Sultan Qaboos University Med J, November 2021, Vol. 21, Iss. 4, pp. 644–647, Epub. 25 Nov 21
Submitted 7 Jul 20
Revisions Req. 19 Aug & 27 Oct 20; Revisions Recd. 4 Oct & 9 Nov 20
Accepted 18 Nov 20
https://doi.org/10.18295/squmj.4.2021.038

CASE REPORT

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

The role of cardiovascular magnetic resonance

*Rashid S. Al Umairi,[1] Khalid Al Manei,[4] Fatma Al Lawati,[2] Yaqoob Al Mahrouqi,[3] Farida Al Balushi[3]

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 non-invasive diagnostic tool for detecting cardiac involvement and guiding the management plan. We report a 39-year-old male patient with a known history of bronchial asthma who was referred to the chest clinic at a tertiary hospital in 2019 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 and confirmed with a lung biopsy. 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 Granulomatous Vasculitis; Vasculitis; Eosinophils; Vascular Diseases; Anti-Neutrophil Cytoplasmic Antibody-Associated Vasculitis; Case Report; Oman.

Eosinophilic granulomatosis with polyangiitis (EGPA), historically known as Churg-Strauss disease, is an uncommon necrotising vasculitis of small- to medium-sized vessels that can involve multiple organs, including the paranasal sinuses, lungs, heart, nervous system, kidneys and gastrointestinal tract.[1–3] 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.[4] Cardiovascular magnetic resonance (CMR) is a non-invasive 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.[4] Herein, we present a case of histologically confirmed EGPA with characteristic findings on chest high-resolution computed tomography (HRCT) and CMR. In addition, the role of cardiac magnetic resonance imaging (MRI) in the assessment of cardiac involvement in patients with EGPA is discussed. To the best of the authors' 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 male patient with a known history of asthma for 24 years and a nasal polypectomy several years earlier presented to a local hospital in 2019 with a history of fever and cough lasting for two 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 × 10^9/L (normal range: 0.1–0.5 × 10^9/L). Sputum examination was negative for acid-fast bacilli and there was no growth in the sputum culture. Further assessment with a chest 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 (1,200 mg three times/day for seven days) but his symptoms did not improve. A repeat chest HRCT scan showed stable lung findings [Figure 2A]. Subsequently, the patient was referred to the chest clinic at a tertiary hospital in 2019 for further management. When the patient was seen, he was still complaining of cough but did not have a fever. His vital signs were stable (temperature = 35.5°C, heart rate = 84 beats per minute, respiratory rate = 20 breaths per minute and blood pressure = 125/68 mmHg). His CBC revealed normal haemoglobin (12.9 g/dL, normal range: 11.5–15.5 g/d) and white cell count (6.5 × 10^9/L, normal range: 2.2–10.5 × 10^9/L); however, the eosinophilic count was high (2.1 × 10^9/L, normal range: 0.1–0.5 × 10^9/L). Other blood investigations were as follows: urea was 4.8 mmol/L (normal range: 2.5–6.7 mmol/L),

Departments of [1]Radiology, [2]Pathology and [3]Medicine, The Royal Hospital, Muscat, Oman; [4]Department of Radiology, Oman Medical Specialty Board, Muscat, Oman
**Corresponding Author's e-mail: alumairi1@yahoo.com*

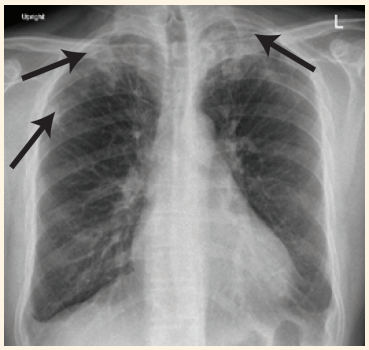

Figure 1: Chest X-ray of a 39-year-old male patient showing bilateral upper lung zone airspace opacities (arrows).

eGFR was >90 mL/min/1.73 m^2 (normal range: >90 mL/min/1.73 m^2), serum C-reactive protein was 78 mg/L (normal value is <5 mg/L), immunoglobulin E was 122 IU/mL (normal 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 HRCT scan at our hospital, performed two months after the initial HRCT 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, in addition to the blood eosinophilia and migratory chest CT findings, EGPA was suspected and a lung biopsy was performed. The tissue biopsy examination confirmed the diagnosis of EGPA [Figure 3]. The patient was assessed for potential cardiac involvement; his electrocardiogram and echocardiogram were unremarkable. His CMR scan showed normal biventricular function and volume, a left ventricle ejection fraction of 66% and right ventricle ejection fraction of 64%. However, patchy areas of midmyocardium LGE were detected, which confirmed cardiac involvement in EGPA [Figure 4].

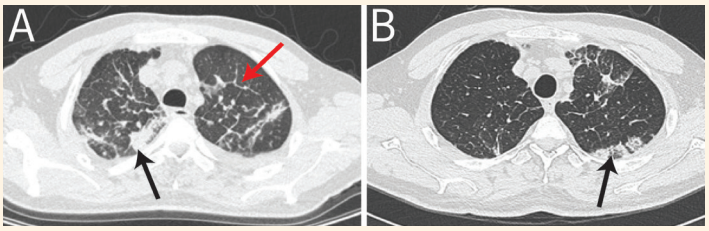

Figure 2: Chest high-resolution computed tomography axial views of a 39-year-old male patient showing **(A)** bilateral ground glass and airspace opacity (black arrow) associated with interlobular septal thickening (red arrow) and **(B)** two months post-initial scan showing improvement of the previously seen airspace opacities and new airspace opacities (black arrow).

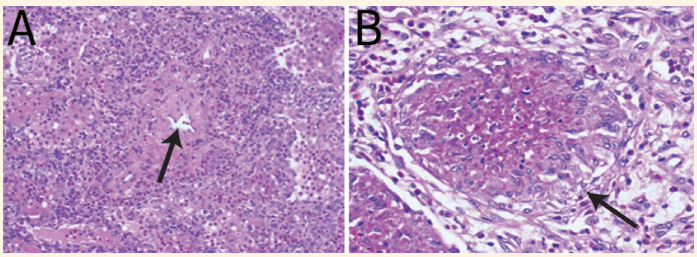

Figure 3: Haematoxylin and eosin stains at **(A)** ×20 magnification showing small- and medium-sized blood vessels with intramural eosinophil infiltrate (arrow) and at **(B)** ×40 magnification showing a non-caseating granuloma with infiltration by eosinophils (arrow).

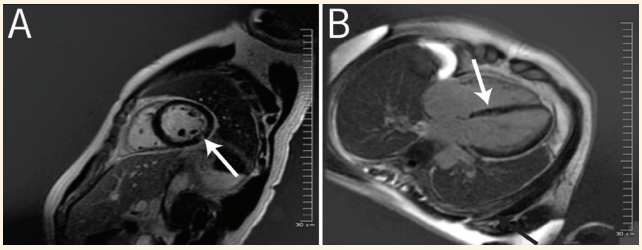

Figure 4: Late gadolinium enhancement short-axis **(A)** oblique and **(B)** 4-chamber views showing patchy midmyocardium enhancement (arrow).

As part of the assessment for EGPA, the patient was tested for ANCA and his results were negative. The patient was started on prednisolone (5 mg once daily) and azathioprine (150 mg once daily) for nine months. The patient remained on regular follow-up every three months and the patient's symptoms improved significantly, with normalisation of inflammatory markers and a decrease in C-reactive protein from 78 mg/L to 1 mg/L (normal value: <5 mg/L). His eosinophilic count was observed to have reduced from 2.1×10^9/L to 0.7×10^9/L (normal range: 0.1–0.5 $\times 10^9$/L). A repeat chest x-ray performed one 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.[1] 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.[3]

The diagnosis of EGPA is widely based on the presence of four of the six criteria proposed by the American College of Rheumatology in 1990: peripheral eosinophilia (10% on differential leukocyte count); (2) paranasal sinus abnormality; asthma; (4) migrating pulmonary opacities; (5) mononeuritis multiplex or polyneuropathy; and (6) biopsy evidence of extravascular eosinophils.[2,5,6] The current patient fulfilled five of these criteria: asthma, peripheral eosinophilia, nasal polyps, migratory pulmonary opacities and a lung biopsy showing eosinophilic infiltration.

There are three distinct phases of EGPA: the prodromal period, consisting of asthma and rhinitis and may last for several years; (2) the eosinophilic phase; and the vasculitis phase.[7]

Cardiac involvement in EGPA varies widely in the literature, ranging from 16–92%, and it has been associated with increased morbidity and mortality.[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.[9]

Cardiac magnetic resonance is a non-ionising imaging modality that has emerged as a non invasive tool for the assessment of structural and functional cardiac abnormalities.[10] CMR is a useful non-invasive 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.[11] The most common CMR findings of cardiac involvement are subendocardial LGE and left ventricle dilatation with decreased left ventricular systolic function. Midmyocardium LGE is less commonly seen, indicating that myocardial necrosis in acute setting and fibrosis is related to myocardial damage.[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.[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 and stabilisation or worsening in the remaining eight patients.[14] Cardiac MRI has certain drawbacks including high cost, limited availability, long examination duration and the need for the patient to repeatedly hold their breath.

The characteristic findings of EGPA in the chest HRCT, seen in up to 90% of patients, includes bilateral predominantly peripheral subpleural consolidation and airspace opacities. Other findings include bronchial wall thickening and dilation along with peribronchial ground-glass nodules.[15] The current patient had characteristic chest HRCT with bilateral predominantly peripheral ground-glass opacities associated with interlobular septal thickening which were migratory.

The Five-Factor Score scale is a widely used prognostic tool for EGPA and consists of five characteristics: age >65 years; (2) renal impairment (proteinuria >1 g/24 h or creatinine > 140 µmol/L); cardiac involvement; (4) severe gastrointestinal symptoms; and (5) central nervous system manifestations. Patients are considered to have a good prognosis if they have a score of zero; they are classified as having a poor prognosis if they score ≥1 point.[16] 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. The current patient had cardiac involvement and was, therefore, considered to have a poor prognosis.[16] Therefore, 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 for stratifying patients according to the risk and guiding their therapy.

AUTHORS' CONTRIBUTION

RSU is responsible for the majority of the work. KU collected the clinical information and wrote the initial manuscript. FL provided the histopathology results and the manuscript was send to be reviewed by her before final submission YM and FB were the treating physicians and the manuscript was send to them to review before submission. All authors approved the final version of the manuscript.

References

1. Churg J, Strauss L. Allergic granulomatosis, allergic angiitis, and periarteritis nodosa. Am J Pathol 1951; 27:277-301.
2. Jennette JC, Falk RJ, Bacon PA, Basu N, Cid MC, Ferrario F, et al. 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. Arthritis Rheum 2013; 65:1–11. https://doi.org/10.1002/art.37715.
3. Gioffredi A, Maritati F, Oliva E, Buzio C. Eosinophilic granulomatosis with polyangiitis: An overview. Front Immunol 2014; 5:549. https://doi.org/10.3389/fimmu.2014.00549.
4. Yune S, Choi DC, Lee BJ, Lee JY, Jeon ES, Kim SM, et al. Detecting cardiac involvement with magnetic resonance in patients with active eosinophilic granulomatosis with polyangiitis. Int J Cardiovasc Imaging 2016; 32S1:155–62. https://doi.org/10.1007/s10554-016-0843-y.
5. Lanham JG, Elkon KB, Pusey CD, Hughes GR. Systemic vasculitis with asthma and eosinophilia: A clinical approach to the Churg-Strauss syndrome. Medicine (Baltimore) 1984; 63:65–81. https://doi.org/10.1097/00005792-198403000-00001.
6. Masi AT, Hunder GG, Lie JT, Michel BA, Bloch DA, Arend WP, et al. The American College of Rheumatology 1990 criteria for the classification of Churg-Strauss syndrome (allergic granulomatosis and angiitis). Arthritis Rheum 1990; 33:1094–100. https://doi.org/10.1002/art.1780330806.
7. Greco A, Rizzo MI, De Virgilio A, Gallo A, Fusconi M, Ruoppolo G, et al. Churg-Strauss syndrome. Autoimmun Rev 2015; 14:341–8. https://doi.org/10.1016/j.autrev.2014.12.004.
8. Szczeklik W, Miszalski-Jamka T. Cardiac involvement in eosinophilic granulomatosis with polyangitis (Churg Strauss) (RCD code: I-3A.7a). J Rare Cardiovasc Dis 2014; 1:91–5. https://doi.org/10.20418/JRCD.VOL1NO3.56.
9. Dalia T, Parashar S, Patel NV, Gautam A, Dai H, Bormann S. Eosinophilic myocarditis demonstrated using cardiac magnetic resonance imaging in a patient with eosinophilic granulomatosis with polyangiitis (Churg-Strauss Disease). Cureus 2018; 10:e2792. https://doi.org/10.7759/cureus.2792.
10. Rajiah P, Tandon A, Greil GF, Abbara S. Update on the role of cardiac magnetic resonance imaging in congenital heart disease. Curr Treat Options Cardiovasc Med 2017; 19:2. https://doi.org/10.1007/s11936-017-0504-z.
11. Eyler AE, Ahmad FA, Jahangir E. Magnetic resonance imaging of the cardiac manifestations of Churg-Strauss. JRSM Open 2014; 5:2054270414525370. https://doi.org/10.1177/2054270414525370.
12. Marmursztejn J, Vignaux O, Cohen P, Guilpain P, Pagnoux C, Gouya H, et al. Impact of cardiac magnetic resonance imaging for assessment of Churg-Strauss syndrome: A cross-sectional study in 20 patients. Clin Exp Rheumatol 2009; 27:S70–6.
13. Greulich S, Mayr A, Kitterer D, Latus J, Henes J, Steubing H, et al. T1 and T2 mapping for evaluation of myocardial involvement in patients with ANCA-associated vasculitides. J Cardiovasc Magn Reson 2017; 19:6. https://doi.org/10.1186/s12968-016-0315-5.
14. Dunogué B, Terrier B, Cohen P, Marmursztejn J, Legmann P, Mouthon L, et al. Impact of cardiac magnetic resonance imaging on eosinophilic granulomatosis with polyangiitis outcomes: A long-term retrospective study on 42 patients. Autoimmun Rev 2015; 14:774–80. https://doi.org/10.1016/j.autrev.2015.04.013.
15. Silva CI, Müller NL, Fujimoto K, Johkoh T, Ajzen SA, Churg A. Churg-Strauss syndrome: high resolution CT and pathologic findings. J Thorac Imaging 2005; 20:74–80. https://doi.org/10.1097/01.rti.0000155268.00125.de.
16. Groh M, Pagnoux C, Baldini C, Bel E, Bottero P, Cottin V, et al. Eosinophilic granulomatosis with polyangiitis (Churg-Strauss) (EGPA) Consensus Task Force recommendations for evaluation and management. Eur J Intern Med 2015; 26:545–53. https://doi.org/10.1016/j.ejim.2015.04.022.