Large left ventricular non-infectious vegetation in patient with eosinophilic granulomatosis with polyangiitis

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Abstract
Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare form of systemic vasculitis in which cardiac involvement is relatively common and accounts for half of EGPA-related deaths. Cardiac involvement is more frequent in patients with an absence of anti-neutrophil cytoplasmic antibody and those with higher eosinophil counts. Clinical manifestations are various, including myocarditis, pericarditis, pericardial effusion, heart failure, arrhythmias, valvular insufficiencies and intra-cardiac thrombus formation. The pathology of cardiac involvement in EGPA is usually endomyocardial and pericardial eosinophilic infiltration. Considering the potentially adverse outcomes associated with cardiac involvement in EGPA, early detection is important. We experienced a rare case of EGPA with cardiac involvement presenting with non-infectious vegetation.

Keywords: eosinophilic granulomatosis with polyangiitis (EGPA), left ventricular non-infectious vegetation

Case report
A 27-year-old man was transferred to our hospital after 10 days of persistent fever, skin rash, and pain and numbness in both ankles. At another hospital he had had antibiotic treatment with ceftriaxone and doxycycline on the presupposition that it was Tsutsugamushi disease, but it had no effect. The patient was regularly followed up at the Department of Allergy and Clinical Immunology for two years because of bronchial asthma and chronic rhinitis.

On admission, his body temperature was 38.1°C, blood pressure was 120/80 mmHg, heart rate was 80 beats/min, and respiratory rate was 20 breaths/min. Breath sounds were slightly decreased on the left lower lung field, and no heart murmur was audible. Petechial rash was found on his whole body. Electrocardiography was in normal sinus rhythm. A chest radiograph showed blunted left costopleural angle and the heart contour seemed to be slightly widened.

Initial laboratory tests showed mild leukocytosis (9.14 × 10^9 cells/l) with marked eosinophilia (39.0%). C-reactive protein was 11.5mg/dl and the cardiac markers, pro-BNP (3548.0 pg/ml), CK-MB (20.9 ng/ml) and troponin-I (2.92 ng/ml) were elevated. On additional laboratory examination, perinuclear anti-neutrophil cytoplasmic antibody (P-ANCA) and cytoplasmic anti-neutrophil cytoplasmic antibody (C-ANCA) were negative. Parasite-specific antibodies were all negative and total Ig E level was high at 2154.0 IU/ml. Blood cultures were all negative.

The absence of platelet-derived growth factor receptor-α and -β (PDGRFA, PDGFRB) gene fusion made a diagnosis of idiopathic hyper-eosinophilic syndrome unlikely. A pleural effusion study revealed neutrophil-predominant exudate, the pH was 7.0, adenosine deaminase was 25 IU/l, glucose was 51 mg/dl (2.83 mmol/l), and Gram and AFB staining were negative. Bacterial and fungal cultures showed no growth.

For lower extremity numbness, a nerve conduction study was performed, which showed decreased sensory nerve action potential amplitude in both sural nerves. Intravenous methyl-
prednisolone (1 mg/kg/day) treatment was started from the second day in hospital, with a possible diagnosis of eosinophilic granulomatosis with polyangiitis (EGPA) or hyper-eosinophilic syndrome. After intravenous steroid treatment, the patient’s clinical conditions, including body temperature, skin rash and numbness of the feet, improved rapidly.

On the fourth day in hospital, the patient had an operation for resection of the mass-like lesions in the left ventricle. Pathological gross findings showed fragments of pinkish-gray soft tissue measuring 3.0 × 1.0 and 2.5 × 1.0 cm (Fig. 2). Microscopic findings revealed non-infective vegetations that comprised a thrombus, granulation tissue, eosinophils, lymphoplasmic cells, neutrophils and histiocyte infiltrations (Fig. 3).

Based on these pathological findings, namely hyper-eosinophilia, history of asthma, chronic sinusitis and polyneuropathy, a diagnosis of EGPA was made. Seven days after starting intravenous steroid treatment, all the laboratory results, including eosinophil count, C-reactive protein and cardiac markers, were normalised. The patient was discharged and is on oral methyl-prednisolone treatment at the out-patient clinic.

Discussion

Eosinophilic granulomatosis with polyangiitis or EGPA, previously named Churg-Strauss syndrome, which was first described in 1951, is a rare form of systemic, necrotising small-vessel vasculitis with accompanying bronchial asthma, eosinophilia and eosinophilic tissue infiltration of various tissues with granuloma formation.\textsuperscript{1,2} The pathogenesis is not well known, however it is considered a T-helper type 2 (Th2)-mediated disease.\textsuperscript{3,4} The immune response may be triggered by genetic or environmental factors such as allergens, infections, drugs or nutrition.\textsuperscript{2,5} Eosinophils, T-lymphocytes, B-lymphocytes and various cytokines may also play a role in the process.\textsuperscript{2,4}

The most commonly involved organ is the lung, followed by the skin and nervous system; however it can affect any organ.
Cardiac involvement is relatively frequent and one of the most serious manifestations of EGPA, accounting for approximately half of the deaths attributable to EGPA. It is more common in patients with an absence of ANCA and those with higher eosinophil counts. Clinical manifestations are various, including myocarditis, pericarditis, pericardial effusion, heart failure, arrhythmias, valvular insufficiencies, intra-cardiac thrombus formation, and others.

The histological features of EGPA are tissue eosinophilia, necrotising vasculitis and extravascular eosinophilic granulomas. However, histological findings may vary according to the organs involved. Cardiac pathology usually shows endomyocardial and pericardial eosinophilic infiltration and only rarely, coronary vasculitis. Because cardiac involvement in EGPA is relatively frequent and could be fatal, early detection is important.

Transthoracic echocardiography can show a wide spectrum of cardiac abnormalities, including systolic dysfunction, valvular insufficiencies, pericardial effusion and intra-cardiac thrombus. Cardiac MRI is the most sensitive technique to evaluate cardiac involvement in EGPA. It can detect clinically silent and undisclosed myocardial involvement. Late gadolinium enhancement in cardiac MRI suggests active endomyocarditis or endomyocardial fibrosis. Most enhancing lesions were apical and mid-cavity segments of the left ventricle. Therefore late gadolinium enhancement of endocardial layers could be associated with eosinophilic Loeffer-like endocarditis.

The general consensus for treatment is based on the usage of systemic glucocorticoids, adding other immunosuppressants if the prognosis is poor. The most commonly used prognostic tool is the Five Factor Score (FFS) scale. According to this scale, one point is given for each of the following: cardiac involvement, severe gastrointestinal manifestation, central nervous system involvement and renal impairment. Patients with a good prognosis have a FFS of 0 points and are treated solely with corticosteroids, while for patients with a poor prognosis (FFS ≥ 1), consider the addition of immunosuppressants, usually cyclophosphamide.

In this presented case, diagnosis was based on the clinical history and laboratory and pathology results. Hyper-eosinophilic syndrome (HES) is probably the most challenging differential diagnosis of EGPA. We could rule out reactive HES from parasitic infection, allergy and drug reaction by clinical history. The absence of PDGFRα and PDGFRβ gene fusion suggested it was less likely to be myeloid or lymphoid HES, and idiopathic HES is rarely accompanied by asthma. After ruling out HES, the diagnosis was made by American College of Rheumatology (ACR) criteria.

Cardiac MRI is known as a sensitive modality to evaluate cardiac involvement, however, we could not use it owing to the patient's refusal. Echocardiographic findings revealed intra-cardiac vegetative formations, which have not been reported before; hence it is quite a rare form of cardiac involvement of EGPA. We considered adding cyclophosphamide however the patient’s clinical aspects rapidly improved after intravenous methyl-prednisolone and surgical treatment.

Conclusion
We experienced a patient with EGPA with cardiac involvement presenting with non-infectious vegetations. There have been reports of intra-cardiac thrombus formation in EGPA patients but there are no reports of EGPA-related vegetative formation. The patient was successfully treated by surgical removal and a systemic corticosteroid.

References
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