

CASE REPORT

ADVANCED

CLINICAL CASE

Atrial Giant Cell Myocarditis as a Cause of Heart Failure



Diagnostic Pathway and Successful Treatment

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ABSTRACT

We present a patient with acute heart failure and new onset atrial fibrillation secondary to giant cell myocarditis with lone atrial involvement. The diagnosis was managed with cardiac magnetic resonance and confirmed by interventionaly guided biopsy. In the future, diagnosis could be managed noninvasively for this rare entity as the gold standard. (**Level of Difficulty: Advanced.**) (J Am Coll Cardiol Case Rep 2022;4:66-71) © 2022 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

HISTORY OF PRESENTATION

A 79-year-old woman presented to the emergency department with exertional dyspnea and palpitations. Additionally, she reported a weight loss of 4 kg (weight, 50 kg; body mass index, 17.5 kg/m²), night

sweats, and low appetite for 4 weeks. She was afebrile, with a blood pressure of 120/70 mm Hg and a heart rate of 126 beats/min. Electrocardiography showed newly diagnosed persistent atrial fibrillation (AF) (CHA₂DS₂-VASc-score of 3).

LEARNING OBJECTIVES

- To diagnose precisely in future this rare entity of atrial GCM and to rule out ventricular inflammation or storage diseases non-invasively by imaging evaluation with CMR as the gold standard.
- To pay special attention to atrial and septal wall thickening as signs of atrial inflammation for clinicians conducting the imaging.

PAST MEDICAL HISTORY

There was no cardiac or other relevant medical history, no recent infections or COVID-19. The patient had undergone regular cancer screening in the past.

DIFFERENTIAL DIAGNOSIS

Possible differential diagnoses included acute heart decompensation resulting from new onset AF or myocarditis or a malignant disease.

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INVESTIGATIONS

Natriuretic peptide levels were elevated (N-terminal pro-B-type natriuretic peptide, 3,063 pg/mL). There were no laboratory signs of infection (no leukocytosis and no value elevation of C-reactive protein, procalcitonin, interleukin 6, or blood sedimentation rate) or acute kidney injury. Results of an extensive infective work-up, including immunoglobulin (Ig) levels (IgM and IgG) for myocarditis-relevant viral agents (ie, coxsackievirus, parvovirus B19, human herpesvirus-6, human cytomegalovirus, adenovirus) and the rheumatologic panel (including cytoplasmic antineutrophil cytoplasmic antibody [c-ANCA], perinuclear ANCA [p-ANCA], antinuclear antibody, rheumatic factor) were negative. Thoracic and abdominal computed tomography, as well as gastroscopy and colonoscopy, ruled out concomitant malignant disease.

Transthoracic echocardiography (Figures 1A to 1C, Videos 1 and 2) revealed a 7-mm pericardial effusion and dilatation of both the left atrium (LA) (surface area, 22 cm²) and the right atrium (RA) (surface area, 18 cm²), with thickening of the free atrial wall (RA, 6 mm; LA, 6 mm). Transesophageal echocardiography (TEE) confirmed the markedly thickened atrial wall, including thickening of the atrial septum (Figure 1F, Videos 3 and 4). Additionally, no valve vegetations were detected. Cardiac magnetic resonance (CMR) showed distinct inflammation isolated to the atrium without ventricular involvement (Figure 2, Videos 5, 6, and 7). The pathognomonic sign was biatrial wall thickening, with isolated bright T₂ edema and enhanced late gadolinium enhancement in both atria. Diffuse myocardial or pericardial inflammation was ruled out by noninvasive tissue characterization. Additionally, CMR showed normal ventricular function.

MANAGEMENT

Heart failure (HF) medication with an oral angiotensin receptor antagonist (candesartan, 8 mg/d) and a beta-blocker (metoprolol, 95 mg/d), as well as oral anticoagulation with a direct oral anticoagulant agent (apixaban, 10 mg/d) was initiated. AF heart rate control was achieved by digitoxin (0.07 mg/d).

The case was discussed within the institutional heart team, and we proposed performing an interventional endomyocardial biopsy of the atrial septum and ventricle. For this purpose, the patient was sedated, and vascular access was obtained through the right femoral vein and artery (Cook 16-F, 45-cm

Check Flo Performer). Guided by TEE and fluoroscopy, multiple biopsy specimens were acquired throughout the atrial and ventricular septum with the biopsy catheter system (Maslanka flexible biopsy forceps) (Figures 1D and 1E). Histopathologic examination of the atrial biopsy specimens revealed necrotic areas, lymphocytic infiltration, and multinuclear giant cells leading to the final diagnosis of giant cell myocarditis (GCM) (Figures 3A to 3F). Ventricular biopsy results were negative, proving lone involvement of the atrium.

Symptomatic HF and the ongoing atrial inflammation, as assessed by CMR and confirmed by biopsy, were the key factors for specific treatment initiation. The patient was treated with prednisolone, starting with 50 mg/d and reduced to 10 mg/d over the course of 3 months. HF symptoms resolved, and spontaneous conversion to sinus rhythm was observed. Follow-up CMR at 3 months revealed normal thickness of both left and right atrial walls, with no signs of inflammatory T₂ edema, compared with pretreatment findings (Figures 4A to 4L, Videos 8, 9, and 10).

DISCUSSION

NOVELTY. GCM is known as a rapidly progressive and frequently fatal myocardial disease in young and middle-aged adults.¹ However, atrial GCM represents a rare, distinct clinicopathologic entity with a more favorable prognosis than the classic ventricular GCM.² Only a few cases have been described so far, and the definitive histopathologic diagnosis was achieved mostly after surgical procedures.^{2,3} Here we present a patient with atrial GCM and an accurate diagnostic pathway, managed primarily with CMR and confirmed by interventional biopsy, followed by selective treatment with prednisolone that led to a full recovery.

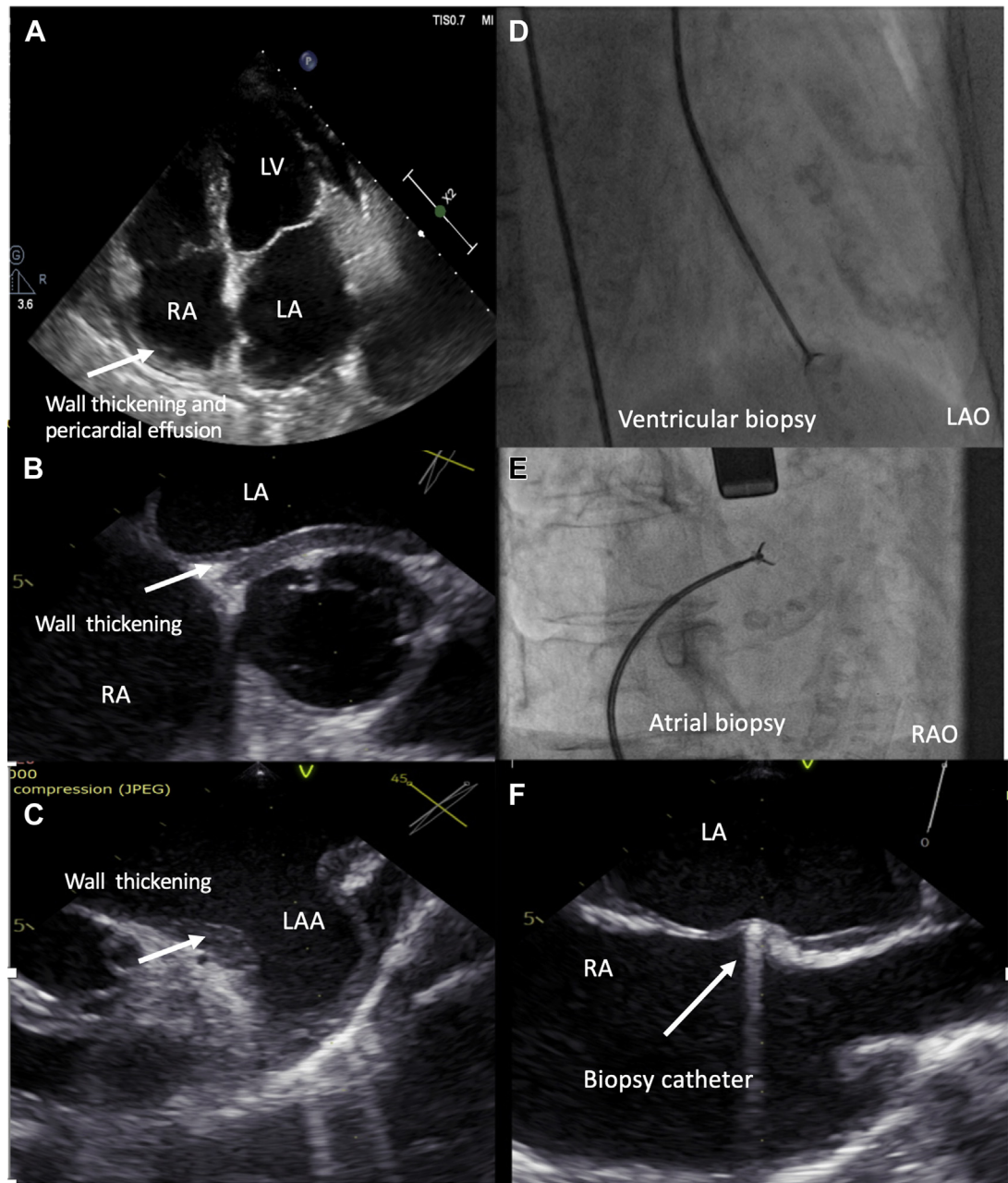
ATRIAL FIBRILLATION DIFFERENTIAL DIAGNOSIS.

Atrial cardiomyopathy may be a cause of recurrent AF. Atrial GCM was first described in 1964 in a case report.⁴ The pathophysiology of GCM is not well understood beyond its recognition as an autoimmune disorder attributable to T-lymphocyte-mediated myocardial inflammation.¹ In published reports, some atrial GCM cases have been associated with autoimmune disorders^{4,5}; however, another series of cases indicated that atrial GCM was a distinct entity.²

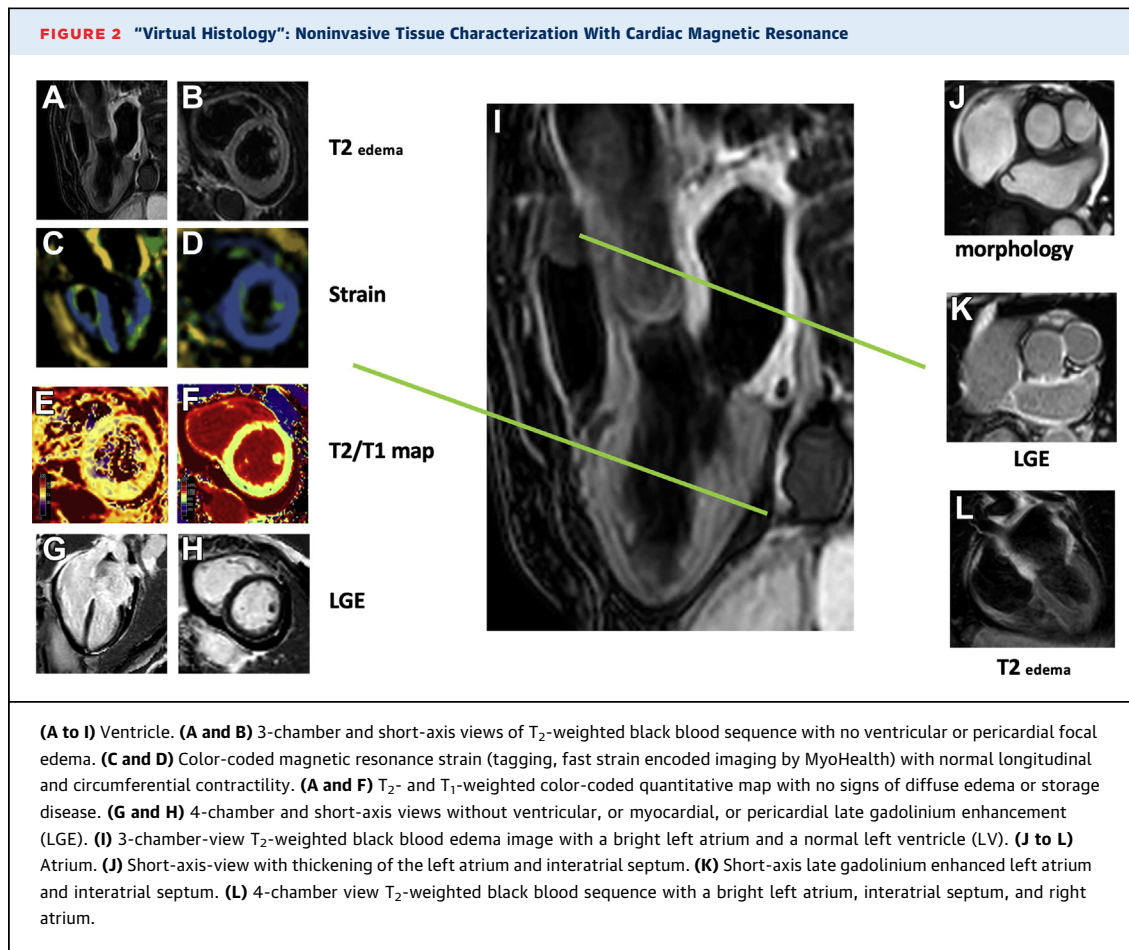
A NEW SPECIFIC DIAGNOSTIC PATHWAY. When GCM involves only the atria, clinical and imaging findings are different from those of ventricular GCM.

ABBREVIATIONS AND ACRONYMS

AF	= atrial fibrillation
ANCA	= antineutrophil cytoplasmic antibody
CMR	= cardiac magnetic resonance
GCM	= giant cell myocarditis
HF	= heart failure
Ig	= immunoglobulin
LA	= left atrium
RA	= right atrium
TEE	= transesophageal echocardiography

FIGURE 1 Echocardiographic Images and Guided Biopsy

(A) Transthoracic echocardiography showing biatrial dilatation, wall thickening, and pericardial effusion. Transesophageal short-axis images depict **(B)** left atrial wall thickening and **(C)** the left atrial appendage (LAA). Biopsies of the atrial septum and left ventricle (LV) were guided by **(D and E)** fluoroscopy and **(F)** transesophageal echocardiography. LA = left atrium; LAO = left anterior oblique; RA = right atrium; RAO = right anterior oblique.

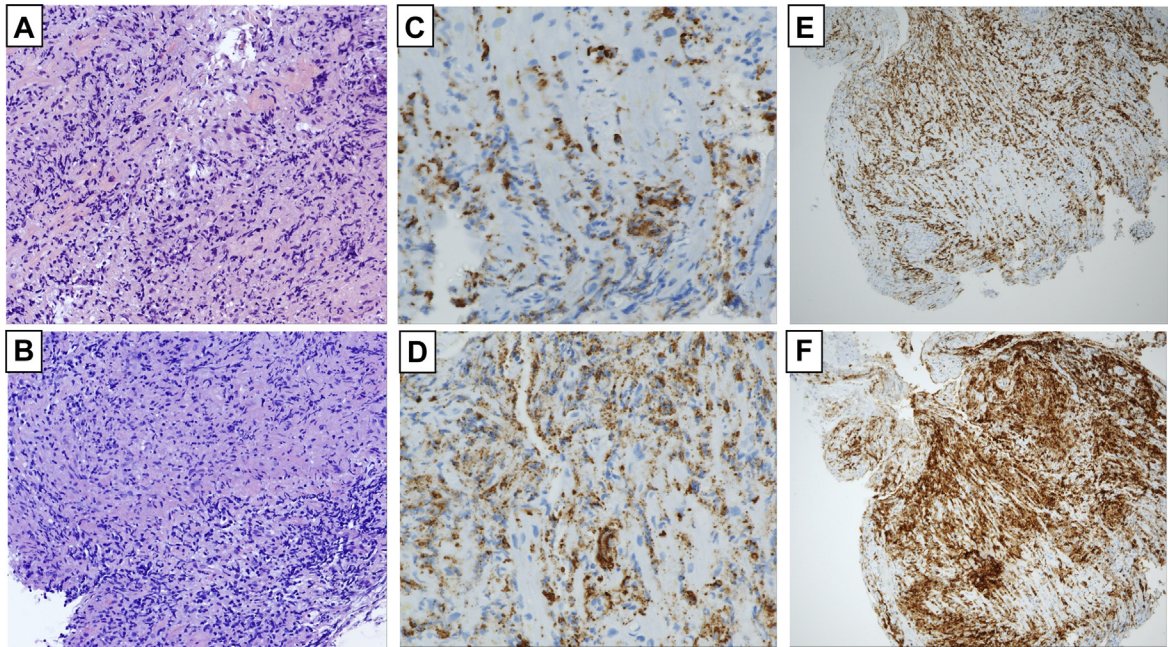


AF seems to be a nearly universal finding in all cases of atrial GCM.^{2,6} Atrial GCM should be included in the differential diagnosis of AF and dilatation, and CMR should be performed, particularly in association with atrial wall thickening.² Ventricular function was preserved in our patient and in all other cases described.² Diagnosis in our patient was achieved by CMR, which showed atrial wall thickening, dilatation, and inflammation limited to the atria and sparing the ventricles. Findings were in line with a previous described CMR case of atrial GCM,² and are in our opinion they were pathognomonic for this rare distinct entity. Although our belief is that in future the diagnosis of atrial GCM can be managed non-invasively by clinical and imaging evaluation, with

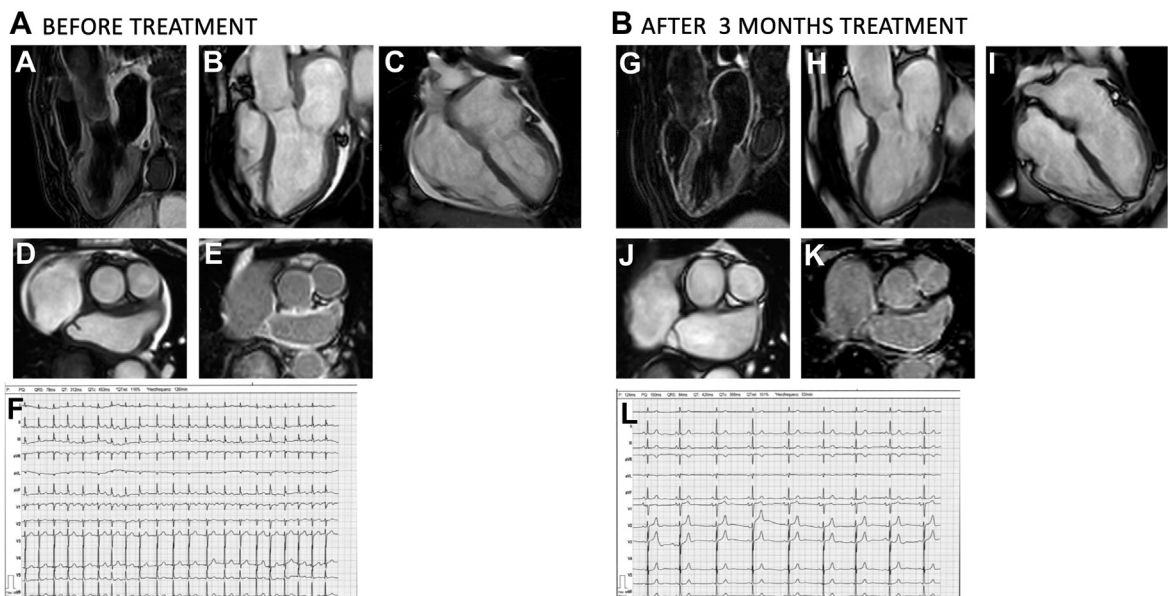
CMR tissue characterization as the gold standard for this rare entity, following our diagnostic pathway, endomyocardial biopsy may be considered in patients without early clinical improvement or resolution after treatment initiation.

FOLLOW-UP

Treatment with prednisolone monotherapy in our patient led to full recovery and conversion to sinus rhythm at 3-month follow-up. However, the role of immunosuppressive treatment remains unknown for this rare entity, and additional studies will therefore be required before conclusions can be made regarding the long-term efficacy of this approach.

FIGURE 3 Histology of Atrial Giant Cell Myocarditis

Atrial biopsy revealed necrotic areas, with lymphocytic infiltrations ($CD8^-$ and $CD4^+$ cells) and multinuclear giant cells, with positive expression of CD68. (A) Hematoxylin and eosin stain of myocardial biopsy. (B) Period acid-Schiff stain. (C and D) Immunohistochemical staining with CD68 antibody, highlighting macrophages and multinuclear giant cells. (E) $CD4^+$ infiltrating lymphocytes. (F) $CD8^+$ infiltrating lymphocytes.

FIGURE 4 Images and Electrocardiography Before and After Treatment

Cardiac magnetic resonance (A to E) before and (G to K) after treatment. (A and G) 3-chamber view T_2 -weighted image (A) with and (G) without a bright left atrium. (B and H) 3-chamber view cine (B) with and (H) without thickening of the left atrial walls. (A and I) 4-chamber view cine with (C) and (I) without thickening of the atrial walls. (D and J) Short-axis view of the left atrium (D) with and (J) without thickening of the left atrial walls. (E and K) Short-axis view late gadolinium enhancement (E) with and (K) without enhanced left atrial walls. Electrocardiography showing (F) atrial fibrillation before treatment and (L) sinus rhythm at 3-month follow-up.

CONCLUSIONS

GCM affecting only the atria differs from the ventricular GCM entity. We show a case of atrial GCM leading to AF and HF in a patient whose accurate diagnosis was managed primarily noninvasively by CMR, followed by atrial septal and ventricular biopsies and selected treatment with prednisolone monotherapy, leading to full recovery.

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The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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KEY WORDS atrial giant cell myocarditis, cardiac magnetic resonance, heart failure, magnetic resonance imaging

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