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ADVANCED

CASE REPORT: CLINICAL CASE

Progressive Thinning of the Basal Interventricular Septum by Giant Cell Myocarditis

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ABSTRACT

We describe a patient with ventricular tachycardia and complete atrioventricular block. Remarkable thinning of the basal interventricular septum preceded left ventricular dysfunction. Endomyocardial biopsy demonstrated giant cell myocarditis. The patient received combined immunosuppressive therapy and a cardioverter-defibrillator. Eligibility screening for heart transplantation was initiated. (**Level of Difficulty: Advanced.**) (J Am Coll Cardiol Case Rep 2020;2:180–5)

HISTORY OF PRESENTATION

A 40-year-old woman was hospitalized with recent-onset palpitations that occurred both at rest and during exercise. She had no dyspnea, chest pain, or syncope, and she denied use of illicit drugs. Upon admission blood pressure was 133/85 mm Hg, heart rate 150 beats/min, oxygen saturation on room air 99%, and respiratory rate 15 ventilations/min. Fever and clinical signs of heart failure were absent. Cardiac auscultation was normal.

LEARNING OBJECTIVES

- GCM should be included in the differential diagnosis of thin basal IVS.
- CMR is useful in determining the etiology of nonischemic cardiomyopathy. Further research is needed to elucidate the mechanism of transmural LGE in GCM.

PAST MEDICAL HISTORY

The patient had no previous medical or surgical history. Her family history of cardiac disease was negative.

INVESTIGATIONS

The electrocardiogram showed a monomorphic ventricular tachycardia (VT) with right bundle branch block morphology at a rate of 150 beats/min. Rhythm monitoring demonstrated episodes of complete atrioventricular block.

Laboratory data revealed a high sensitive troponin T level of 609 ng/l and an N-terminal pro-B-type natriuretic peptide level of 3,275 ng/l. C-reactive protein level was 26 mg/l. Complete blood cell count, kidney function, electrolytes, liver tests, and the creatine phosphokinase and thyroid-stimulating hormone levels were within normal ranges. Antinuclear factor and antineutrophil cytoplasmic antibody levels were normal.

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Informed consent was obtained for this case.

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Invasive evaluation demonstrated mildly depressed left ventricular (LV) function (left ventricular ejection fraction [LVEF] 45% upon ventriculography) with normal coronary arteries. Hemodynamic measurements were within the normal range.

SEE PAGE 178

Transthoracic echocardiography showed slightly reduced LV systolic function and normal diastolic function without evidence of valvular or pericardial disease. The basal segment of the interventricular septum (IVS) was remarkably thin (Figure 1).

On cardiac magnetic resonance imaging (CMR), transmural late gadolinium enhancement (LGE) was observed in the basal segments of the IVS and anterior wall, whereas the middle segments of the IVS had a subepicardial distribution of LGE (Figure 2). Tissue characterization with T_2 imaging showed substantial myocardial edema, compatible with very intense focal myocardial inflammation, as observed in myocarditis or sarcoidosis. LV function appeared slightly reduced (LVEF 45%) with moderate dilation of the LV (end-diastolic volume 186 ml). Polymerase chain reaction for common viruses and serological testing were negative. Total-body positron emission tomography-computed tomography (PET-CT) showed no signs of systemic or cardiac disease activity. No elevated 18F-fluorodeoxyglucose uptake in the heart was noted.

Subsequent LV endomyocardial biopsy (EMB) revealed the presence of numerous multinucleated giant cells with histiocytes, lymphocytes, eosinophils, and clearly damaged myocytes (Figure 3). Granulomas, amyloid deposition, and molds were absent. These hallmark histological findings confirmed the diagnosis of giant cell myocarditis (GCM).

DIFFERENTIAL DIAGNOSIS

A thin basal IVS has been observed in ischemic heart disease (myocardial infarction with scar tissue

ABBREVIATIONS AND ACRONYMS

CMR = cardiac magnetic resonance imaging

CS = cardiac sarcoidosis

EMB = endomyocardial biopsy

GCM = giant cell myocarditis

IVS = interventricular septum

LGE = late gadolinium enhancement

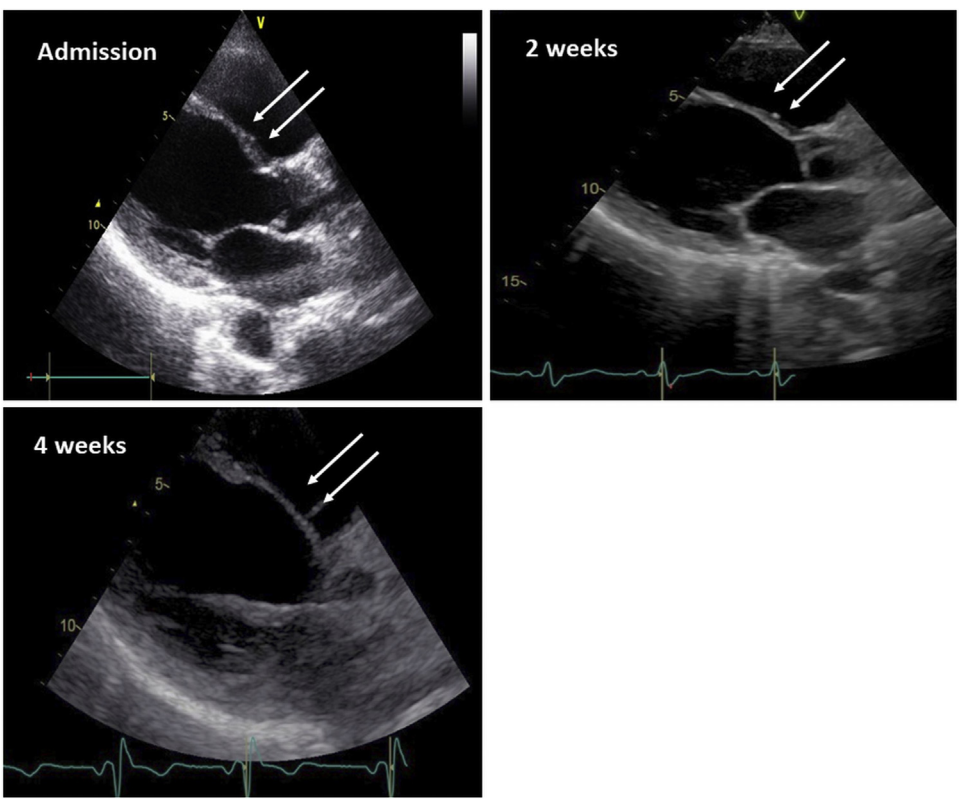
LV = left ventricle

LVEF = left ventricular ejection fraction

PET-CT = positron emission tomography-computed tomography

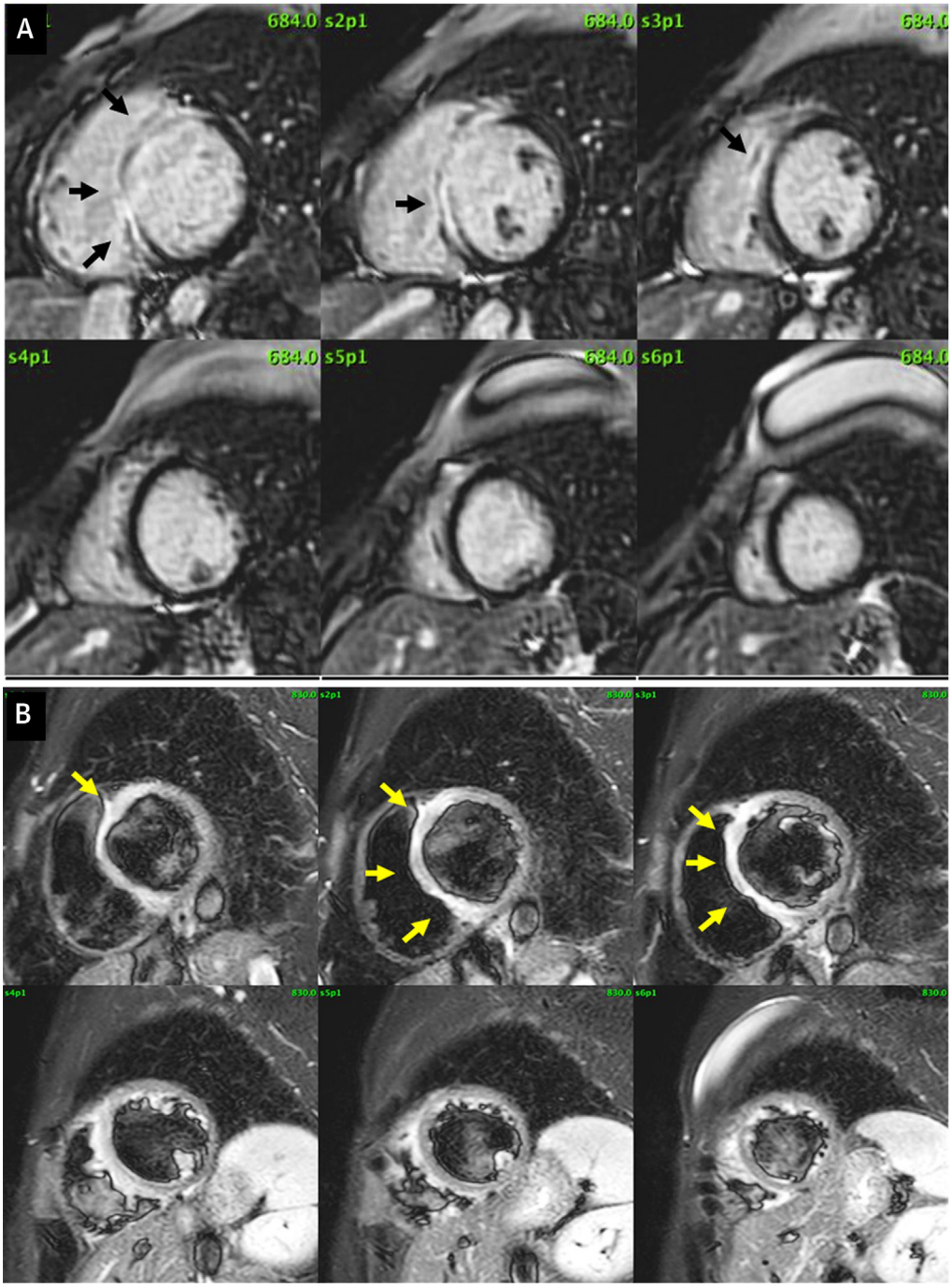
VT = ventricular tachycardia

FIGURE 1 Transthoracic Echocardiography



Serial parasternal long-axis views showing progressive thinning of the basal portion of the interventricular septum, measuring 5 mm on admission, 4 mm after 2 weeks, and 3 mm after 4 weeks.

FIGURE 2 Representative CMR Images



(A) Late gadolinium enhancement (LGE) (inversion recovery gradient recalled echocardiography) short-axis images showing a nonischemic hyper-enhancement pattern in the basal to middle interventricular septum (IVS) and lateral wall. **Arrows** indicate transmural, midmyocardial, and subepicardial involvement. **(B)** Dark blood T_2-weighted (short T_1 inversion recovery) short-axis images showing increased signal intensity in the IVS **(arrows).** T_2 values for IVS, lateral wall and skeletal muscle were 152, 72, and 46 ms, respectively. **(C)** LGE short-axis images after 5 weeks showing transmural and subepicardial scar in the basal to mid-IVS **(arrows).** T_2 values for IVS, lateral wall and skeletal muscle were 59, 55, and 38 ms, respectively (image not shown).

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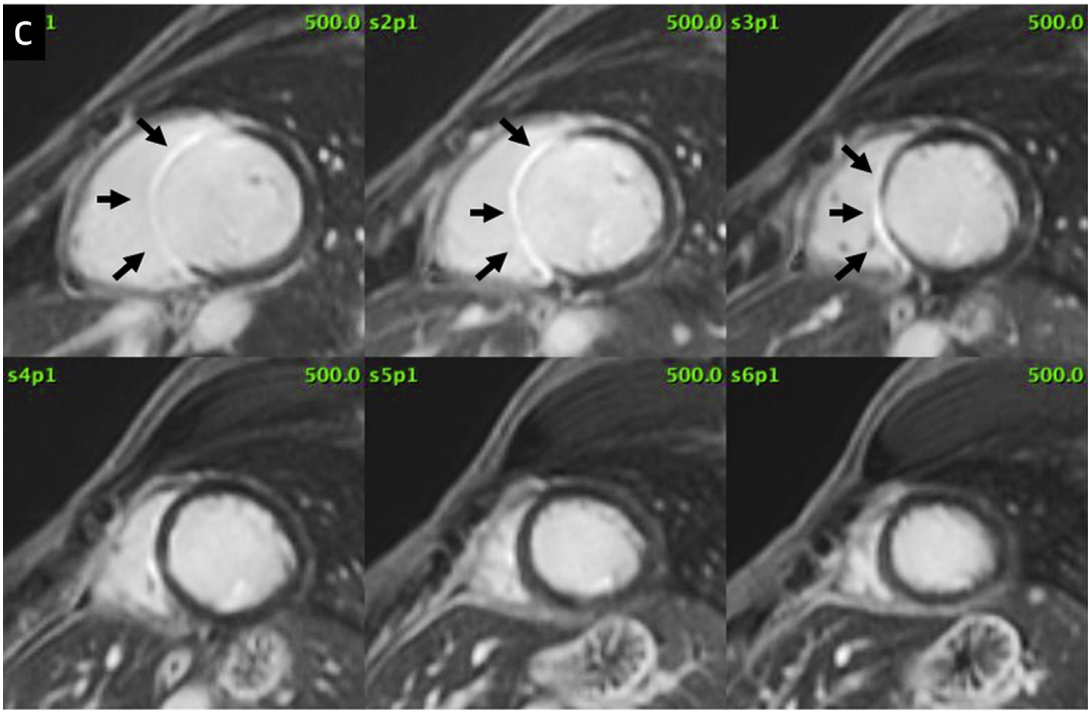
FIGURE 2 Continued



formation), cardiac sarcoidosis (CS) (scar tissue formation after granulomatous inflammation), and trauma.

MANAGEMENT

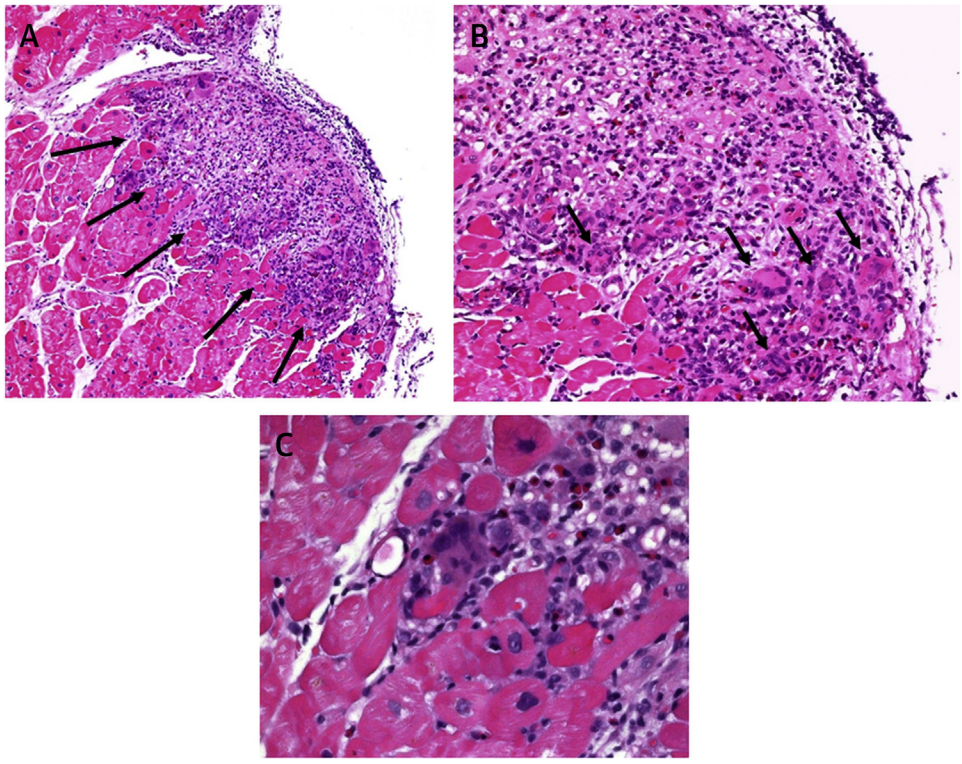
Bisoprolol administration was started because of frequent runs of nonsustained VT. Despite beta-blocker therapy, the patient developed sustained VT necessitating electrical cardioversion. Amiodarone, lisinopril, and spironolactone were added to the therapy. After diagnosis, immunosuppressive treatment with methylprednisolone, azathioprine, and cyclosporine was initiated.

DISCUSSION

A clinical suspicion of GCM is a Class I indication for EMB (1). Multinucleated giant cells can be observed in both GCM and CS. GCM is associated with a widespread inflammatory infiltrate and extensive myocyte necrosis, whereas CS is characterized by tight non-necrotizing granulomatous inflammation and prominent fibrosis. Unlike GCM, eosinophils are rare in CS, and Schaumann bodies are frequently found in giant cells associated with sarcoidosis. A limitation of EMB is a high rate of sampling error. The sensitivity of EMB for detecting GCM is 68% but can be substantially improved to 93% by repeated or targeted EMBs (2).

CMR with analysis of LGE distribution has emerged as a valuable imaging method to differentiate between various types of nonischemic cardiomyopathies. The typical pattern of LGE in CS is a subepicardial and midmyocardial distribution along the basal septum, spreading into all LV segments. Transmural involvement is a rare feature in CS (3). Myocardial edema on T_2 imaging is considered a hallmark finding in myocarditis but may also be seen in acute lesions of CS (4). A series of 5 histologically proven GCM cases found that LGE tends to be widespread in GCM involving all layers of the myocardium, as opposed to other forms of myocarditis, which typically have subepicardial LGE (4,5). This transmural distribution of LGE could reflect extensive myocardial inflammation in GCM (5). Nonetheless, the underlying mechanisms leading to LGE are still under debate. Previously thought to be caused by myocardial fibrosis or inflammation, LGE has been associated with increased ventricular wall stress in dilated cardiomyopathy (6). This evidence is supported by temporary LGE seen in stunned ventricles, for example, in stress cardiomyopathy, in which scar formation is unlikely to contribute to LGE. In our case, we hypothesize that, due to the thinned and

FIGURE 3 Microscopy



The presence of multiple giant cells, numerous eosinophils, and myocyte necrosis is indicative of giant cell myocarditis. Fibrosis and epithelioid granulomas are absent. Eosinophilic myocarditis was excluded because of the absence of inciting drugs, peripheral blood eosinophilia, and skin rash. **(A)** Dense band of inflammatory cells **(arrows).** Hematoxylin and eosin stain (magnification ×100). **(B)** Mixed inflammatory infiltrate containing eosinophils, lymphocytes and numerous multinucleated giant cells **(arrows).** Hematoxylin and eosin stain (magnification ×200). **(C)** Detail of a Langhans giant cell with adjacent damaged myocytes. Schaumann bodies are absent. Hematoxylin and eosin stain (magnification ×400).

hypocontractile IVS, increased ventricular wall stress in the anteroseptal and inferoseptal walls may explain the LGE localizations.

We describe a case of biopsy-proven GCM with extreme thinning of the basal IVS. Thinning of the basal IVS is a major diagnostic feature of CS, thus raising suspicion of possible misdiagnosis. Although the concomitant presence of GCM and undiagnosed CS is possible, it is an extremely unlikely explanation for our observation. The fulminant clinical course favored GCM above CS. Our findings of transmural LGE and intense myocardial edema on CMR do not reliably exclude CS but are more likely caused by GCM. Furthermore, our histopathological analysis was clearly diagnostic of GCM. Also, the fact that PET-CT, a reliable examination for diagnosing active CS, was negative for sarcoidosis does not align with the rapid clinical progression and septal thinning in our case, which would only be explainable by a very active form of CS. Therefore, the negative PET-CT also favors the diagnosis of GCM compared with CS.

FOLLOW-UP

Five weeks later, CMR showed progressive disease with further thinning of the IVS, especially in the inferior part (Figure 2), with akinesia of the basal anteroseptal and inferoseptal walls and hypokinesia of the middle segment of the IVS. LVEF dropped to 26%. A cardiac resynchronization therapy-defibrillator was implanted, and screening for heart transplantation was started.

CONCLUSIONS

This clinical case illustrates that thinning of the basal IVS, previously thought to be predictive of CS in the absence of ischemic heart disease, may very well be caused by GCM. To the best of our knowledge, this

association has not yet been reported. This finding highlights an important relationship between GCM and CS. The basal IVS seems to be a predilection spot for accumulation of inflammation that nevertheless conveys nothing about its origin.

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KEY WORDS **cardiac magnetic resonance imaging, cardiovascular disease imaging, palpitations, ventricular tachycardia**