

What's behind your eosinophilic myocarditis? A case of Churg–Strauss syndrome diagnosed during acute heart failure

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Abstract

Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare multisystem disorder; cardiac involvement may include eosinophilic myocarditis. A 67-year-old woman presented with 1-week history of dyspnoea and orthopnoea. She had a history of adult-onset asthma and peripheral eosinophilia. The investigations showed T-wave inversion on lateral leads, peripheral eosinophilia, elevated troponin and BNP values, and severe biventricular systolic dysfunction with diffuse hypokinesia and apical akinesia. Computed tomography excluded coronary disease and showed bilateral basal ground-glass opacities, air-space consolidation, and bilateral reticular-nodular pattern. Cardiac magnetic resonance findings were compatible with active myocardial inflammation. An endomyocardial biopsy (EMB) confirmed the diagnosis of eosinophilic myocarditis, and a therapy with oral corticosteroids and heart failure medications was started.

Keywords Eosinophilic granulomatosis with polyangiitis (Churg–Strauss); Eosinophilic myocarditis; Heart failure; Endomyocardial biopsy; Cardiac magnetic resonance

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Introduction

Eosinophilic myocarditis (EM) is a rare and potentially life-threatening form of myocarditis, presenting with acute chest pain with signs and symptoms of acute or chronic heart failure (HF).¹ It ranges from mild localized disease to multifocal widespread infiltrates associated with myocardial necrosis, thrombotic complications, and endomyocardial fibrosis.² Despite a wide variety of severity in clinical presentation and the possibility of slower evolving, paucisymptomatic forms, EM is often fatal with high in-hospital mortality, in particular when it presents as fulminant form. The diagnosis mainly depends on endomyocardial biopsy (EMB).³ Eosinophilic granulomatosis with polyangiitis (EGPA), previously known as Churg–Strauss, is a rare multisystem disorder characterized by chronic rhinosinusitis, asthma, and prominent

peripheral blood eosinophilia.⁴ One-third of the patients have anti-myeloperoxidase antineutrophil cytoplasm antibodies, and their presence seems to differentiate between two phenotypes, with different clinical characteristics and prognoses. Overall survival has improved markedly since the use of glucocorticoids and immunosuppressants, but relapse rates remain high. Cardiac involvement may include EM.⁵

Case report

A 67-year-old woman presented with 1-week history of progressive dyspnoea, orthopnoea, and weakness. She suffered from adult-onset bronchial asthma and recurrent sinusitis, and she was known for eosinophilia in the peripheral blood from at least 8 years. In March 2021, she underwent right

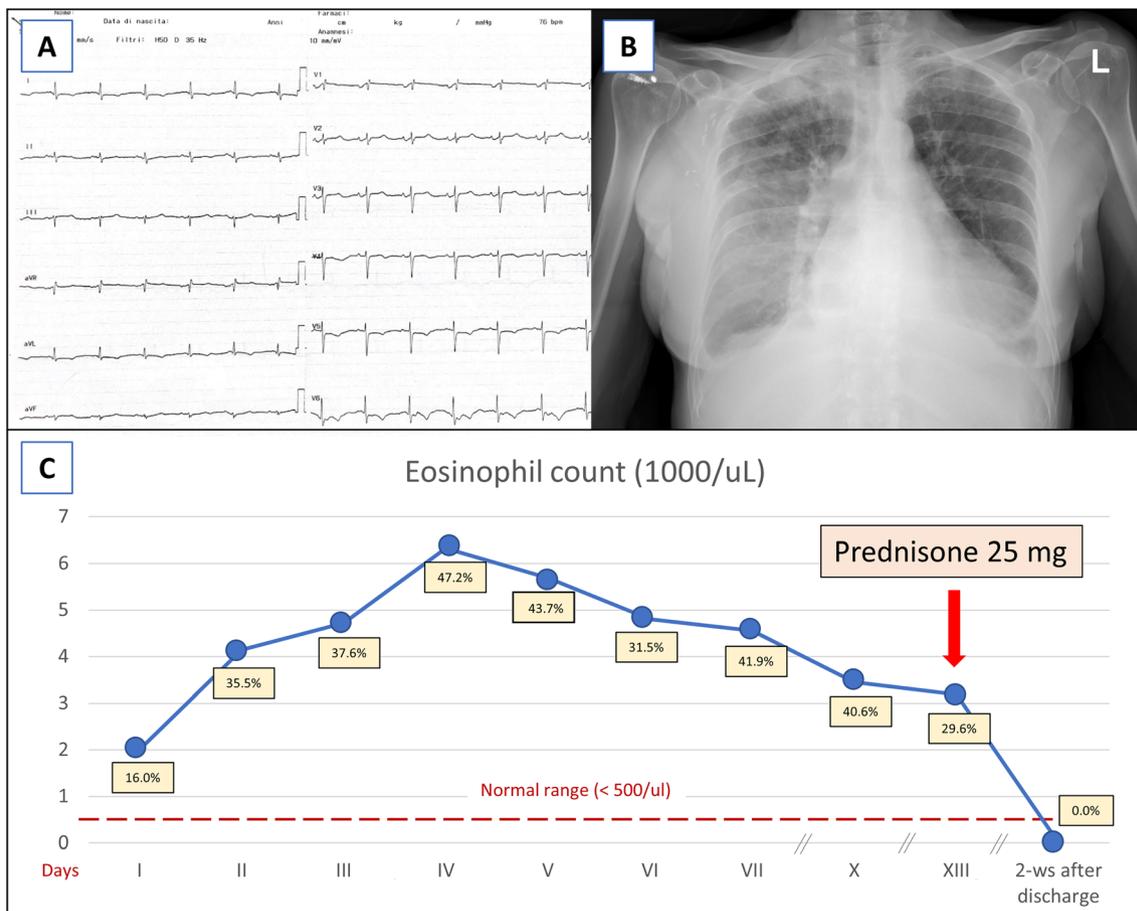
mastectomy due to breast cancer, treated with adjuvant radiotherapy, and she was under treatment with letrozole.

One month before admission (September 2021), she presented a first episode of atrial fibrillation (AF), and she underwent a successful direct-current electrical (DCE) cardioversion, complicated by an early arrhythmia recurrence after 5 days. At that time, an echocardiogram revealed a preserved ejection fraction (EF). A chest computed tomography (CT) showed no signs of pulmonary embolism and consolidation on the superior right pulmonary lobe with bilateral pleural effusion. She underwent four more failed DCE cardioversion attempts.

One month after (October 2021), she was admitted at our centre with worsening dyspnoea. Vital signs were normal (BP 110/70 mmHg, HR 72 bpm, SpO₂ 98%). Breath sounds were reduced at the base of the lung bilaterally. The ECG showed sinus rhythm at 76 bpm and negative T waves in lateral leads (Figure 1A). A blood gas analysis (FiO₂ 21%) was performed, showing hypoxia and mild elevation of lactates (pH 7.48,

pCO₂ 27 mmHg, pO₂ 66 mmHg, lactates 2.1 mmol/L). A chest X ray showed enlargement of cardiac area, bilateral hilar congestion and pleural effusion, and opacity of right lung field (Figure 1B). The blood analysis showed mild anaemia, leucocytosis with marked eosinophilia (Figure 1C), high values of high-sensitivity troponin I (hsTnI) and BNP (Hb 10.7 g/dL, leucocytes 12 600/uL, eosinophils 2010/uL, AST 92.2 UI/L, ALT 120 UI/L, hsTnI 4440.12 ng/L, BNP 2551 pg/mL). An echocardiography showed a non-dilated left ventricle (LV) with a severe systolic dysfunction (EF 31%) due to diffuse hypokinesia and apical akinesis, high filling pressures (E/e' 20), mild right ventricle dilatation with reduced longitudinal and radial function (TAPSE 10 mm, FAC 31%), bi-atrial enlargement, mild aortic regurgitation, and moderate mitral regurgitation. The diagnostic hypotheses were mainly oriented towards myocarditis presenting with acute biventricular dysfunction, whereas an acute presentation of decompensated hypokinetic dilated cardiomyopathy was unlikely because the heart chamber volumes were normal. As differential diag-

Figure 1 Chest X-ray, ECG and blood sample findings. The ECG showed sinus rhythm at 76 bpm and negative T waves in lateral leads (A). A chest X-ray showed enlargement of cardiac area, bilateral hilar congestion and pleural effusion, and opacity of right lung field (B). Leucocytosis with marked eosinophilia (C) was noted at admission and during the hospitalization.



nosis, an acute coronary syndrome or a tachycardiomyopathy needed to be ruled out. The patient was treated with i.v. furosemide and levosimendan. She presented a recurrence of AF and 300 mg i.v. amiodarone was administered without successful cardioversion. Optimal HF medical therapy was started (Figure 2). The blood analysis showed persistent leucocytosis with eosinophilia, with a progressive reduction of hsTnI and BNP values. We investigated other possible causes of eosinophilia: The autoimmune panel showed anti-nuclear antibodies positivity (1:160), normal complement levels, and negative ANCA. A faecal parasitological exam was negative. Six days after admission, the patient underwent spontaneous cardioversion to sinus rhythm. Although acute coronary syndrome was unlikely, a coronary anatomy evaluation was required to rule out haemodynamically significant stenosis. We performed a cardiac CT (Figure 3A–C) showing no coronary artery stenosis, a consolidation area in the apical segment of the right upper lobe, ground-glass opacities in the lower lobes, interlobular septal thickening, and bilateral pleural effusion (Figure 3D).

To confirm the clinical suspicion of myocarditis, and obtain an advance cardiac tissue analysis, a cardiac magnetic resonance (CMR) was performed demonstrating improvement of left ventricular function (LVEF 50%), prolonged native T1 (Figure 3E), and T2 times (Figure 3F) in the interventricular septum, left ventricle anterior, and inferolateral wall, augmented extracellular volume (ECV): 36 ± 6% (Figure 3G). There is no late gadolinium enhancement (LGE) (Figure 3H). A diagnosis of acute myocarditis was made, according to 2018 Lake Louise criteria.^{6,7}

To establish an aetiological diagnosis of myocarditis, we performed an electro-anatomical LV voltage mapping showing areas of low voltages only at the unipolar map. Four EBM samples were taken in these areas (Figure 4A). At biopsy analysis in all samples, there were eosinophilic infiltrates, focal necrosis of cardiomyocytes, and signs of initial replacement with fibroblasts with no signs of vasculitis (Figure 4B). The molecular investigation resulted negative for both DNA and RNA viruses' genomes. The diagnosis of EM was established, and therapy with prednisolone 25 mg b.i.d. was started (Figure 2). To exclude a maxillofacial involvement related to the hypereosinophilic syndrome, a maxillofacial CT was done showing signs of chronic sinusitis with no nasal polyps. According to 1990 American College of Rheumatology criteria, diagnosis of EGPA was made. We repeated an echocardiogram showing non-dilated LV with mild systolic dysfunction (EF 50%), non-dilated RV with normal longitudinal systolic function (TAPSE 21 mm), mild MR, and absence of pericardial effusion.

Two weeks after discharge, the patient did not present HF symptoms/signs. Blood analysis showed no leucocytosis, eosinophils 0%, and normal hsTnI (26.9 ng/L). The ECG showed sinus rhythm, without repolarization abnormalities. She underwent a pre-discharge cardiopulmonary exercise test demonstrating only a mild reduction of functional capacity assessed by peak oxygen intake (VO₂ peak 15.4 mL/kg/min, 68% of predicted value) and slight increase in ventilation to carbon dioxide production (VE/VCO₂; 38.4), with no peripheral desaturation and no signs of ventilatory limitation. The patient started to taper the

Figure 2 Therapeutic management. Day-by-day therapeutic approach during hospitalization. IV, intravenous; PO, per os; SGLT2, sodium-glucose transport protein 2; Sc, subcutaneous.

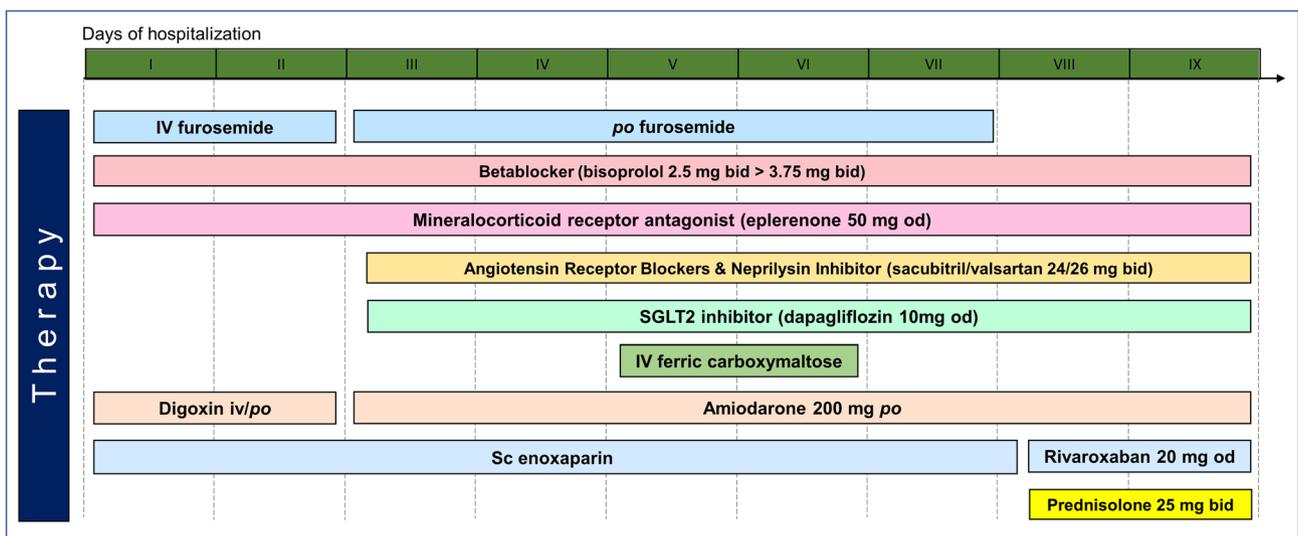
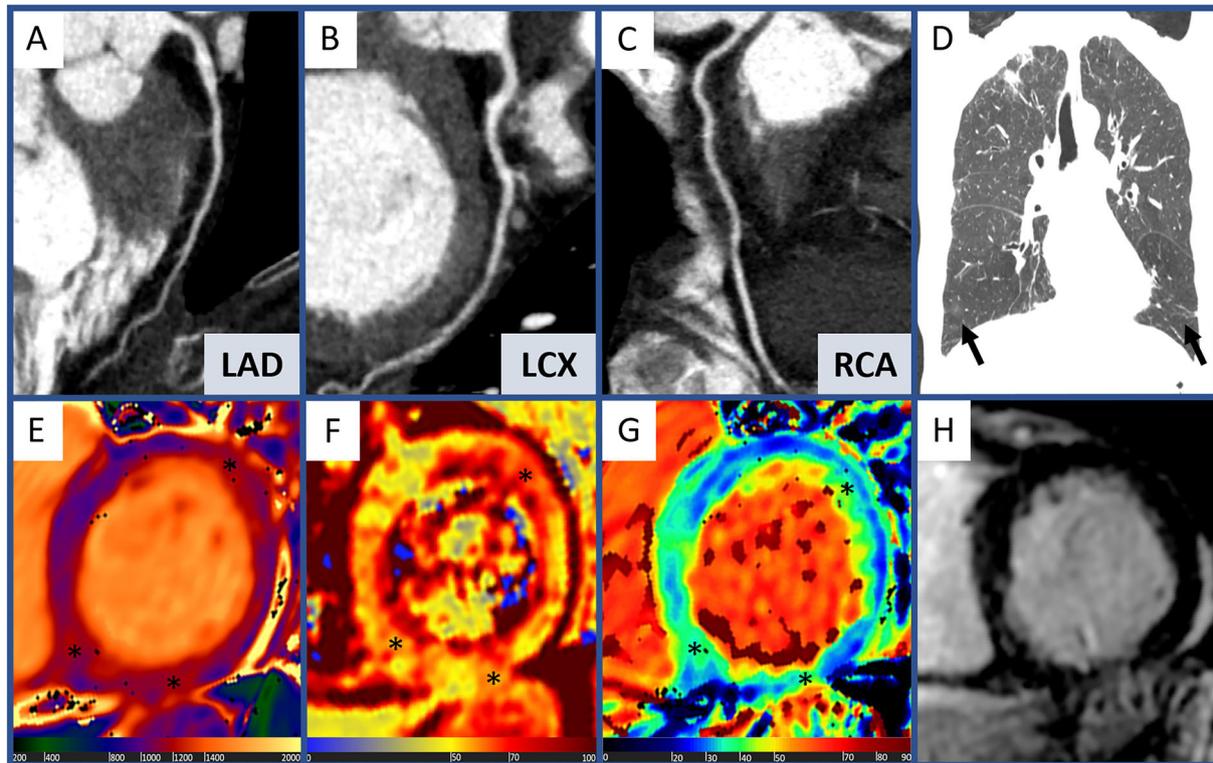


Figure 3 Cardiovascular imaging findings. (A–C) CCTA showing no coronary stenosis. (D) CT thorax showing nodular consolidation in the apical segment of the right upper lobe (asterisk) and ground-glass opacities in the lower lobes (arrows). Interlobular septal thickening and bilateral pleural effusion were also present. (E–H) CMR images showing increased native T1 (E; mean normal T1 value: 975 msec, abnormal T1 values, marked by asterisks, ranged between 1146 and 1230 msec), T2 (F; mean normal T2 value: 44 msec; abnormal T2 values, marked by asterisks, ranged between 58 and 78 msec) and ECV (G; mean normal ECV value: 26%; abnormal ECV values, marked by asterisks, ranged between 34% and 43%) at the level of interventricular septum, anterior wall and inferolateral lateral wall (asterisks). No overt late gadolinium enhancement was noted (H). CCTA, computed tomography coronary angiography; CMR, cardiac magnetic resonance; ECV, extracellular volume; LAD, left anterior descending artery; LCX, left circumflex; RCA, right coronary artery.



steroid therapy under careful supervision of the pneumologist who took charge of the EPGA follow-up after hospital discharge. At 6-month follow-up (April 2022), the patient is asymptomatic, and eosinophil values persistently remain in the normal range even with minimal dose prednisolone (5 mg o.d.). In addition, a follow-up CMR showed normalization of LV systolic function and resolution of cardiac tissue changes present at onset (Figure 5).

The patient signed a consent form for her data to be anonymously presented.

Discussion

Cardiac involvement is not rare in EGPA (50% of autopsied EPGA patients), and it seems more frequent in ANCA (–) patients.⁸ It is well known that persistent eosinophilia can

cause cardiac tissue damage, typically in the form of EM.² After having excluded an acute coronary syndrome, EM was the most probable cause of biventricular dysfunction in our patient. CMR was useful to identify myocardial inflammation and non-ischaemic myocardial injury, establishing the diagnosis of myocarditis according to 2018 Lake Louise criteria, and to guide EMB.^{9,10} The EMB, the gold standard for the diagnosis, demonstrated eosinophilic infiltrates associated with focal necrosis of cardiomyocytes and signs of initial replacement with fibroblasts. Despite the lack of standardized medical treatment for various types of myocarditis, immunosuppressive therapy is the mainstay EM therapy.¹¹ Asthma, a feature present in our patient, is a cardinal clinical feature of EGPA, being reported in more than 90% of patients.¹² Pulmonary findings are present in 50–70% including pulmonary opacities with eosinophilia, pleural effusion, and nodules that are rarely cavitory.¹³ Ear, nose, and throat involvement, including re-

Figure 4 Electro-anatomic mapping and endomyocardial biopsy. (A,B) Electro-anatomical voltage mapping of the left ventricle. The bipolar mapping is mainly normal (purple, A); low-voltage area (red) is noted in the inferolateral basal wall (unipolar mapping, B); the empty dots (white asterisks) show the sites of bioptic samples at the inferolateral wall (target area for CMR). (C) Haematoxylin and eosin staining of bioptic fragment shows infiltrates of phlogistic cells with a pronounced eosinophilic component (white arrows), associated with focal cardiomyocyte necrosis and fibrosis. CMR, cardiac magnetic resonance.

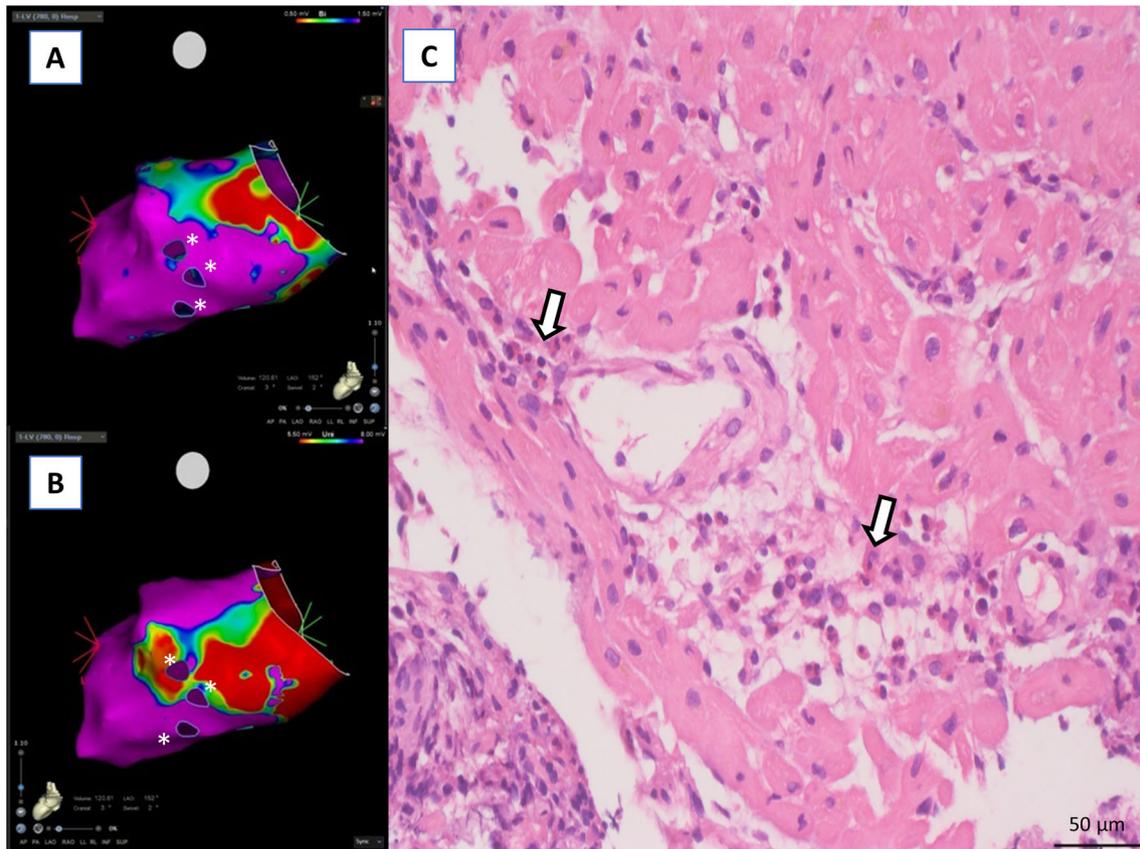
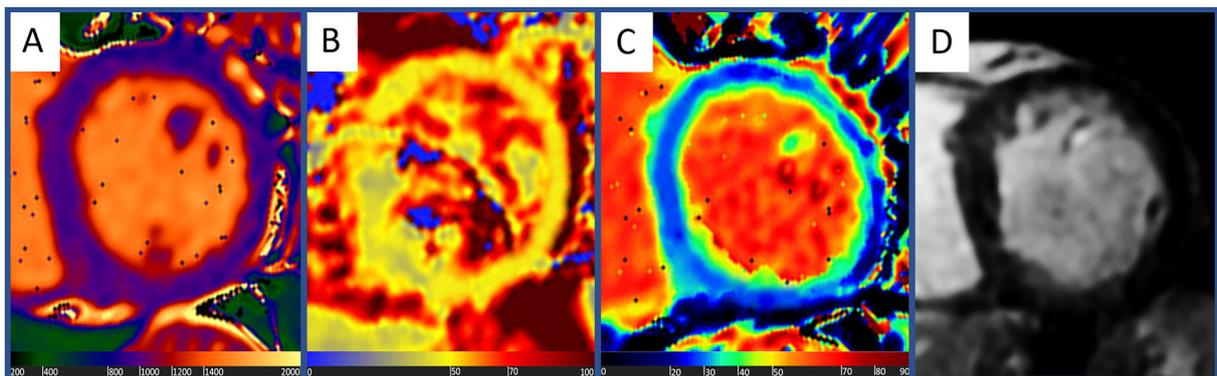


Figure 5 Follow-up CMR findings. (A–D) Compared with the tissue abnormalities described in first CMR scan (Figure 3), at follow-up CMR, exam normalization of T1 values (A; mean normal T1 value: 963 msec), T2 values (B; mean normal T2 value: 43 msec) and ECV values (C; mean normal ECV value: 24%) was noted. Absence of overt late gadolinium enhancement was also confirmed (D). CMR, cardiac magnetic resonance; ECV, extracellular volume.



current sinusitis, is reported in 70–85% patients with EGPA.¹² Peripheral blood eosinophilia is the most characteristic finding, and an absolute eosinophil count ≥ 1500 cells/microL (or greater than 10% of the total leucocyte count) should raise suspicion for EGPA.¹³ All these clinical features were present in our patient. A number of different sets of criteria for the diagnosis of EGPA have been proposed, but the most commonly used classification is the one from American College of Rheumatology.¹⁴ According to these criteria, a diagnosis of EGPA was made in our patient. We observed a favourable evolution of cardiac dysfunction in our patient probably due to a combination of HF treatment and immunosuppressive therapy. Thrombotic complications (i.e. LV thrombosis) are not a rare complication in EM,² as described by Zampieri *et al.* showing a prevalence of three out of 52 patients.¹⁵ Thus, an anticoagulation therapy was maintained. Monitoring responsiveness to treatment and the development of recurrence is best achieved by following symptoms, eosinophil count, and any previously abnormal laboratory parameters.¹⁶ We believe that the laboratory findings observed 2 weeks after discharge (eosinophils 0%, hsTnI 26.9 ng/L) suggest an adequate immunosuppressive therapy, and this favourable acute response to treatment can be an indicator of long-term good prognosis.

In conclusion, we described a multimodality evaluation of an EGPA-associated EM, complicated by HF. A prompt recognition of signs and symptoms involving all appropriate diagnostic methods (including EMB) can lead to a favourable short-term and medium-term outcome.

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Timeline

Since adulthood	Asthma
Since at least 2013	Eosinophilia
Seven months before admission (March 2021)	Right mastectomy. Adjuvant radiotherapy for the next 3 months
Two months before admission (August 2021)	Low-grade fever and dyspnoea treated with azithromycin
One month before admission (September 2021)	Asymptomatic AF treated with CVE
Three weeks before admission	Recurrence of AF; 4 failed attempts of CVE
One week before admission	Onset of worsening dyspnoea
Day of presentation (October 2021)	Dyspnoea and orthopnoea
During hospitalization	12 days of hospitalization, discharge in good clinical status
Two weeks after discharge	NYHA I, eosinophilic count 0%, hsTnI 26.9 ng/L

Conflict of interest

None declared.

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