Cardiac Involvement in Eosinophilic Granulomatosis with Polyangiitis (Churg-Strauss Disease)

The Role of Cardiovascular Magnetic Resonance (CMR)

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Abstract

Eosinophilic granulomatosis with polyangiitis (EGPA), previously known as Churg-Strauss disease, is a rare vasculitis that affects small- to medium-sized vessels and has a propensity to involve the heart. Patients with cardiac involvement have a poor prognosis and usually require immunosuppressive treatment along with corticosteroids. Cardiovascular magnetic resonance (CMR) is a noninvasive diagnostic tool that can detect cardiac involvement and guide the management plan. Herein, we present the case of a 39-year-old man with a known history of bronchial asthma who was referred to the chest clinic at the Royal Hospital for further assessment of persistent lung parenchymal changes on chest computed tomography. Given the clinical context of the patient and the radiological findings, EGPA was suspected. Lung biopsy confirmed the diagnosis of EGPA. CMR was performed for further assessment, which confirmed cardiac involvement. The patient was started on prednisolone and azathioprine and showed significant radiological and clinical improvement.

Keywords: Eosinophilic Granulomatosis with Polyangiitis, Vasculitis, Eosinophils, Vascular Diseases, ANCA-associated Vasculiti
Introduction

Eosinophilic granulomatosis with polyangiitis (EGPA), historically known as Churg-Strauss disease, is an uncommon necrotising vasculitis of small- to medium-sized vessels\textsuperscript{1,2} that can involve multiple organs, including the paranasal sinuses, lungs, heart, nervous system, kidneys and gastrointestinal tract.\textsuperscript{3} Cardiac involvement in EGPA is seen in approximately 45–62% of patients and can present as eosinophilic myocarditis, coronary vasculitis, congestive heart failure, pericarditis or valvular disease.\textsuperscript{4} Cardiovascular magnetic resonance (SCMR) is a noninvasive diagnostic tool that can be used to detect cardiac involvement in EGPA. Typically, myocardial involvement in EGPA manifests as subendocardial and midmyocardial late gadolinium enhancement (LGE).\textsuperscript{4} Herein, we present the case of a 39-year-old man with a histologically confirmed diagnosis of EGPA who showed characteristic findings on chest high-resolution computed tomography (HRCT) and CMR. We also discuss the role of cardiac MRI in the assessment of cardiac involvement in patients with EGPA. To the best of our knowledge, this is the first case of EGPA with cardiac involvement detected by MRI to be reported in Oman.

Case report

A 39-year-old man with a known history of bronchial asthma since 24 years of age and a nasal polypectomy several years earlier presented to a local hospital with a history of fever and cough lasting 2 months. On chest auscultation, bilateral scattered rhonchi were detected. Other systemic examinations were unremarkable. His chest x-ray showed bilateral upper lung airspace opacification suggestive of an acute infective process (Figure 1). Complete blood count (CBC) showed eosinophilia, with a value of 4.7 10\textsuperscript{*9}/L (normal range 0.1–0.5 10\textsuperscript{*9}/L). Sputum examination was negative for acid-fast bacilli (AFB) and there was no growth in the sputum culture. Further assessment with a chest computed tomography (CT) scan revealed bilateral upper lobe airspace opacities associated with nodular interlobular septal thickening, predominantly with peripheral subpleural distribution. The patient was treated with amoxiclav 1200 mg TID for 7 days, but his symptoms did not improve. A repeat chest CT showed stable lung findings (Figure 2A). Therefore, the patient was referred to our hospital, The Royal Hospital, Muscat, Oman, for further management. When the patient was seen in our hospital, he was still complaining of cough but did not have a fever. His vital signs were stable (temperature of 35.5\degree C, heart rate of 84 bpm, respiratory rate of 20 breaths per minute and blood pressure of 125/68 mmHg). His complete blood count revealed normal
haemoglobin (12.9 g/dl, reference range 11.5–15.5 g/dl) and white cell count (6.5 10^9/L, reference range 2.2–10.5 *9/L); however, the eosinophilic count was high (2.1 10^9/L, reference range 0.1–0.5 *9/L). Other blood investigations were as follows: urea was 4.8 mmol/L (reference range 2.5–6.7 mmol/L), eGFR was >90 mL/min/1.73 m^2 (reference range >90 mL/min/1.73 m^2), serum reactive protein (CRP) was 78 mg/L (normal value <5 mg/L), immunoglobulin E (IgE) was 122 iU/mL (reference range 0–100 iU/mL), P- and C-antineutrophil cytoplasmic antibodies (ANCA) were not reactive, and the protein creatine ratio in urine was 5.2 mg/mmol/L (normal value <20 mg/mmol/L). A repeated chest CT scan at our hospital, performed 2 months after the initial CT scan, showed improvement in the previously observed airspace opacities; however, new airspace opacities had developed (Figure 2B). Given the patient’s clinical history of asthma, together with the blood eosinophilia and migratory chest CT findings, EGPA was suspected and a lung biopsy was performed. The tissue biopsy examination (Figure 3) confirmed the diagnosis of EGPA. The patient has been worked up to assess potential cardiac involvement. His electrocardiogram and echocardiogram were unremarkable. His CMR showed normal biventricular function and volume, a left ventricle ejection fraction (LVEF) of 66% and right ventricle ejection fraction (RVEF) of 64%. However, patchy areas of midmyocardium LGE (Figure 4) were detected, which confirmed cardiac involvement in EGPA. As part of the workup for EGPA, the patient was tested for anti-neutrophil cytoplasmic antibodies (ANCA) and he was negative. The patient was started on prednisolone (5 mg once daily) and azathioprine (150 mg once daily) for 9 months. The patient has been on regular follow-up every 3 months. On follow-up, the patient’s symptoms had improved significantly, with normalisation of inflammatory markers and a decrease in C-reactive protein from 78 mg/L (normal value <5 mg/L) to 1 mg/L. His eosinophilic count was reduced to 0 10^9/L (reference range 0.1–0.5 10^9/L) from 2.1 10^9/L. A repeat chest x-ray performed 1 month after starting treatment showed complete resolution of the lung abnormalities. Consent to publish the present clinical details and clinical images was obtained from the patient.

Discussion
Eosinophilic granulomatosis with polyangiitis is a rare, systemic disease that was first described by Churg and Strauss in 1951. It has an annual incidence of approximately 0.9 to 2.4 per million individuals, with no difference in distribution between males and females. The median age of onset is usually between 49 and 59 years. Approximately 40–60% of patients
with EGPA are ANCA-positive; therefore, EGPA is classified as ANCA-associated vasculitis.\textsuperscript{3}

The diagnosis of EGPA is widely based on the presence of four out of six criteria proposed by the American College of Rheumatology (ACR) in 1990: (1) peripheral eosinophilia (10% on differential leukocyte count), (2) paranasal sinus abnormality, (3) asthma, (4) migrating pulmonary opacities, (5) mononeuritis multiplex or polyneuropathy, and (6) biopsy evidence of extravascular eosinophils.\textsuperscript{2, 5, 6} Our patient had five of these criteria: asthma, peripheral eosinophilia, nasal polyps, migratory pulmonary opacities, and lung biopsy showing eosinophilic infiltration.

There are three distinct phases of EGPA: (1) prodromal period, consisting of asthma and rhinitis and may last for several years; (2) eosinophilic phase; and (3) vasculitis phase.\textsuperscript{7}

Cardiac involvement in EGPA varies widely in the literature, ranging from 16% to 92%, and it has been associated with increased morbidity and mortality.\textsuperscript{8, 9} EGPA with cardiac involvement is more frequently encountered in patients who are ANCA-negative, and patients can present with acute myocarditis, coronary vasculitis, congestive heart failure, pericarditis and valvular disease.\textsuperscript{8}

Cardiac magnetic resonance is a nonionising imaging modality that has emerged as a noninvasive tool for the assessment of structural and functional cardiac abnormalities.\textsuperscript{10} CMR is a useful noninvasive diagnostic tool that can be used to detect cardiac involvement in EGPA. It has been shown that CMR has a sensitivity of 88% and specificity of 72% for detecting cardiac involvement in EGPA.\textsuperscript{8, 11} The most common CMR findings of cardiac involvement are subendocardial late gadolinium enhancement and left ventricle dilatation with decreased left ventricle systolic function.\textsuperscript{4} Midmyocardium LGE is less commonly seen, indicating myocardial necrosis in acute sitting, and fibrosis related to myocardial damage.\textsuperscript{12} Native T1 and T2 are promising mapping techniques that can be used to detect myocardial fibrosis related to EGPA. Greulich et al. showed that patients with ANCA-associated vasculitis, including EGPA, had higher values for native T1, ECV and T2 compared to controls, irrespective of the presence of LGE.\textsuperscript{13} Cardiac MRI can also be used to follow up patients with cardiomyopathy related to EGPA. Dunogué et al. used CMR to follow up 15 patients with EGPA who showed evidence of cardiac involvement on baseline CMR and
received treatment. He reported an improvement in seven patients but stabilisation or worsening of the remaining eight patients.\textsuperscript{14} Cardiac MRI has some drawbacks, including high cost, limited availability, long examination duration and the need for the patient to repeatedly hold their breath.\textsuperscript{15}

The characteristic findings of EGPA in the chest HRCT, seen in up to 90\% of patients, include bilateral predominantly peripheral subpleural consolidation and airspace opacities. Other findings include bronchial wall thickening and dilation, along with peribronchial ground-glass nodules.\textsuperscript{16} Our patient had characteristic chest HRCT with bilateral predominantly peripheral groundless opacities associated with interlobular septal thickening that were migratory.

The Five Factor Score (FFS) scale is a widely used prognostic tool for EGPA and consists of five characteristics: (A) age >65 years, (B) renal impairment (proteinuria >1 g/24 h or creatinine >140 μmol/L), (C) cardiac involvement, (D) severe gastrointestinal symptoms, and (E) central nervous system manifestations. Patients are considered to have a good prognosis if they have a score of 0, and are classified as having a poor prognosis if they score ≥1 point.\textsuperscript{17} Corticosteroids are classically used for the treatment of patients with a good prognosis, with the addition of immunosuppressive medication, usually cyclophosphamide, for patients with a poor prognosis.\textsuperscript{17} Our patient had cardiac involvement and was therefore considered as having a poor prognosis, so azathioprine was prescribed in addition to the corticosteroid.

**Conclusion**
Eosinophilic granulomatosis with polyangiitis is a rare, necrotising vasculitis that has the propensity to involve the heart, leading to increased mortality and morbidity. CMR is a useful tool, not only for the assessment of cardiac involvement in EGPA patients, but also to help to stratify patients according to risk and guide their therapy.

**References**


**Figure 1:** Chest radiograph showing bilateral upper lung zone airspaces opacities (red arrow)

**Figure 2A:** Chest high resolution computed tomography (HRCT) axial view showing bilateral ground glass and airspace opacity (red arrow) associated with interlobular septal
thickening (green arrow). (B) Chest HRCT after 2 months from the initial scan, showed improvement of the previously seen airspace opacities, however, new airspace opacities had developed (blue arrow).

Figure 3A: Haematoxylin & Eosin X20- Sections show small and medium sized blood vessels with intramural eosinophil infiltrate (red arrow). (B) Haematoxylin & Eosin X40- Sections show a non caseating granuloma with infiltration by eosinophils (green arrow)

Figure 4: Late gadolinium enhancement short axis oblique (A) and 4-chamber views (B) showing patchy midmyocardium enhancement (red arrow).