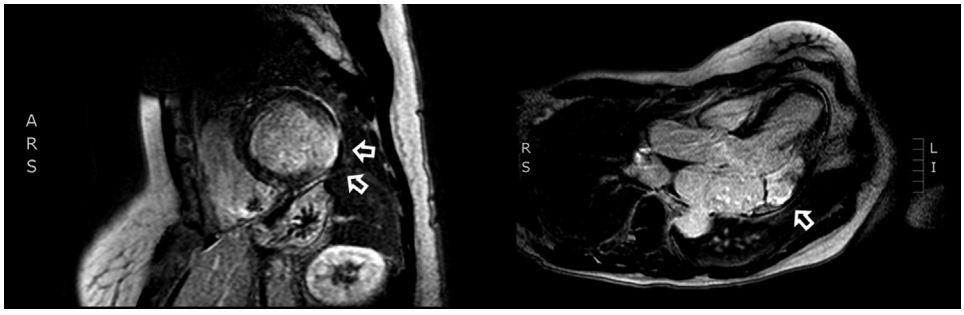


Electrocardiogram demonstrating sinus bradycardia with prolonged atrioventricular conduction.

CASE 3

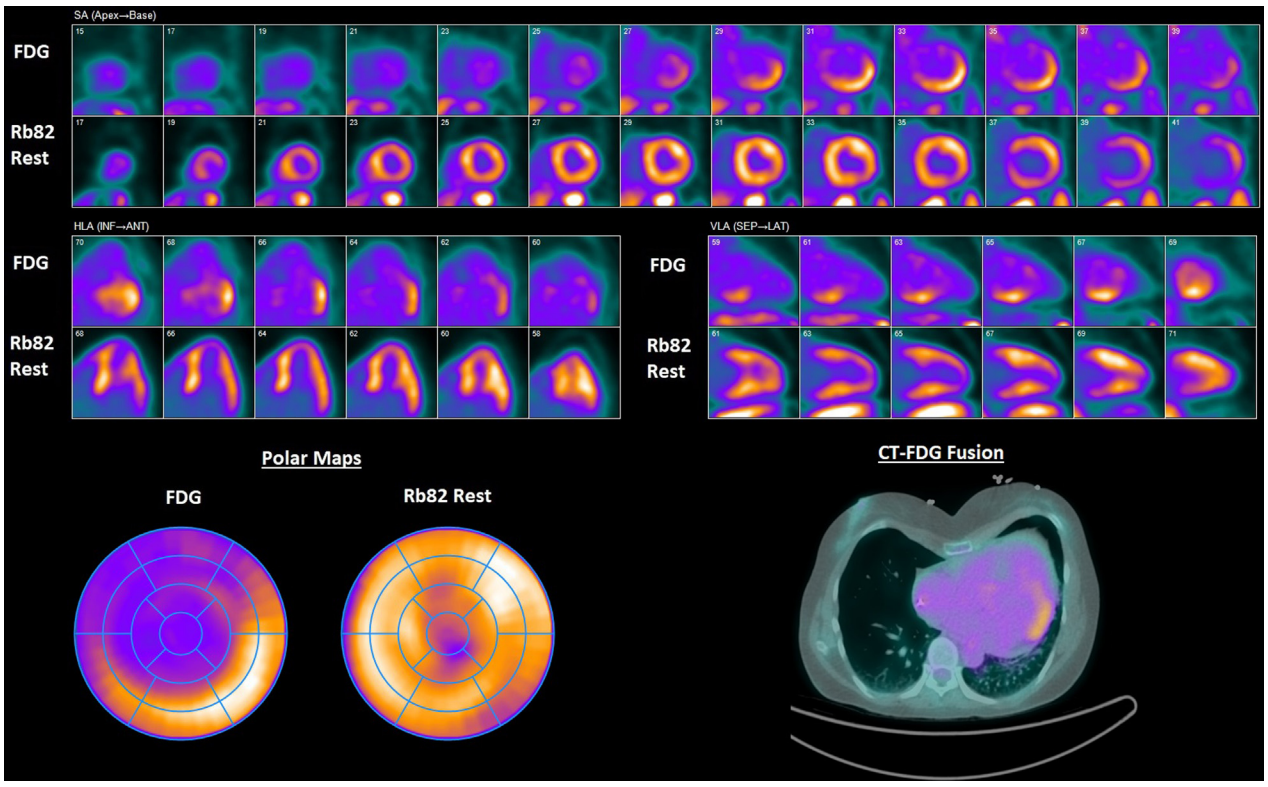
A 58-year-old woman who had undergone ICD placement for aborted sudden cardiac arrest of unknown etiology presented to the hospital with appropriate ICD discharges. Electrocardiography showed sinus bradycardia with first-degree atrioventricular block (**Figure 8**). Echocardiography showed preserved biventricular systolic function with normal chamber dimensions (Videos 9 to 14). There was moderate posterior mitral valve leaflet prolapse with moderate anteriorly directed mitral regurgitation. Cardiac magnetic resonance imaging confirmed bi-leaflet prolapse and moderate mitral regurgitation, and showed mitral annular disjunction with associated transmural delayed enhancement in the basal to mid-inferolateral wall (**Figure 9,** Video 15). Cardiac catheterization revealed unremarkable

FIGURE 9 **Case 3: Cardiac Magnetic Resonance Imaging**



Delayed gadolinium-enhancement cardiac magnetic resonance images in the short-axis view at the left ventricular base **(left)** and in the 3-chamber view **(right)**. There is delayed enhancement in the basal inferolateral wall **(arrows)**. In the absence of coronary disease, this is suggestive of inflammation progressing to fibrosis.

FIGURE 10 Case 3: PET



Resting Rb82 and FDG PET in a patient with mitral valve prolapse and mitral annular dysjunction. Resting perfusion shows a small inferolateral segment perfusion defect. FDG localizes to this region as well, suggesting inflammation. Coronary angiography was normal (Videos 16 and 17). Polar maps and fusion images with CT are shown at the bottom. Abbreviations as in **Figures 2, 5, and 6**.

coronary arteries (Videos 16 and 17). Resting perfusion and metabolic cardiac PET/CT was done to rule out an inflammatory etiology of her ventricular tachycardia.

The patient underwent rest Rb82 imaging with 30 mCi RB82 as well as FDG imaging with 9 mCi FDG (**Figure 10**). There was evidence of a small perfusion defect in the basal inferolateral wall. This region exhibited focal FDG uptake consistent with active inflammation. The patient was diagnosed with malignant mitral valve prolapse. The patient was treated with amiodarone and metoprolol. Follow-up was scheduled at discharge.

DISCUSSION

Ultimately, no single imaging modality is infallible in the diagnosis of cardiac inflammation. The clinical presentation of the patient must be foremost in the minds of the providers ordering and interpreting tests in pursuit of these elusive diagnoses. Even with modern optimization protocols, pathologic studies demonstrate that sarcoidosis remains frequently misdiagnosed.[5] PET/CT with FDG is a crucial tool used to assess myocardial inflammation. As new tracers and imaging techniques emerge and improve, safe noninvasive diagnosis of cardiac inflammation will become more accurate and reproducible. These tools must be evaluated in longitudinal trials and registries for their diagnostic and therapeutic implications.

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APPENDIX For a supplemental figure, please see the online version of this paper.