ESC European Society of Cardiology

European Heart Journal - Case Reports (2024) **8**, ytae569
https://doi.org/10.1093/ehjcr/ytae569

CASE REPORT
Medical management of arrhythmias

Eosinophilic granulomatosis with polyangiitis associated with malignant arrhythmias: a case report

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Received 7 March 2024; revised 2 July 2024; accepted 14 October 2024; online publish-ahead-of-print 22 October 2024

Background Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare vasculitis associated with significant cardiac morbidity and mortality. This case report presents the diagnostic and management challenges of EGPA-related arrhythmias in a remote general hospital setting.

Case summary A 64-year-old Caucasian male presented with an indolent prodrome of fatigue, shortness of breath and anorexia, that culminated in an acute presentation with pulmonary embolism. His complicated clinical course included intracranial haemorrhage and refractory ventricular arrhythmias. Eosinophilia and sub-endocardial hypoattenuation observed on chest computed tomography were key findings that led to the diagnosis of EGPA. Multiple anti-arrhythmic therapies were required as temporary measures whilst control of the underlying eosinophilic inflammation was achieved.

Once stable, the patient was transferred to a tertiary cardiac centre for further investigation and cardioverter-defibrillator implantation. With EGPA now well controlled, he has experienced no further ventricular arrhythmias and has fully recovered.

Conclusion Cardiac complications of EGPA, including ventricular arrhythmias, are difficult to manage without concurrent immunosuppression, which may itself further destabilize cardiac electrophysiology. The role of multiple imaging modalities in the diagnosis and monitoring of EGPA is emphasized, with cardiac magnetic resonance imaging playing a crucial role in detecting sub-endocardial fibrosis.

Keywords Eosinophilic granulomatosis with polyangiitis • Hypereosinophilia • Ventricular tachycardia • Implantable cardioverter defibrillator • Cardiac magnetic resonance imaging • Case Report

ESC curriculum 5.6 Ventricular arrhythmia • 2.3 Cardiac magnetic resonance

Learning points

- Cardiac manifestations of eosinophilic granulomatosis with polyangiitis (EGPA) include life threatening arrhythmias such as ventricular tachycardia and torsades des pointes
- Whilst cardiac involvement is more common in anti-neutrophil cytoplasmic antibody (ANCA)-negative cases, cardiac manifestations may still be present in ANCA-positive cases of EGPA
- Cardiovascular magnetic resonance imaging is invaluable in demonstrating cardiovascular involvement and can show thrombi, endomyocardial fibrosis, active inflammation, and decreased myocardial perfusion

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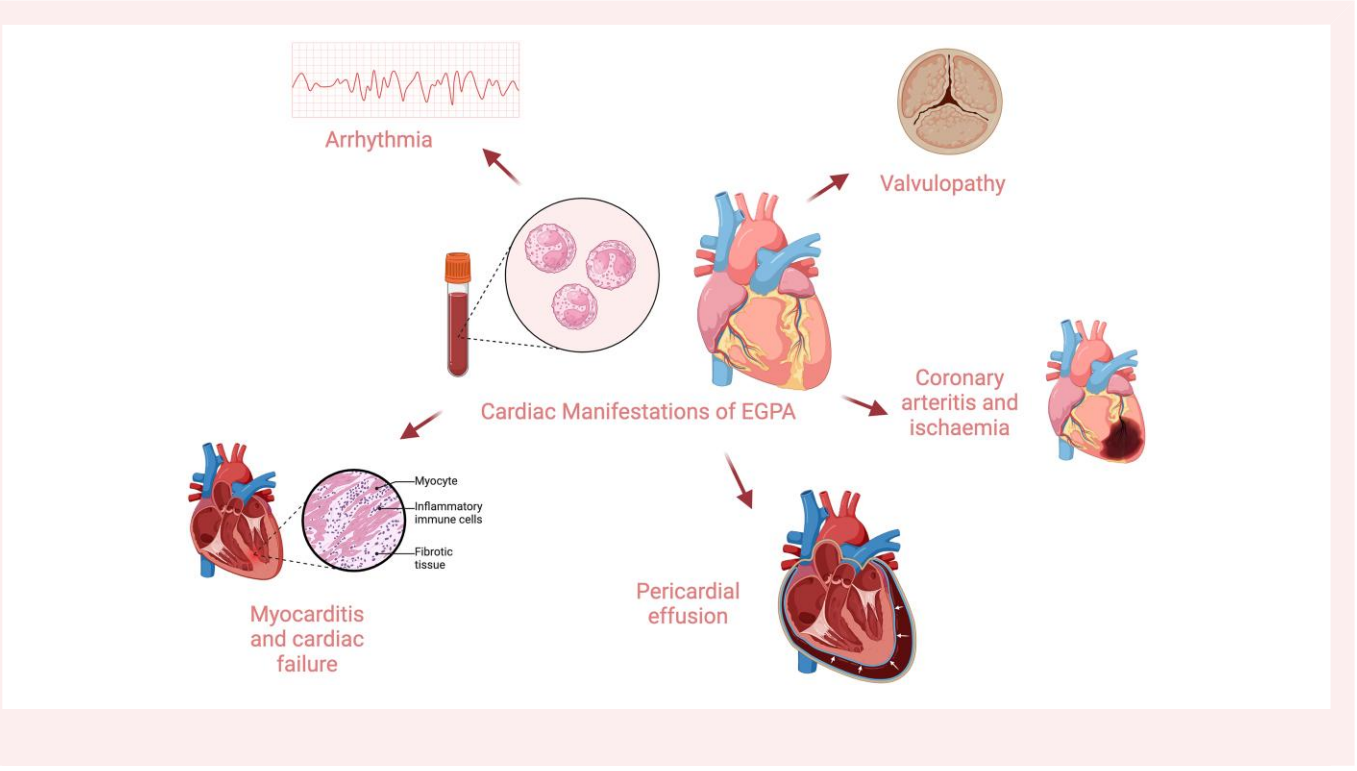
Handling Editor: Giulia Ferrannini
Peer-reviewers: Carlos Minguito Carazo; Alessandro Villaschi
Compliance Editor: Niklas Schenker

Introduction

Eosinophilic granulomatosis with polyangiitis (EGPA, previously known as Churg-Strauss syndrome) is a rare anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis typically characterized by eosinophilia, rhinosinusitis and asthma. Cardiovascular involvement however has been documented in up to 50% of EGPA cases and carries a significant morbidity and mortality.[1,2] This has included myopericarditis, heart failure, coronary vasculitis causing ischaemia and valvular involvement (*Summary Figure*).

Here, we present a complex case of newly diagnosed EGPA complicated by multiple ventricular arrhythmias resulting in cardiac arrest. We highlight some of the challenges in managing ventricular arrhythmias in these patients, underscoring the importance of monitoring the QTc interval in patients with inflammatory conditions who have received QTc prolonging drugs. We also discuss the importance of multimodality imaging in confirming cardiovascular involvement and how this can be achieved despite presentation to a remote general hospital.

Summary figure



Case presentation

A 64-year-old Caucasian male presented to his primary care physician with symptoms of fatigue, breathlessness, and malaise. He had been using a steroid inhaler for a year but had not received a formal diagnosis. Additionally, he reported anorexia, difficulty walking, urinary incontinence, and cognitive fogging, including worsening memory.

Upon examination, the patient exhibited tachycardia and tachypnoea, with widespread wheeze upon chest auscultation and bipedal oedema. He was referred to the emergency department where initial laboratory results showed a normocytic anaemia (Hb 12.0 g/dl; 13.0–17.0 g/dl), elevated eosinophils (1.04×10^9/l; 0.01–0.5×10^9/l) and a raised C-reactive protein (86 mg/l; < 10 mg/l). Elevations in D-dimer (2729 ng/ml; < 250 ng/ml), troponin I (28.3 ng/l; < 11.0 ng/l), and NTproBNP (15 200 pg/ml; < 400 pg/ml) were also present.

The patient was admitted with suspicion of a pulmonary embolism (PE). Admission electrocardiogram (ECG) revealed sinus rhythm with deep T-wave inversion in the lateral leads (*Figure 1A*). Bilateral PEs were confirmed by computed tomography pulmonary angiography (CTPA) (*Figure 1B*). Echocardiography demonstrated right heart strain with elevated pulmonary pressures, alongside apical and posterolateral left ventricular (LV) hypertrophy with preserved LV systolic function (LVEF 62%).

Despite initiation of anti-coagulation and antibiotics for a lower respiratory tract infection, the patient's condition deteriorated rapidly, requiring emergency intubation and ventilation for acute respiratory distress syndrome. New neurological signs led to concerns for intracranial bleeding, with a subtle sub-arachnoid haemorrhage over the right motor cortex identified on non-contrast CT imaging. A chest x-ray (CXR) showed diffuse bilateral infiltrates (*Figure 2A*). Repeat echocardiography showed moderate to severe left ventricular hypertrophy, preferentially affecting the apex, creating a 'punched-out' appearance with preservation of systolic function (*Figure 2B*). A review of chest CT imaging revealed marked sub-endocardial hypoattenuation (*Figure 2C*), with the notable absence of any evidence of coronary artery calcification.

The patient developed atrial fibrillation with rapid ventricular response. A rhythm control strategy was enacted with amiodarone therapy given the evidence of structural heart disease. This resulted in restoration of sinus rhythm but at the cost of marginal prolongation of his QTc. Amiodarone was therefore discontinued in favour of beta blockade.

Multiple concurrent pathologies prompted a search for a unifying diagnosis. Sera were analysed for thrombophilia and vasculitis screening

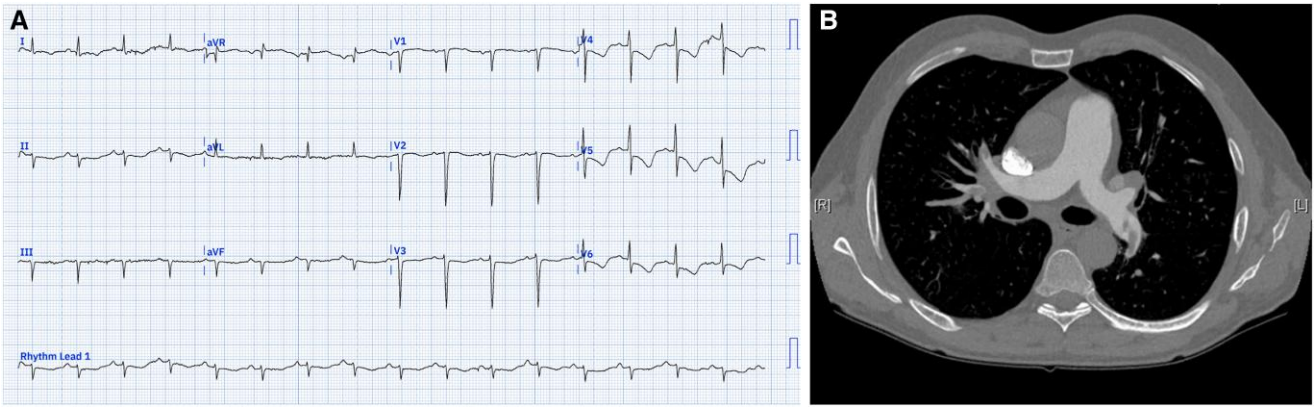


Figure 1 (*A*) 12 Lead electrocardiogram (ECG) on presentation showing borderline sinus tachycardia with left axis deviation and lateral t wave inversion. Heart rate 98 bpm, QTc 482 ms, 40 Hz, 25.0 mm/s, 10.0 mm/mV. ECG digitalized using PMCardio. (*B*) Computed tomography pulmonary angiogram (CTPA) showing bilateral filling defects in keeping with bilateral PEs.

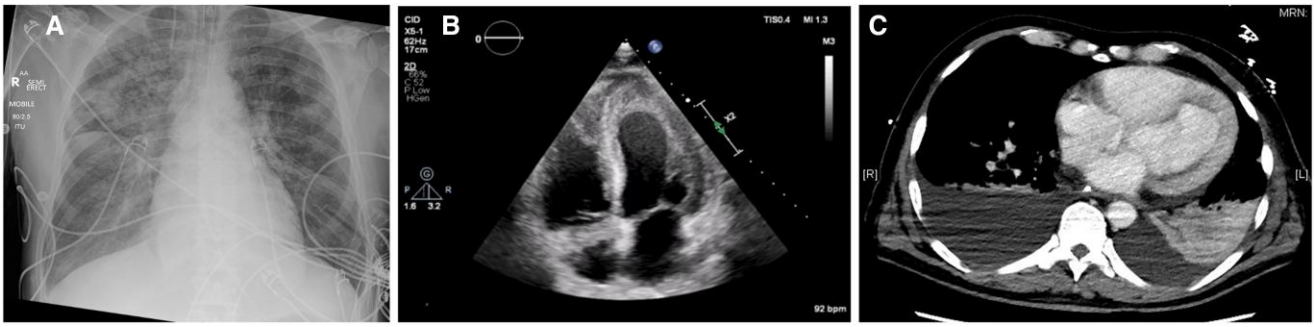


Figure 2 (*A*) Chest x-ray (CXR) at time of acute respiratory failure demonstrating bilateral diffuse hazy infiltrates. (*B*) Apical four chamber echocardiogram demonstrated apical left ventricular hypertrophy in a 'punched-out' appearance. (*C*) CT chest imaging showing bilateral pleural effusions and sub-endocardial hypoattenuation.

panels. Given the history of presumptive asthma, peripheral eosinophilia with no travel history or risk factors for parasitic infection and sub-endocardial hypoattenuation of CT, a presumptive diagnosis of EGPA was made. Further review of CT imaging showed ground glass opacities and interlobular septal thickening and ANCA testing was positive for perinuclear ANCA (p-ANCAs) further supporting the diagnosis. Immunosuppressive treatment was initiated with high-dose methylprednisolone (1000 mg intravenous for 3 days) and cyclophosphamide (2 mg/kg/day oral), with prophylactic use of acyclovir and co-trimoxazole.

The patient developed repeated episodes of self-terminating monomorphic ventricular tachycardia (VT). This was initially managed with IV beta blocker infusion. He then developed polymorphic VT with torsades des pointes morphology which deteriorated into ventricular fibrillation (*Figure 3A* and *B*). Cardiopulmonary resuscitation, electrical cardioversion and magnesium infusion were successful in restoring sinus rhythm. However, over the subsequent days the patient suffered from further intra-hospital cardiac arrest (IHCA) episodes, requiring the addition of a lidocaine infusion before transitioning onto oral therapy with mexiletine and verapamil therapy.

Once stabilized, plans were put in place for transfer off island to a tertiary centre for cardiac magnetic resonance (CMR) imaging. This was delayed for 3 weeks due to development of Enterococcus sepsis and Covid-19 infection with the patient being deemed too unwell for transfer. CMR imaging showed a small apical thrombus in the left ventricle (*Figure 3C*). It also showed features typical of eosinophilic endomyocardial fibrosis with a widespread rim of sub-endocardial late gadolinium enhancement (LGE) (*Figure 3D*). A CT coronary angiogram showed normal coronary arteries. Although the long-term risk of VT recurrence is not well characterized, the patient received a sub-cutaneous implantable cardioverter defibrillator. A sub-cutaneous system was chosen over a transvenous system due to the lower risk of infection in a patient on systemic immunosuppression, and the potential complications of lead placement in an eosinophilic myocardium.

In the year since his initial presentation, the patient has made a remarkable recovery, returning to work and training for a cross-country cycle. Repeat echocardiography showed resolution of left ventricular hypertrophy. He is maintained on Azathioprine as a steroid sparing agent.

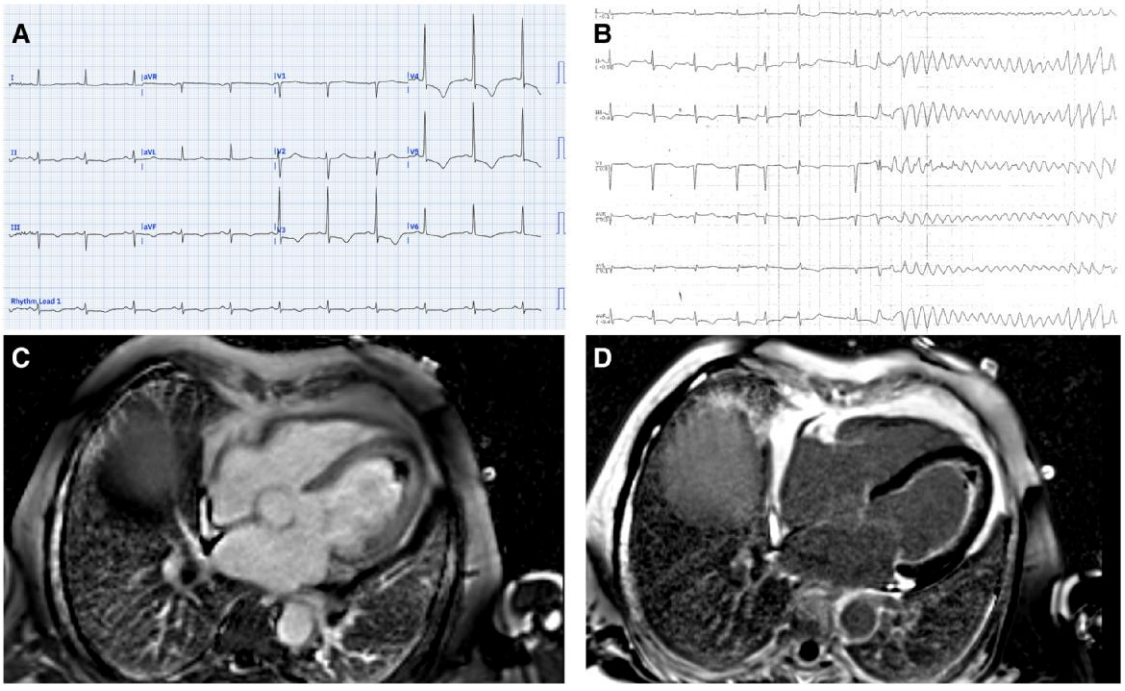


Figure 3 (*A*) 12 lead ECG showing QTc prolongation of 582 ms and widespread t wave inversion. Heart rate 64 bpm, 40 Hz, 25.0 mm/s, 10.0 mm/mV. ECG digitalized using PMCardio. (*B*) ECG monitor showing transition from sinus rhythm with prolonged QT interval into torsades des pointes. (*C*) Cardiac magnetic resonance (CMR) imaging horizontal long axis image showing early gadolinium enhancement. (*D*) CMR imaging horizontal long axis image showing sub-endocardial late gadolinium enhancement.

Discussion

EGPA is rare condition, with a prevalence of ~10–13 cases per million, and often goes unrecognized by physicians.[2] Estimates of cardiac involvement vary between 15% and 50%,[1,3] cardiac involvement being the leading cause of death in EGPA-patients.[2] Cardiac involvement is more likely in ANCA-negative cases[4]; however, here we present a case with a p-ANCA positive patient with cardiac involvement.

Ventricular arrhythmias in EGPA

Ventricular arrhythmias in patients with EGPA are uncommon, with prevalence reported in small studies ranging from 0–4%.[1,5] There are isolated case reports of ventricular arrhythmias attributed to EGPA: Budanova *et al.*, described a 66-year old female presenting with palpitations, which were found to be recurrent non-sustained monomorphic VT.[6] The introduction of cyclophosphamide therapy suppressed ventricular arrhythmia, with a reduction from over 12 000 beats of ventricular complexes to one ventricular ectopic per day. Lopes *et al.*, present a case of a 47-year-old female with fulminant eosinophilic myocarditis secondary to EGPA. She suffered an out-of-hospital cardiac arrest with recurrent VT requiring extracorporeal membrane oxygenation as a bridge to ablation therapy.[7]

This case underscores the critical interplay between QTc prolongation and the heightened risk of arrhythmias in patients with EGPA. There is growing evidence that chronic inflammatory conditions are associated with QTc prolongation, and that systemic inflammatory activation correlates with QTc duration.[8] This prolongation may have been exacerbated by amiodarone therapy which is well recognized to increase the QTc. Evidence regarding cyclophosphamide's impact on the QT interval is limited, however, a small study reported a 20 ms prolongation in patients with non-Hodgkin lymphoma following high-dose treatment.[9] Intravenous methylprednisolone has also been shown to increase the both the QTc interval[10] and QTc dispersion,[11] an independent predictor of cardiac death.[12]

Cardiac magnetic resonance imaging

CMR remains the gold-standard cardiac imaging modality, and is recommended as the most sensitive investigation for cardiac hypereosinophilic syndromes.[13] LGE alongside parametric mapping offers a comprehensive evaluation of active myocardial inflammation and/or fibrosis, whilst perfusion imaging may detect deficits secondary to coronary arteritis. In this case, LGE confirmed sub-endocardial fibrosis, whilst early gadolinium enhancement revealed an unexpected LV thrombus. Intracardiac thrombus is not a well-recognized complication of EGPA, but hypercoagulability from systemic inflammation and endomyocardial damage due to eosinophilic infiltration likely increase the risk. Despite a lack of local CMR infrastructure at our island-based remote general hospital, strong links with a UK based tertiary centre allowed our patient to receive optimal cardiac imaging and confirmation of this rare diagnosis.

Conclusion

EGPA has a myriad of clinical manifestations with cardiovascular involvement described to include myocarditis, heart failure, coronary vasculitis and valvulopathies. Here, we report a case of EGPA leading to ventricular arrhythmias, where treatment of the disease and its sequalae lead to further problems, namely QT prolongation and Torsades des Pointes. Multi-modality imaging proved useful in confirming cardiac

manifestations of the disease. Aggressive immunosuppressant therapy lead to significant clinical improvement and resolution of the arrythmias and left ventricular hypertrophy.

Lead author biography

Dr Christopher Brown is an acute medic with interests in cardiology and digital health. Alongside clinical practice, he is a researcher at The Allan Lab, collaborating with the Jersey Heart Team to bridge the gap between research and patient care.

Consent: The authors confirm that written informed consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: None declared.

Funding: None.

Data availability

No new data were generated or analysed in support of this research.

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