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Spontaneous Remission in a Case of Giant Cell Myocarditis with Preserved Left Ventricular Ejection Fraction

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Data Interpretation D
Manuscript Preparation E
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Conflict of interest: None declared

Patient: Female, 28
Final Diagnosis: Giant cell myocarditis
Symptoms: Progressive shortness of breath and palpitation
Medication: None
Clinical Procedure: Endomyocardial biopsy • MRI • PET
Specialty: Cardiology

Objective: Unusual clinical course

Background: Giant cell myocarditis (GCM) is rapidly progressive fulminant myocarditis causing death or requiring cardiac transplantation despite various immunosuppression therapies.

Case Report: A 28-year-old woman with progressive shortness of breath and palpitation following an upper respiratory infection was referred to our institution. On admission, transthoracic echocardiography (TTE) revealed a preserved left ventricular ejection fraction (LVEF) with mildly impaired LV diastolic function despite extensive ECG abnormalities, a mildly elevated troponin I concentration, and moderately elevated N-terminal pro-brain natriuretic peptide (NT-pro-BNP) concentration. The diagnosis of GCM was made by endomyocardial biopsy (EMB), which revealed extensive fibrosis and inflammatory infiltration with multinucleated giant cells, as well as scattered eosinophils and lymphocytes in the absence of granuloma formation. However, the patient's symptoms began to improve without any specific therapy within 2 weeks, followed by the normalization of the ECG abnormalities, TTE-determined diastolic function, and troponin I and NT-pro-BNP concentrations. In sub-acute phase, ^{18}F-fluorodeoxyglucose positron emission tomography showed no evidence of inflammation, and repeat EMB showed a significant decrease in the inflammatory infiltration and fibrosis, including absence of giant cells. Given the favorable clinical course, the patient was discharged without medications. At the 6-month follow-up, the patient had no LV functional impairment, cardiovascular events, or arrhythmia.

Conclusions: We encountered a rare case of atypical GCM in which clinical and histologic remission was achieved without immunosuppression therapy. There seems to be a population of GCM patients who improve without immunosuppression therapy. In monitoring GCM patients, clinicians should be aware of the possibility of spontaneous remission.

MeSH Keywords: Biopsy • Myocarditis • Remission, Spontaneous

Full-text PDF: http://www.amjcaserep.com/abstract/index/idArt/895253

Background

Giant cell myocarditis (GCM) is a rare, often fatal myocardial disease caused by extensive infiltration of inflammatory cells with multinucleated giant cells in the absence of granuloma formation [1]. Typically, the clinical course is one of rapidly progressive fulminant myocarditis leading to acutely decompensated heart failure. Patients have severely reduced ventricular function and 1 or more ventricular arrhythmias causing death or requiring cardiac transplantation despite being placed on various immunosuppression therapies [2,3]. Here, we describe a case of GCM in which the left ventricular ejection fraction (LVEF) was preserved and clinical remission was reached without any specific therapy.

Case Report

A 28-year-old woman presented to her primary care physician with progressive shortness of breath (New York Heart Association functional class II) and palpitation that had lasted for 3 weeks. These symptoms had followed an upper respiratory infection that had been treated for 1 week with cefditoren pivoxil (CDTR-PI). The 12-lead electrocardiogram (ECG) and chest X-ray appearance resembled those seen in cases of acute myocardial infarction, so the patient was referred to our institution for further evaluation and treatment.

On admission, the patient appeared pale and unwell. Her body temperature was 37.3°C, blood pressure was 92/67 mmHg, heart rate was 88 beats/min, respiratory rate was 14 breaths/min, and oxygen saturation (via pulse oximetry) was 97% on room air. Cardiopulmonary auscultation revealed no gallop but did show minimal bibasilar crackles. Some lower-extremity edema was seen. The ECG showed normal sinus rhythm, low limb lead QRS voltage, diffuse Q waves, and ST- and T-wave abnormalities in the precordial leads (Figure 1A). The chest X-ray appearance was suggestive of mild ventricular enlargement without pulmonary edema. Transthoracic echocardiography (TTE) revealed a preserved LVEF of 63% with global thickening and a mildly elevated E/e' of 13, which suggested impaired LV diastolic function. No significant valvular abnormality or pericardial effusion was detected. Laboratory tests revealed a leukocyte count of 5900/mm^3 with 3.1% eosinophils, a slightly elevated C-reactive protein level of 0.5 mg/dl, a mildly elevated troponin I concentration of 3.62 ng/ml, and moderately elevated N-terminal pro-brain natriuretic peptide (NT-pro-BNP) concentration of 12,525 pg/ml. The creatine kinase and creatine kinase MB isoenzyme concentrations were within normal range. Serologic analyses showed no evidence of acute or subacute systemic infection with any cardiotropic virus, fungus, or parasite, and there was no evidence of sarcoidosis or autoimmune disorder. Cardiac magnetic resonance

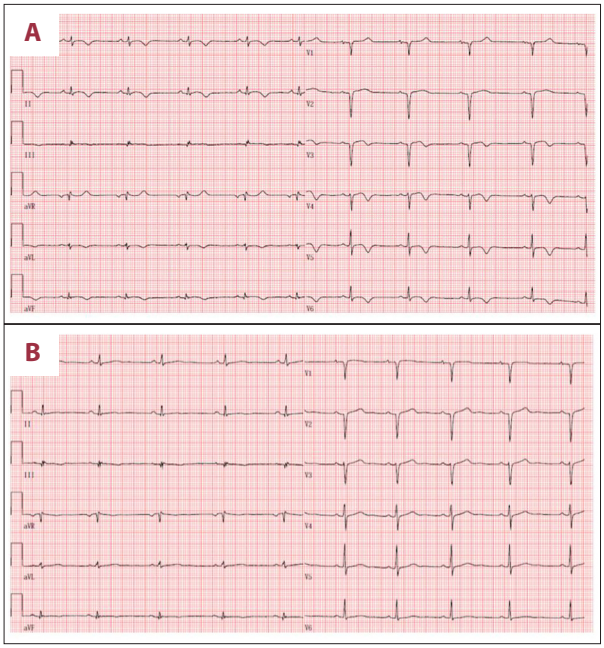
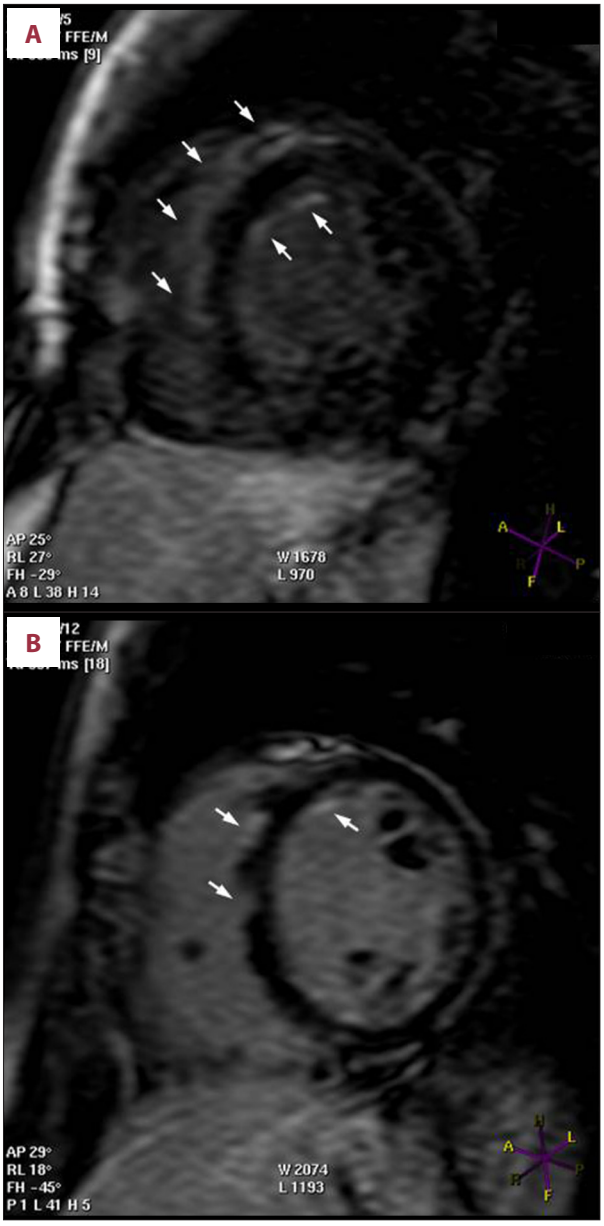


Figure 1. Twelve-lead electrocardiograms obtained (**A**) on admission and (**B**) on hospital day 44.

imaging (CMR) showed late gadolinium enhancement (LGE) on both sides of the interventricular septum (Figure 2A). Coronary angiography showed no evidence of coronary artery disease, and right heart catheterization yielded a cardiac index of 4.23 L/min/m^2 and pulmonary capillary wedge pressure of 11 mmHg. Subsequent endomyocardial biopsy (EMB) of the right ventricular (RV) septum revealed extensive fibrosis and inflammatory infiltration with multinucleated giant cells, scattered eosinophils and lymphocytes in the absence of granuloma formation, amyloid deposition, and iron deposition (Figure 3A, 3B). Finally, GCM was diagnosed.

Within 2 weeks of admission, the patient's symptoms began to improve with standard therapy for heart failure. Follow-up CMR on hospital day 28 depicted persistent LGE lesions on the interventricular septum and scattered LGE lesions on the LV posterior wall (Figure 2B, 2C). However, on hospital day 30, ^{18}F-fluorodeoxyglucose positron emission tomography and 67-gallium citrate scintigraphy showed no evidence of inflammation. By hospital day 44, the ECG abnormalities (Figure 1B), TTE-determined diastolic function, and troponin I and NT-pro-BNP concentrations normalized. Repeat RV EMB performed on hospital day 45 showed a significant decrease in the inflammatory infiltration and fibrosis, including absence of giant cells (Figure 3C). Given the favorable clinical course, the patient was discharged without medications. At the 6-month follow-up visit, the patient reported feeling well and no cardiovascular events or arrhythmia had ensued. Her cardiac parameters assessed by ECG, TTE and serological tests remained within normal range.



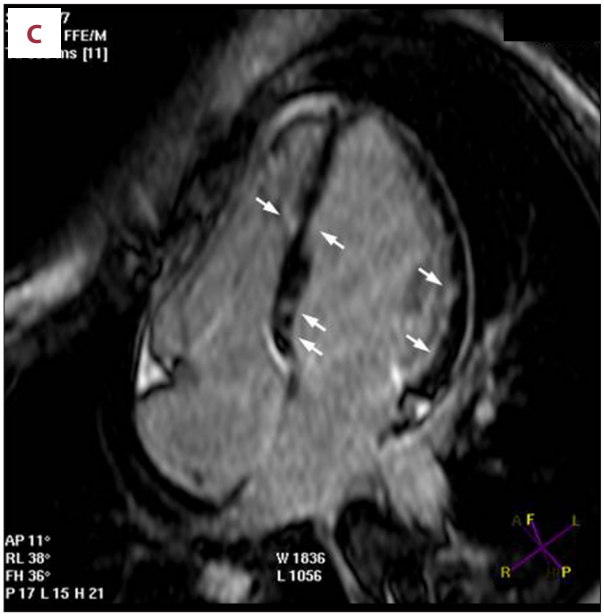


Figure 2. Cardiac magnetic resonance images obtained on the day of admission and hospital day 28. (**A**) Short-axis view on the day of admission, (**B**) short-axis view on day 28, and (**C**) apical 4-chamber view on day 28. (**A**) Late gadolinium enhancement (LGE) is identified on both sides of the interventricular septum (arrows) on the day of admission. (**B**) and (**C**) Persistent LGE lesions on the interventricular septum and scattered LGE lesions on the LV posterior wall are seen on day 28 (arrows).

Discussion

GCM usually presents as fulminant myocarditis and leads to severe decompensated heart failure within a few weeks. Therefore, EMB is crucial for a correct diagnosis and proper management. The reported sensitivity of EMB of the RV is 80–85% in cases of GCM [1,4] and the sensitivity can be enhanced if the target site is assessed by means of CMR before EMB [5,6]. The histologic differential diagnosis of GCM includes cardiac sarcoidosis and hypersensitivity myocarditis [4,7]. The most common histologic feature of cardiac sarcoidosis is noncaseating granulomas, with limited lymphocyte infiltration and patchy fibrosis [4]. Hypersensitivity myocarditis is typically characterized by pancarditis with a perivascular mixed inflammatory infiltrate that is rich in eosinophils [7]. However, these hallmarks were not observed in our case. The histologic identification of extensive fibrosis and inflammatory infiltration with numerous giant cells and scattered eosinophils and lymphocytes in the absence of granuloma formation is strongly suggestive of GCM rather than cardiac sarcoidosis or hypersensitivity myocarditis, although these findings are not diagnostic.

The median transplant-free survival time reported for GCM patients given a combination immunosuppression therapy that included corticosteroids, cyclosporine, and muromonab-CD3 was 12.3 months, whereas that of patients who were not given any immunosuppression therapy was only 3 months [1]. Our patient, however, showed marked clinical and histologic improvement without any immunosuppression therapy. A possible EMB sampling error should be considered, but, as recommended, 3 EMB samples were taken each time to minimize the possibility of this type of error [7]. There seems to be a population of patients who improve without immunosuppression therapy.

In a recent prospective multicenter study that included 11 GCM patients treated by immunosuppression therapy [2], all 7 patients with an LVEF >40% had a good clinical outcome, whereas 3 of the 4 patients with an LVEF <40% died or underwent

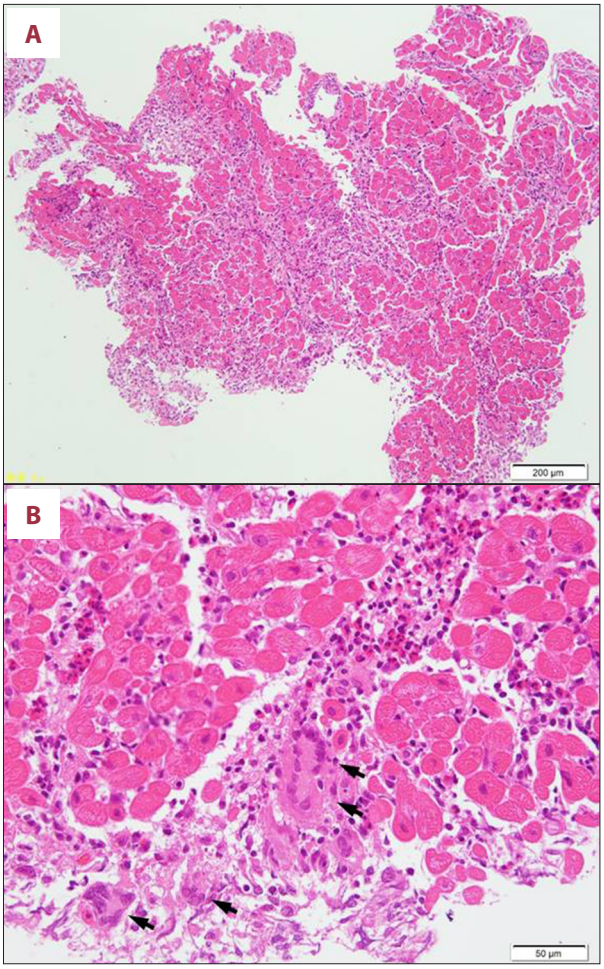


Figure 3. Endomyocardial biopsy specimens of the right ventricular septum obtained (**A, B**) upon admission and (**C**) on hospital day 45. Hematoxylin and eosin (HE)-stained sections show (**A**) extensive fibrosis and inflammatory infiltration with (**B**) multinucleated giant cells (arrows) and scattered eosinophils and lymphocytes in the absence of granuloma formation (original magnification: A, ×100; B, ×400). (**C**) A significant decrease in inflammatory infiltration and fibrosis without giant cells is seen on hospital day 45 (original magnification: ×100).

heart transplantation. The clinical course in our case along with the results of the multicenter study suggests that baseline LVEF might serve as a prognostic indicator in patients with GCM. Further studies to identify predictors of GCM outcome and optimal immunosuppression strategies are warranted.

Conclusions

We encountered a rare case of atypical GCM in which the patient's cardiac function improved and histologic remission was achieved without immunosuppression therapy. In monitoring patients with GCM, clinicians should be aware of the possibility of spontaneous remission.

Acknowledgments

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Disclosures

None.

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