CASE OF THE MONTH

Incessant PVCs and Cardiomyopathy: Think Outside the Box

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CLINICAL PRESENTATION

A 74-year-old African American male with nonischemic cardiomyopathy, premature ventricular contraction (PVC) status post ablation in 2010 and 2015, hypertension and hyperlipidemia presented with recurrent symptomatic PVCs. Prior work up included transthoracic echocardiogram in 2010, which showed LVEF 35-39% that improved to LVEF 50-55% post PVC ablation. Coronary angiogram at that time showed nonobstructive coronary artery disease. Due to recurrent symptomatic PVCs, he underwent further evaluation with a 48-hour Holter monitor, which showed 43,000 PVCs burden. Current medications, patient was on carvedilol 12.5 mg BID, lisinopril 40 mg daily, amlodipine 10 mg daily, atorvastatin 40 mg daily and aspirin 81 mg daily. Physical exam was otherwise unremarkable. Laboratory work up was otherwise unremarkable with normal electrolytes and low platelet count.

LAB RESULTS

Laboratory results were as follows:
Sodium 140 mEq/L
Potassium 4.3 mEq/L
Chloride 101 mEq/L
CO2 26 mEq/L
Bun 18 mg/dL
Creatinine 1.0 mg/dL
White blood cell count 4.7 K/uL, hemoglobin 15.3 g/dL, and platelet count 106 K/uL

A 12-lead electrocardiogram (Figure 1) showed normal sinus rhythm with frequent PVCs.

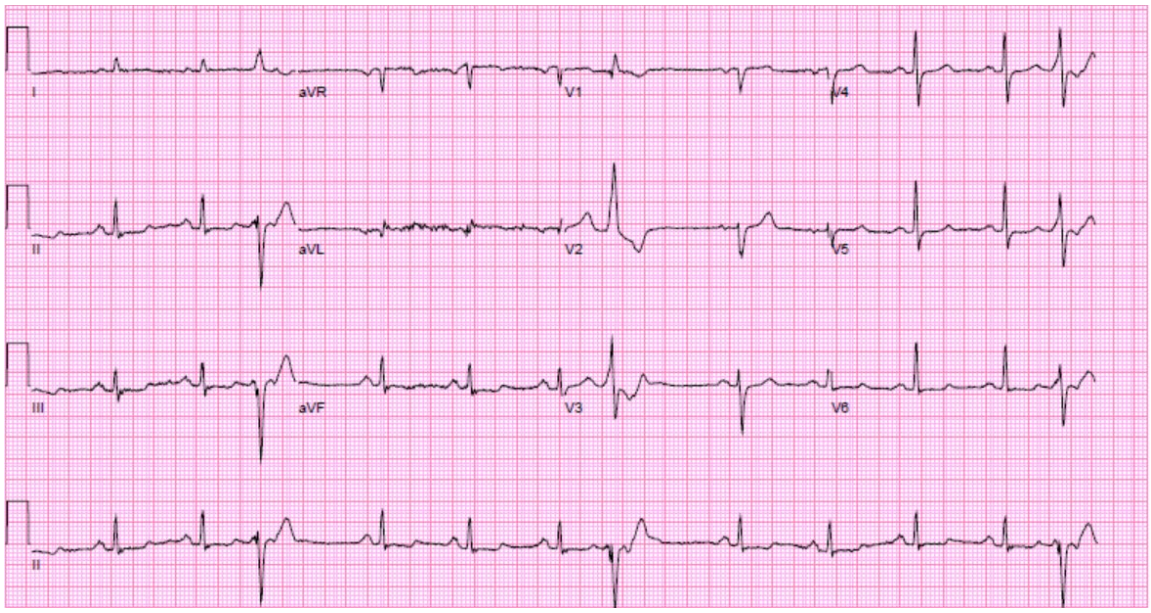

Figure 1. A 12-lead electrocardiogram with sinus rhythm with frequent PVCs.

QUESTION 1: What are potential causes of PVCs in this patient?

A. Myocardial scar
B. Valvular heart disease
C. Electrolyte disturbance
D. All the above

ANSWER

D. All the above

All the above are potential causes for PVCs and need to be considered. In our patient with depressed left ventricular function, coronary angiogram was performed to rule out obstructive coronary artery disease (CAD) and showed nonobstructive CAD with 30% stenosis in the mid to distal right coronary artery. Prior echocardiogram did not show significant valvular heart disease and laboratory work up was otherwise unremarkable for electrolyte or metabolic disturbances. Frequent PVCs that exceed 20,000/day are more likely to cause PVC-related cardiomyopathy. In our patient, frequent PVCs were the likely culprit for his cardiomyopathy, which improved after his prior PVC ablation.[1,2]

CASE CONTINUED

The patient was not found to have significant electrolyte disturbances, valvular heart disease or obstructive CAD. Contrast enhanced cardiac magnetic resonance imaging (CMR) with late gadolinium enhancement (LGE) was performed for myocardial scar assessment prior to repeat PVC ablation and showed depressed biventricular function (LVEF 43%, RVEF 44%), mild biventricular enlargement, and basal inferoseptal and anteroseptal LGE uptake (Figure 2).

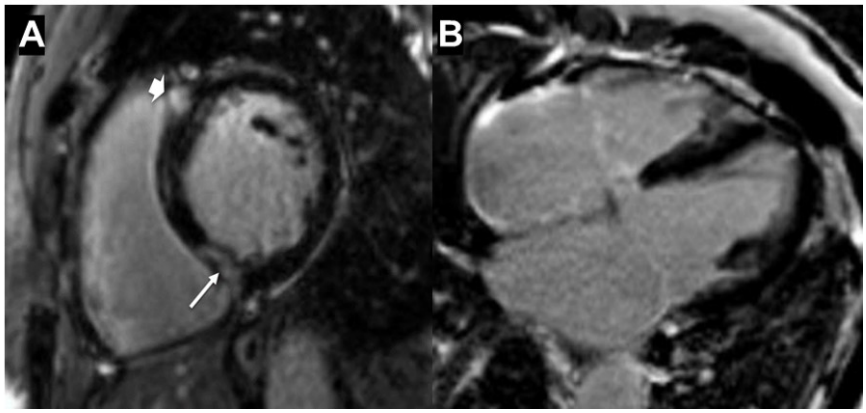

Figure 2. CMR-LGE demonstrating (A) basal inferoseptal (arrow) and anteroseptal (arrowhead) LGE uptake (B) without evidence in other segments on 4-chamber long axis of the left ventricle.

QUESTION 2: Which of the following is NOT a differential diagnosis for the LGE pattern in this patient?

A. Coronary artery disease
B. Cardiac sarcoidosis
C. Idiopathic dilated cardiomyopathy
D. Myocarditis

ANSWER

A. Coronary artery disease

The LGE pattern on CMR is important and informs us on the etiology of the acute myocardial injury or chronic scar and helps further narrow down differential diagnoses. The LGE patterns in Figure 2 are a non-CAD pattern at the basal anteroseptal site and mid-myocardial pattern at the basal inferoseptal site. These suggest a nonischemic etiology such as myocarditis, cardiac sarcoid or dilated cardiomyopathy. The LGE pattern for CAD is a subendocardial pattern in a coronary distribution.[3]

CASE CONTINUED

The patient underwent successful PVC ablation with relief of symptoms. A repeat 24-hour Holter monitor showed reduced PVC burden down to 1700 from 43,000. A repeat CMR performed 3 months post ablation showed normal LVEF 57%, mild depressed RVEF 50% and mild biventricular enlargement. There was no evidence of significant valvular disease, intracardiac shunts and no evidence of arrhythmogenic right ventricular dysplasia. On LGE imaging, there was now new non-CAD LGE uptake in the lateral segments (Figure 3 A, B) and transmural involvement in the basal inferoseptum (Figure 3 C) with associated microvascular obstruction (Figure 3 D).

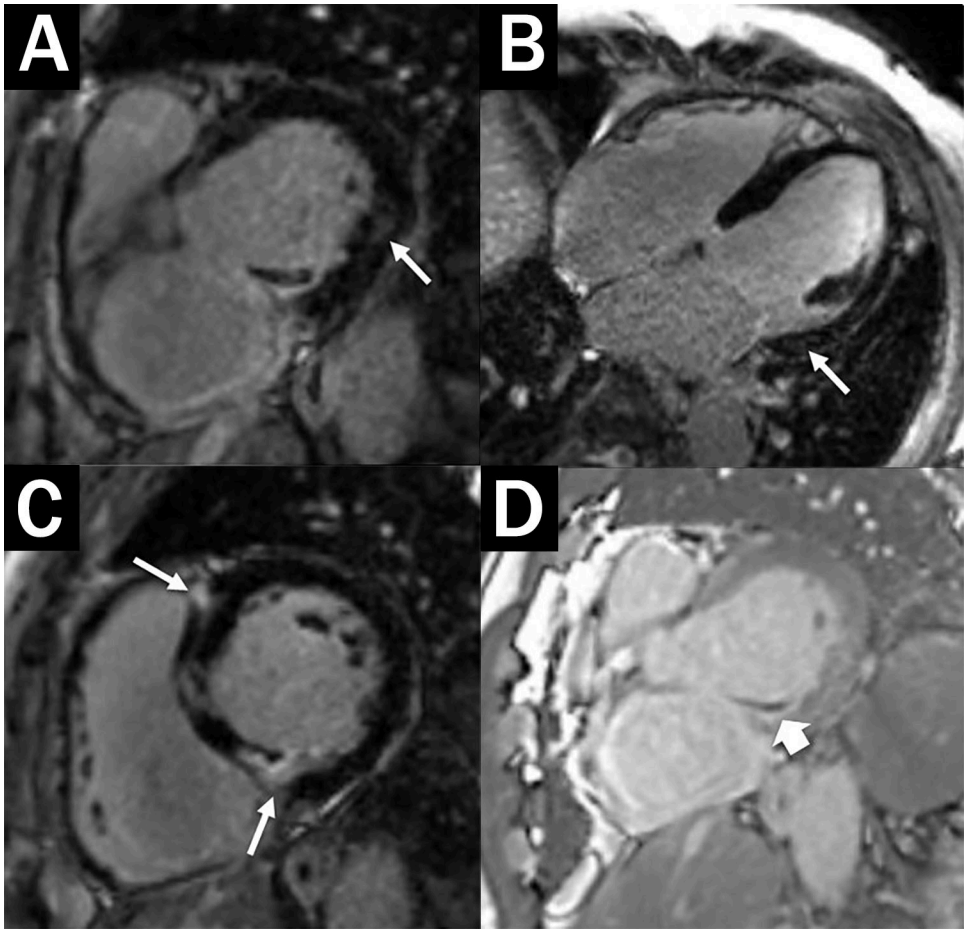

Figure 3. CMR LGE demonstrating (A, B) non-CAD pattern with mid-myocardial LGE pattern in the lateral segments, (C) non-CAD pattern in the basal anteroseptal segment, and transmural involvement in the basal inferoseptal segment with (D) linear dark hypodensity with contrast uptake on delayed imaging suggestive of microvascular obstruction.

Though there was improvement in symptoms and PVC burden post ablation, concerns for progression of LGE uptake and persistent right ventricular dysfunction raised suspicion for an inflammatory cardiomyopathy, such as cardiac sarcoidosis (CS).

QUESTION 3: What is the next best step in diagnosis of this patient?

A. Repeat cardiac MRI
B. Endomyocardial biopsy
C. Cardiac fluorodeoxyglucose-positron emission tomography (FDG-PET)
D. None of the above

ANSWER

C. Cardiac FDG-PET

Cardiac FDG-PET is a noninvasive imaging test that uses a glucose analog (FDG) to help differentiate between normal myocardium versus active myocardial inflammation, where there

is higher FDG uptake.[4] Endomyocardial biopsy is invasive and would not be the next best step in this case. Biopsy has lower sensitivity due to the focal nature of CS; however, imaging-guided (CMR or PET) biopsies have increased yield in up to 50% of cases.[5,6] Repeating the cardiac MRI would not be useful in this case because LGE pattern is unlikely to change or reveal the underlying cause.

CLINICAL COURSE

The patient underwent cardiac PET following appropriate preparation. This showed increased FDG uptake in the basal septal and lateral walls, which coincided with the areas of LGE on CMR.[7] He was then referred to CS specialist and started on prednisone and mycophenolate mofetil (CellCept). A repeat cardiac PET performed 5 months later while the patient was on this therapy showed significant reduction in FDG uptake in the myocardium compared to the initial study (Figure 4). There was a significant drop in the standard uptake value (SUV max) from 7.5 to 3.

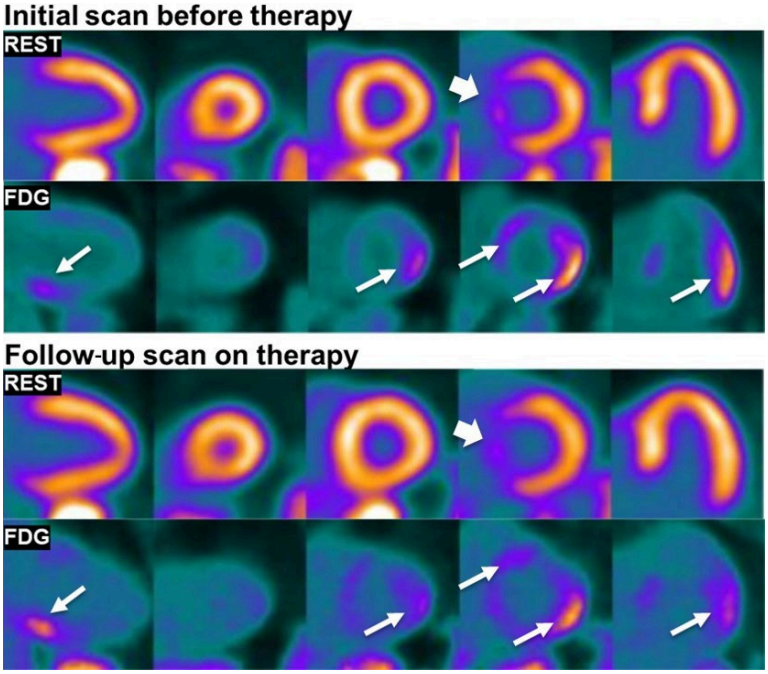

Figure 4. Initial and follow-up cardiac FDG-PET demonstrating resting perfusion defect in the septal segments (arrowheads). There is FDG uptake in the septal, lateral ,and inferolateral segments with improvement, especially in lateral segments, on follow-up scan (arrows).

The patient continued to do well clinically on steroids and immunosuppressive therapy without recurrence of significant PVCs. He did not have obvious evidence of extracardiac sarcoid, so endomyocardial biopsy was considered pending clinical response to therapy. A repeat cardiac PET scan in 6 months is planned to evaluate clinical response to therapy.

DISCUSSION

Frequent PVCs can lead to reversible cardiomyopathy and are often a marker for underlying structural heart disease. PVC-induced cardiomyopathy is a diagnosis of exclusion. Therefore, a thorough evaluation is warranted, often requiring CMR to evaluate for myocardial

scar.[2] Our patient demonstrates an example where PVC-induced cardiomyopathy was suspected due to recurrent PVCs requiring multiple ablations, but the underlying etiology was progression of inflammatory cardiomyopathy.

Cardiac sarcoidosis is a multisystem inflammatory disorder characterized by formation of noncaseating granulomas. Clinically manifest cardiac involvement can occur in 5% of patients and portends a worse prognosis, with up to 25% of patients showing cardiac involvement in autopsy studies.[5] Current diagnostic criteria are based on the modified Japanese Ministry of Health and Welfare guidelines and Heart Rhythm Society consensus statement, both requiring either a histologic diagnosis of CS or integration of clinical and imaging features.[8,9] CMR-LGE and cardiac FDG-PET have emerged as important diagnostic tools to detect CS and following response to therapy. In patients with suspected CS, complementary use of CMR-LGE and cardiac FDG-PET has been shown to have good diagnostic accuracy and help guide management.[10]

There is no specific CMR-LGE pattern for CS; however, patterns include patchy or multifocal involvement of the mid-wall LGE along the basal septum and inferolateral walls as seen in our patient.[11] While CMR-LGE provides myocardial injury or scar assessment, cardiac FDG-PET informs us on the degree of inflammation by quantifying myocardial FDG uptake and response to therapy. The use of serial cardiac FDG-PET has been shown to be essential in diagnosing and guiding immunosuppressive therapy in patients with CS.[12] Prognosis in CS is largely based on clinical symptoms and left ventricular ejection fraction. Additionally, findings on CMR-LGE and cardiac FDG-PET provide strong prognostic information and risk stratification in patients with CS.[13,14]

TAKE-HOME POINTS

- PVC cardiomyopathy is a diagnosis of exclusion, and further investigation of underlying cause and structural heart disease is required.
- A high index of suspicion for inflammatory cardiomyopathies, such as cardiac sarcoid, is required in patients with recurrent arrhythmias and nonischemic cardiomyopathy with evidence of LGE on CMR.
- CMR-LGE and cardiac FDG-PET are important and complementary diagnostic tools for diagnosis, risk stratification, and evaluating clinical response to therapy in patients with cardiac sarcoid.

Key words: cardiomyopathy, cardiac sarcoid, cardiac magnetic resonance imaging, cardiac fluorodeoxyglucose-positron emission tomography

Conflict of Interest Disclosure: The authors have completed and submitted the *Methodist DeBakey Cardiovascular Journal* Conflict of Interest Statement and none were reported.

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