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CASE REPORT
Cardiac imaging

Severe biventricular thrombosis in eosinophilic granulomatosis with polyangiitis: a case report

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Background Eosinophilic granulomatosis with polyangiitis (EGPA), formerly known as Churg–Strauss syndrome, is a rare multisystem disease characterized by asthma, rhinosinusitis, and eosinophilia. Cardiac involvement, present in half the patients, may be life threatening.

Case summary A young woman with long-standing asthma and nasal polyposis was admitted with new-onset dyspnoea, sinus tachycardia, and eosinophilia. She had severe biventricular thrombosis and severe tricuspid regurgitation (TR) on echocardiography, with preserved ejection fraction of both ventricles. Cardiac magnetic resonance (CMR) imaging showed diffuse subendocardial late gadolinium enhancement (LGE). She had a positive test for perinuclear antineutrophil cytoplasmic antibodies (p-ANCA) confirming the diagnosis of ANCA positive EGPA. She was treated with anticoagulation, high-dose corticosteroids, cyclophosphamide, and rituximab with gradual resolution of her symptoms. Follow-up echocardiography showed significant improvement in ventricular thrombi and TR but could not reliably exclude residual ventricular thrombus. Repeat CMR at 11 months confirmed complete resolution of both ventricular thrombi and near complete resolution of LGE.

Discussion Cardiac involvement in EGPA, a rare cause of heart failure, can manifest as severe biventricular thrombosis and severe TR, resulting in heart failure with preserved ejection fraction. Combined immunosuppression and anticoagulation can lead to complete remission within a year. CMR is instrumental for both diagnosis and follow-up of EGPA, allowing for safe discontinuation of oral anticoagulation.

Keywords Eosinophilic granulomatosis with polyangiitis • Echocardiography • Cardiac magnetic resonance imaging • Heart failure • Cardiac thrombosis • Case report

Learning points

- Cardiac involvement in eosinophilic granulomatosis with polyangiitis can present with severe biventricular thrombosis and heart failure with preserved ejection fraction.
- Cardiac magnetic resonance is instrumental for both diagnosis and long-term management.
- Contemporary medical therapy, including corticosteroids, cyclophosphamide, and rituximab can induce complete remission.

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Introduction

Eosinophilic granulomatosis with polyangiitis (EGPA), first described in 1951 by J. Churg and L. Strauss, is a rare multisystem disorder characterized by asthma, rhinosinusitis, and prominent peripheral blood eosinophilia.[1] It is classified as an antineutrophil cytoplasmic antibodies (ANCA) associated vasculitis of small sized arteries, although vasculitis is seldom apparent early in the disease course and ANCA is not always positive.[2] The most commonly involved organs are lung and skin but any organ system may be affected. Cardiovascular involvement is described in about 50% of patients and had been associated with poor prognosis, accounting for 50% of deaths in EGPA.[3,4]

We describe the imaging workup and outcome in a rare case of a young woman with cardiac involvement in EGPA, manifesting as heart failure with preserved ejection fraction (HFpEF) and severe biventricular thrombosis. This case highlights the utility of multimodality imaging, and in particular cardiac magnetic resonance (CMR) imaging, for the diagnosis and long-term management of these patients.

Timeline

Time	Events
One week prior to admission	Progressive dyspnoea
Hospital admission	Heart failure with preserved ejection fraction and biventricular thrombosis on echo. hypereosinophilia. Anticoagulation started
Day 2	Eosinophilic granulomatosis with polyangiitis (EGPA) suspected. Corticosteroids initiated
Day 4	Cardiac magnetic resonance (CMR) confirms EGPA. Antineutrophil cytoplasmic antibodies test was positive. Cyclophosphamide started
Month 3	Steroids and cyclophosphamide substituted with rituximab
Month 4	Reduced thrombi size and tricuspid regurgitation (TR) on echo
Month 9	No thrombi seen on echo
Month 11	No thrombi or late gadolinium enhancement on CMR. Warfarin stopped
Month 20	Patient doing well, moderate residual TR and no thrombi

Case presentation

A 23-year-old woman with long-standing asthma and nasal polyposis was referred to the emergency department for progressive shortness of breath during daily activities in the week prior to her admission. Physical examination was unremarkable, except for sinus tachycardia 110/min. Electrocardiogram showed T-wave inversion in precordial leads. Chest X-ray was normal. Troponin T was mildly elevated at 15 ng/L (normal <13). She had marked eosinophilia in her peripheral blood count (1570/mm^3, normal < 500/mm^3). Pulmonary computed tomography angiography ruled out pulmonary embolism. Transthoracic echocardiography, in search of cardiac disease as the source of her symptoms, showed large biventricular apical thrombi, occupying half of the left ventricle and most of the right ventricle in the four-chamber view with estimated pulmonary systolic pressure of 29 mmHg (*Figure 1A*, Supplementary material online, *Video S1*, short-axis view: *Video S2*). There was good contraction of the basal segments in both ventricles but ventricular contraction appeared to be reduced at the apex. Colour-flow and spectral Doppler revealed severe tricuspid regurgitation (TR) (*Figures 1B and 2*). N-terminal pro-brain natriuretic peptide (NT-proBNP) was 5022 pg/mL (normal < 300 pg/mL), confirming the diagnosis of HFpEF.

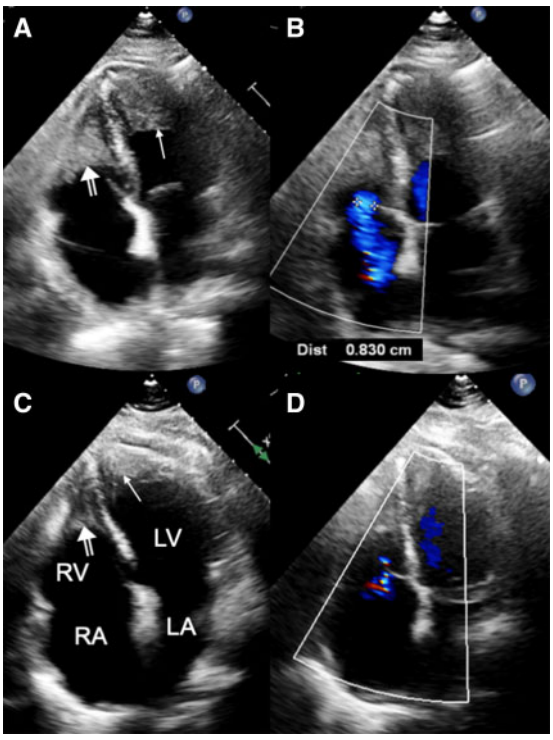

Figure 1 Echocardiography. (*A*) Transthoracic echocardiography using the four-chamber view, showing large left ventricular (arrow) and right ventricular (double-arrow) thrombi. (*B*) Colour-flow Doppler showing severe TR with a vena contracta of 8 mm. (Repeat echo at four months: *C*) Decreased thrombus size in both ventricles and (*D*) decrease in TR. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle; TR, tricuspid regurgitation.

Based on her clinical and echocardiographic findings, in combination with asthma, nasal polyposis and eosinophilia, the diagnosis of EGPA with cardiac involvement was suggested. CMR imaging was performed, confirming the presence of biventricular thrombi and showing diffuse subendocardial late gadolinium enhancement (LGE) in both ventricles (*Figure 3A–C*, Supplementary material online, *Videos S3* and *S4*). There was evidence of subendocardial oedema (suggesting inflammation) on the T2-weighted double inversion recovery short-axis image (*Figure 4*). Although ventricular contraction

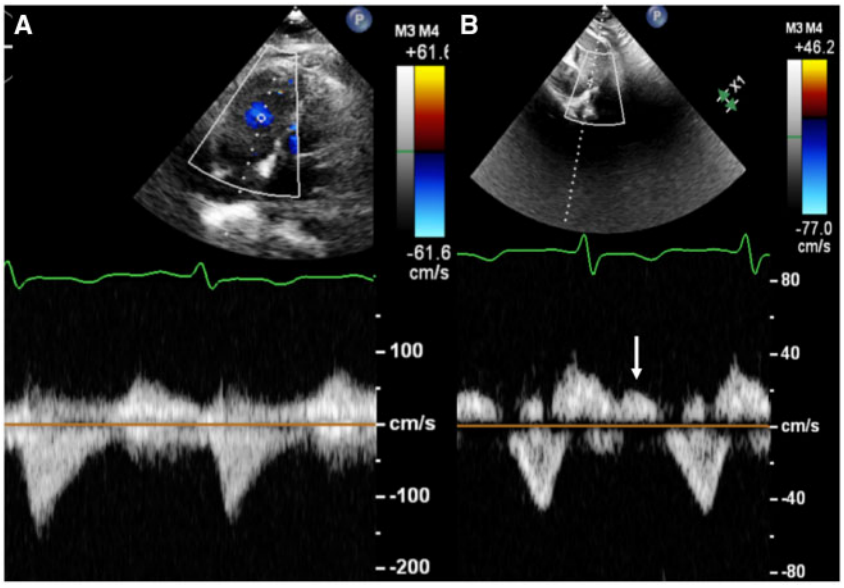

Figure 2 Spectral Doppler of the tricuspid regurgitation. (*A*) Continuous wave Doppler of the TR jet, showing a low velocity triangular shape, typical of severe TR. (*B*) Pulsed wave Doppler of the hepatic veins showing systolic flow reversal (arrow). TR, tricuspid regurgitation.

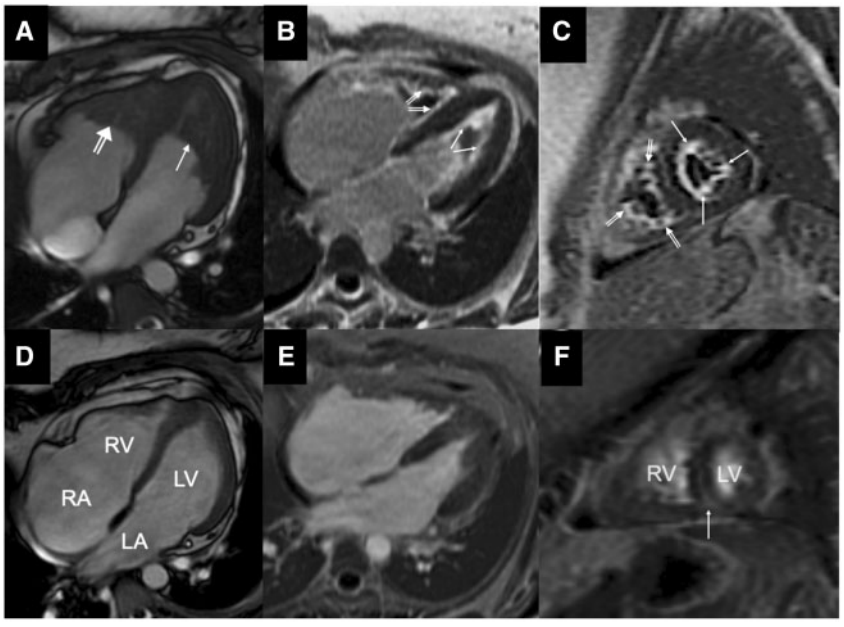

Figure 3 Cardiac magnetic resonance imaging (CMR). (*A*) Cine image using SSFP sequence, four-chamber view, confirming the left (arrow) and right (double-arrow) ventriculi thrombi. In this view the thrombus occupies half of the left ventricle and most of the right ventricle. Four-chamber, (*B*) and short-axis, (*C*) contrast-enhanced images using inversion recovery sequences (normal myocardium is black), showing diffuse subendocardial LGE in left (arrows) and right (double-arrows) ventricles. (Repeat CMR at 11 months: *D*) Cine image showing no residual thrombus in both ventricles. There is moderate right atrial and tricuspid annular dilatation (moderate TR is evident in the corresponding cine loop in Supplementary material online, *Video S5*). (*E* and *F*) No residual thrombus and minimal LGE in contrast CMR using inversion recovery sequences (arrow, showing inferior right ventricular insertion point LGE extending into the mid septum). LA, left atrium; LGE, late gadolinium enhancement; LV, left ventricle; RA, right atrium; RV, right ventricle; SSFP, steady-state free precession; TR, tricuspid regurgitation.

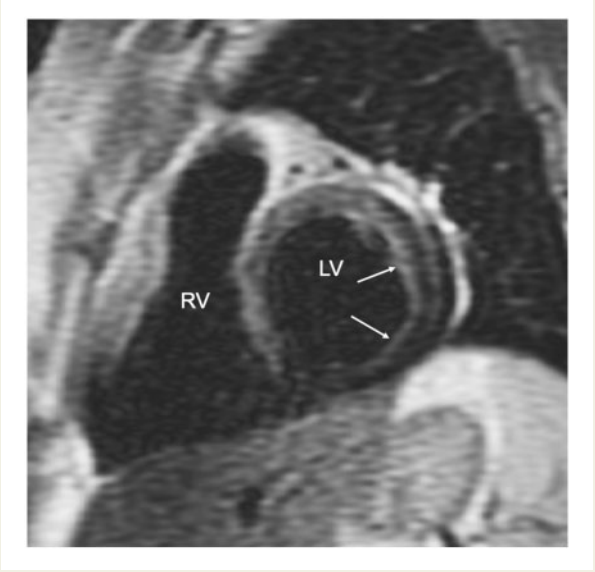

Figure 4 Cardiac magnetic resonance imaging (CMR) T2-weighted sequence. T2 weighted double inversion recovery short-axis image showing subendocardial left ventricular oedema (arrows), mainly in the lateral wall, suggesting acute inflammation. LV, left ventricle; RV, right ventricle.

Table 1 Ventricular volumes and ejection fractions by CMR

	Baseline		Follow-up	
	Left ventricle	Right ventricle	Left ventricle	Right ventricle
EDV (mL)	82	67	82	92
ESV (mL)	41	32	36	44
EF	50%	52%	56%	52%

Volumes were measured by the sum of discs method using short-axis views, including papillary muscles and thrombi. Normal CMR EF range: left ventricle 57–77%, right ventricle 51–71%.
CMR, cardiac magnetic resonance; EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume.

appeared to be reduced at the apex, ejection fraction of both ventricles was generally preserved (*Table 1*). Haematologic workup excluded primary eosinophilia and further laboratory tests were positive for perinuclear ANCA (p-ANCA), supporting the diagnosis of ANCA positive EGPA. Cardiac computed tomography angiography demonstrated normal coronary arteries, excluding major coronary arteries involvement.

The patient was treated with enoxaparin and long-term warfarin, diuretics, high-dose corticosteroids, and cyclophosphamide for 3 months, followed by rituximab, an anti B-cell CD20 chimeric monoclonal antibody. She experienced gradual symptomatic relief with parallel decrease in NT-proBNP. Fortunately, the patient did not suffer any embolic events. A repeat echo at 4 months showed decrease in thrombi size and TR (*Figure 1C and D*) with further decrease in thrombi size at 9 months. Since residual mural thrombi could not be reliably excluded, a second CMR was performed 11 months after her initial presentation, confirming the complete resolution of both left and right ventricular thrombi and showing minimal residual LGE (*Figure 3D–F*, Supplementary material online, *Videos S5–S7*), thus enabling warfarin discontinuation.

Current treatment at 20 months follow-up includes methotrexate as steroid sparing and remission maintenance and rituximab. She has residual moderate TR, tricuspid annular, and right atrial dilatation, and she is maintained on furosemide 20 mg/day.

Discussion

Diagnosis of EGPA based on the American College of Rheumatology criteria requires at least four out of six criteria (asthma, >10% peripheral blood eosinophilia, neuropathy, non-fixed lung opacities, paranasal sinus abnormality and biopsy containing a blood vessel showing extravascular eosinophils).[5] The diagnosis in our patient was based on the presence of asthma, eosinophilia, nasal polyposis, heart involvement (as documented by the CMR findings, showing extensive biventricular subendocardial LGE) and the presence of p-ANCA. Baccouche *et al.*[6] demonstrated the correlation between CMR LGE and endomyocardial biopsy findings of extravascular infiltrating eosinophils and fibrosis. The finding of ANCA, present in 40% of EGPA patients, represent a major argument for the diagnosis of EGPA and is important for the differentiation of EGPA from other hypereosinophilic syndromes with systemic manifestations where ANCA is negative.[7] The type of ANCA detected in our patient—anti-myeloperoxidase or p-ANCA—is typical of EGPA.[8] There is probably no association between ANCA status and cardiac involvement in EGPA, but this issue is controversial.[3,4,9]

Cardiac involvement in EGPA is the result of two main mechanisms: eosinophilic infiltration of the myocardium and vasculitis-related myocardial ischaemia. These can result in myocarditis and heart failure, acute myocardial infarction, intracardiac thrombi, pericarditis, pericardial effusion, and valvular involvement. Our patient presented with HFpEF, manifesting as dyspnoea, tachycardia and elevated NT-ProBNP. The cause of HFpEF in this case was extensive biventricular subendocardial inflammation and massive biventricular mural thrombi, accompanied by severe TR, producing the striking echocardiographic and CMR images. The large mural thrombi occupying both ventricles restricted filling and reduced stroke volume, playing an important role in the mechanism of HFpEF in this case. Valvular dysfunction is not uncommon in EGPA, usually affecting the atrioventricular valves resulting in mild to moderate regurgitation. Our patient presented with severe TR which contributed to her heart failure. The mechanism of TR is not entirely clear. It may have been caused by subvalvular involvement in the disease process, since we did not observe any tricuspid valve leaflet involvement, pulmonary hypertension or right ventricular remodelling. With treatment TR improved but did not completely resolve, probably due to right atrial and tricuspid annular dilatation, necessitating continued low-dose diuretic treatment, in order to decrease right ventricular preload and prevent TR progression.

Several small studies have shown that in patients with EGPA CMR often detects cardiac involvement, even in the absence of clinical or echocardiographic findings.[3,4,10,11] CMR may show impaired left ventricular function or mural thrombi in both ventricles (but usually not as large as in our case). On T2-weighted imaging, myocardial or pericardial oedema as a result of inflammation may be evident. Nodular or band-like LGE pattern, which is usually subendocardial but can be centromyocardial or subepicardial, can reflect either eosinophilic infiltration or fibrosis. In our case, due to the presence of p-ANCA antibodies, treatment with high-dose corticosteroids, cyclophosphamide and rituximab was chosen, resulting in complete elimination of LGE, thus confirming the fact that in this case LGE was the result of active disease and not fibrosis. Echocardiography in our case could not reliably rule out residual endocardial disease or thrombi, and CMR was instrumental, enabling safe discontinuation of anticoagulation.

Saito *et al.*[12] reported a case of a large apical left ventricular thrombus in the setting of ANCA negative EGPA. Hypereosinophilic syndrome can also present with eosinophilia and organ damage, including cardiac involvement similar to ours. Saito *et al.* needed a renal biopsy documenting angionecrosis to rule out hypereosinophilic syndrome. In our case, the presence of long-term asthma and nasal polyposis, together with a positive ANCA, pointed to the diagnosis of EGPA and not hypereosinophilic syndrome.

Conclusion

In this young patient presenting to the emergency department with dyspnoea, long-standing asthma, nasal polyposis, and eosinophilia, the striking echocardiographic images showing large biventricular thrombi and severe TR led to the diagnosis of HFpEF as a result of EGPA with severe cardiac involvement. CMR had a key role in both diagnosis and long-term management of heart involvement in EGPA, demonstrating a favourable response to the combined anti-inflammatory therapy.

Lead author biography

Dr Jihad Hamudi, MD, graduated from the Hebrew University—Hadassah Medical School in Jerusalem, Israel. He was a resident in internal medicine and he is finishing his fellowship in cardiology in Lady Davis Carmel Medical Centre in Haifa, Israel. He is now planning his fellowship in invasive cardiology.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

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Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

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