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Case Report

Acute Pericarditis Revealing Eosinophilic Granulomatosis with Polyangiitis

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Abstract

Eosinophilic Granulomatosis with Polyangiitis (EGPA), commonly known in the past as Churg-Strauss syndrome, is a necrotizing systemic vasculitis accompanied by remarkable eosinophilia. Heart involvement occurs in approximately 15-60% of EGPA patients, especially those who are ANCA negative. Any cardiac structure can be involved. Heart involvement carries a poor prognosis and causes 50% of the deaths of these patients. It is often insidious and underestimated. Early diagnosis of cardiac involvement and subsequent therapy may prevent progression of cardiac disease. To our knowledge, so far

there are only few cases reported in the literature describing pericarditis as a presenting feature of EGPA. Here we report a case of a 54- year- old male with history of repeated sinusitis and mild asthma admitted to our department for worsening dyspnea and chest pain with consequent diagnosis of acute pericarditis due to unknown EGPA. This case suggests that acute pericarditis can be the initial clinical feature of onset EGPA, even in patients with mild asthma history. Early diagnosis of cardiac involvement prevents progression of cardiac disease.

Keywords: Acute pericarditis; Dyspnea; Eosinophilia; Eosinophilic granulomatosis with polyangiitis; Cardiac involvement

Abbreviations: EGPA: Eosinophilic granulomatosis with polyangiitis; ANCA: Antineutrophil cytoplasm antibody; AAV: ANCA-associated vasculitis; MRI: Magnetic resonance imaging; CT: Computed Tomography Scan; EULAR: European League Against Rheumatism; ACR: American College of Rheumatology

1. Introduction

Eosinophilic Granulomatosis With Polyangiitis (EGPA) was first described by Churg and Strauss in 1951 [1]. The disease, newly recognised as part of Anti- Neutrophil Cytoplasm Antibody (ANCA)-Associated Vasculitis (AAV), is characterized by eosinophil-rich granulomatous inflammation and small to medium-size vessel vasculitis associated with asthma and eosinophilia [2]. ANCA are positive in 40-60% of cases, mainly anti-myeloperoxidase. Typical clinical features include asthma, sinusitis, transient pulmonary infiltrates and neuropathy. Blood eosinophils are often >1500/µl or more than 10% on the differential leukocyte count. Heart involvement occurs in approximately 15-60% of EGPA patients, especially those who are ANCA negative. Any cardiac structure can be involved, and patients present with myocarditis, heart failure, pericarditis, arrhythmia, coronary arteritis, valvulopathy, intracavitary cardiac thrombosis. All patients with EGPA should be studied not only with a detailed history of cardiac symptoms and ECG, but also with echocardiography; if abnormalities are detected, a cardiac magnetic resonance study should be performed. Coronary angiography and endomyocardial biopsy should be reserved to selected cases. Heart involvement causes 50% of the deaths of these patients. It is often insidious and underestimated. Early diagnosis of cardiac involvement and subsequent therapy may prevent progression of cardiac disease [3]. Here, we present a case of a 54-year-old male with asthma-like symptoms and sinus pathology refractory, as well as eosinophilia and unexplained cardiac disorder. This case highlights the need to collect a complete clinical history, involving a multidisciplinary team for prompt intervention in EGPA once the disease is identified. It also demonstrates the benefit of prompt intervention, through the rapid improvement seen in the patient thanks to high-dose corticosteroids plus immunosuppression.

2. Case Presentation

A 54-year-old male with general fatigue, fever and a 1-year history of asthma was admitted to our hospital for dyspnea and chest pain associated with first finding of peripheral eosinophilia. He suffered from grass pollen allergy, polyposis and chronic rhinosinusitis since several years. Treatment with inhaled fluticasone/formoterol was ineffective. Few months before he complained episodes of migrating pain in left shoulder, ankles, wrists and hands. On admission to the unit, the patient had severe dyspnea, pulse

75 beats/min, and blood pressure 94/60 mm Hg. Auscultation of the chest demonstrated pericardial friction rub. During the hospitalization, electrocardiogram, cardiac echocardiography, cardiac MRI, chest CT, abdominal echography, blood tests, electromyography and ophthalmology examination were performed.

2.1. Clinical evaluation

Levels of B-type natriuretic peptide (568 pg/mL; normal range <125 pg/mL), sequential troponin-T levels (79 ng/L; normal range <14 ng/L), myoglobin (95 µg/L, normal range <80 µg/L), creatine kinase-MB (5.8 µg/L, normal range <5 µg/L), lactate dehydrogenase (335 U/L, normal range <225 U/L) were elevated, such as eosinophilic count (3.05 10^9/L, normal range <0.45 10^9/L). Hypersensitive C-reactive protein level was 10 mg/dL (normal range <0.5). Serum total IgE level was 251 KUI/l (normally < 100 KUI/l). D-dimer level was 2.83 µg/mL (normal range <0.57). Serum tests were negative for antinuclear antibodies, antineutrophil cytoplasm antibodies (ANCA), rheumatoid factor, anti-citric-citrullinated peptide, double-strands DNA, extractable nuclear antigens, antiphospholipid antibodies, anti- transglutaminase, anti-thyroid peroxidase, anti-thyroglobulin and immunoglobulins. Serum levels of complement were within normal range. Serological markers for Human Herpes virus 6, 8, Parvovirus B19, Cytomegalovirus virus, Epstein-Barr virus, Hepatitis B virus, Hepatitis C virus, Chlamydia pneumoniae, Mycoplasma pneumoniae, Human immunodeficiency virus, Coxsackie virus were negative. Tuberculin skin test as well as quantiferon-TB Gold (QFT-G) were negative. Nasal swab for respiratory viruses, bacteria and SARS-CoV-2 was negative. Test for treponema pallidum was negative. Screening for parasites was negative. Blood and urine cultures were sterile. Electrocardiography revealed sinusal rhythm, slight right delay, non-specific anomalies of ventricular repolarization. Transthoracic echocardiography showed ubiquitous pericardial effusion mostly represented in the inferolateral site (21 mm in the parasternal long axis, 10 mm anterior to the right ventricle, 6 mm in proximity of diaphragmatic wall of right ventricle); biventricular systolic function within limits; no signs of obstruction to right ventricular filling. Treatment with ibuprofen and colchicine was started before doing magnetic resonance imaging (MRI) that revealed ubiquitous pericardial effusion of moderate-severe degree with a maximum detachment of 3 cm in the inferolateral wall without signs of haemodynamic compromise, with signs of organization and presence of voluminous fibrin aggregates. Pericardial leaflets were slightly thickened, edematous and with late enhancement. There were also signs of mild myocardial edema on T2 mapping and possible coexisting mild diffuse fibrosis. Mild myocardial enhancement with non-ischemic pattern was observed on late post-contrast images (Figure 1). Chest Computed Tomography (CT) scan revealed peri bronchial interstitial thickening associated with some bilateral bronchiolectasis, left pleural effusion with a maximum basal thickness of 2 cm, abundant pericardial effusion with a maximum thickness of 2.5 cm, lymphnodes of likely reactive significance. No signs of pulmonary embolism were seen on CT scan (Figure 2). Pulmonary aspergillosis and sarcoidosis were ruled out for absence of biochemical and instrumental diagnostic elements. Complete abdomen ultrasound and fecal occult blood tests were negative, allowing to exclude the paraneoplastic nature of eosinophilia. Electromyography showed no signs of neuropathy. Ophthalmologic examination showed an initial mild episcleritis. Early in admission, patient was carefully reviewed by our multidisciplinary team made up of internists, cardiologists, allergologists and rheumatologists.

Persistent eosinophilia and acute pericarditis were the most important findings that leaded to EGPA diagnosis, along with his history of pollen grass allergy, chronic sinus infections and asthma. According to EULAR recommendations for the management of primary small and medium vessel vasculitis, we used high-dose glucocorticoids followed by a combination of parenteral methotrexate and glucocorticoids. Since the patient's renal function was normal, this was a less toxic alternative to cyclophosphamide to induce clinical remission. Concomitant therapies included folic acid, colchicine, along with proton pump inhibitor, oral bisphosphonates, vitamin D and calcium supplementation for prophylaxis against steroid-induced side effects [4-6]. Almost immediately on commencing treatment, the patient reported less chest pain, resolution of dyspnea, increased energy levels and improved mood. Considering the possibility of an eventual cyclophosphamide treatment, semen cryopreservation was performed. Initial episcleritis was treated with tobramycin and dexamethasone eye drops. The patient's pericardial effusion rapidly resolved once corticosteroids treatment was started, as well as left pleural effusion (Figure 3). He was successfully discharged 20 days after admission. A repeat echocardiogram at 2 months revealed absence of pericardial effusion and good left ventricular systolic function. Eosinophil count after two months kept being low (0.01 10^9/L after two months, 0.04 10^9/L after four months).

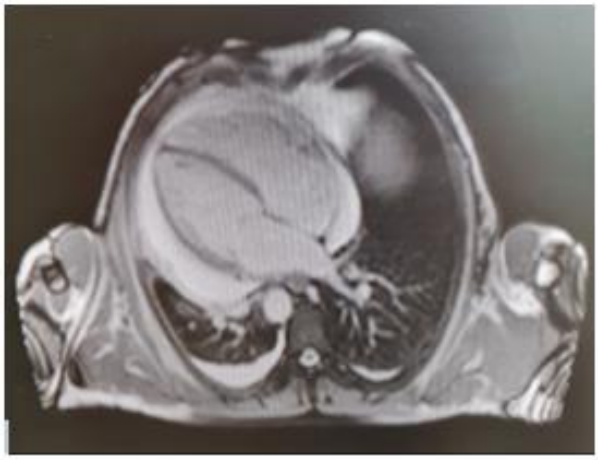

Figure 1: MRI revealed ubiquitous pericardial effusion of moderate-severe degree with a maximum detachment of 3 cm without signs of haemodynamic compromise.

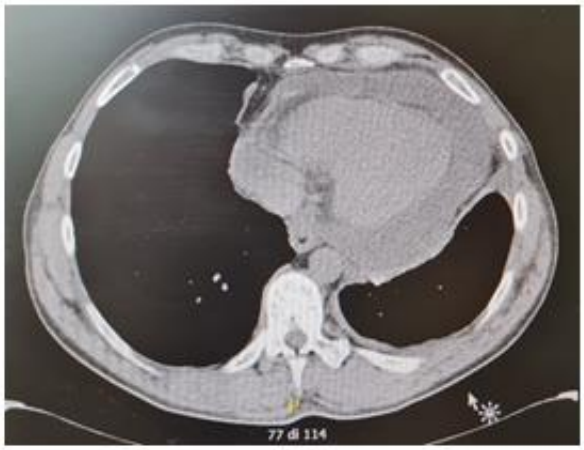

Figure 2: CT scan revealed left pleural effusion with a maximum basal thickness of 2 cm and abundant pericardial effusion.

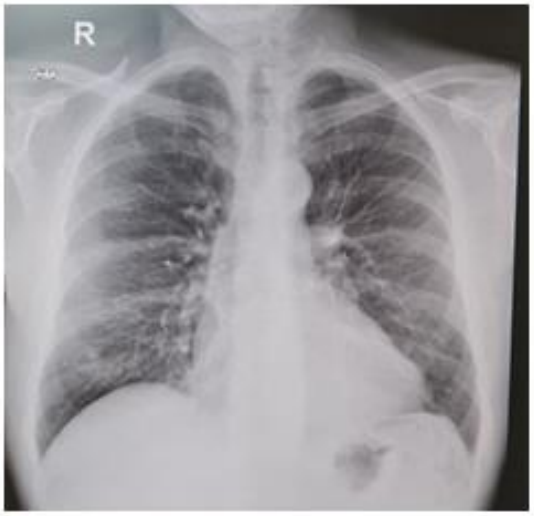

Figure 3: Pericardial and pleural effusion rapidly resolved once corticosteroids treatment was started.

3. Discussion and Conclusions

Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare subtype of ANCA-associated vasculitis characterized by asthma, rhinosinusitis, peripheral eosinophilia and manifestations due to small-vessel vasculitis [7] (Table1). EGPA has been classically described to evolve through three different phases, starting with a prodromic allergic phase characterized by asthma and rhinosinusitis, followed by an increase in blood and tissue eosinophilia, and in the last phase patient show systemic symptoms and organ involvement due to small-vessel vasculitis [8]. Heart involvement occurs in approximately 15-60% of EGPA

patients and is one of the most severe manifestations in EGPA, often leading to death. Interestingly, it has been shown that cardiac involvement is often found in ANCA-negative patients [9]. Typical manifestations include myocarditis, heart failure, arrhythmia and pericarditis, though it has been suggested that many patients with cardiac involvement may be asymptomatic [10]. Pericarditis, which is one of the major cardiac manifestations in EGPA, presents typically with slight pericardial effusion, even though few cases of cardiac tamponade have been reported [11]. To our knowledge, so far there are only few cases reported in the literature describing pericarditis as a presenting feature of EGPA [12-14]. Here we present the case of a 50-year-old male with a history of asthma, polyposis and chronic rhinosinusitis who was admitted to our hospital for dyspnea and chest pain. Laboratory test revealed an increased in eosinophilic count as well as inflammatory markers and radiological investigations showed sign of pericarditis and pleural effusion. Other causes of pericarditis were ruled out and the diagnosis of EGPA was made based on ACR/EULAR criteria [15] (Table 2). In order to avoid toxicity of cyclophosphamide and considering his clinical status, we decided to treat our patient with high dose of glucocorticoids followed by a combination of parenteral methotrexate and glucocorticoids. We would have added cyclophosphamide if systemic glucocorticoids alone had not achieved remission. Instead, the chosen treatment produced a progressive reduction in the size of the pericardial and pleural effusion, as well as the normalization of the eosinophil count and inflammatory markers. In summary, here we report a case of acute pericarditis leading to a new diagnosis of EGPA. This case highlights the need to consider EGPA as differential diagnosis in patients with pericarditis presenting with asthma-like symptoms and sinus pathology, as well as persistent eosinophilia. Blood eosinophils should always be tested in unexplained cardiac disorders and may normalize even after low doses of corticosteroids.

ANCA-associated vasculitis	Necrotizing vasculitis, with few or no immune deposits, predominantly affecting small vessels, associated with MPO-ANCA or PR3-ANCA. Not all patients have ANCA.
Microscopic polyangiitis	Necrotizing vasculitis, with few or no immune deposits, predominantly affecting small vessels. Necrotizing arteritis involving small and medium-sized arteries may be present. Necrotizing glomerulonephritis is very common. Pulmonary capillaritis often occurs. Granulomatous inflammation is absent
Granulomatosis with polyangiitis (Wegener's)	Necrotizing granulomatous inflammation usually involving the upper and lower respiratory tract, and necrotizing vasculitis affecting predominantly small to medium- sized vessels. Necrotizing glomerulonephritis is common.
Eosinophilic granulomatosis with polyangiitis (EGPA)	Eosinophil-rich and necrotizing granulomatous inflammation often involving the respiratory tract, and necrotizing vasculitis predominantly affecting small to medium-sized vessels, and associated with asthma and eosinophilia. ANCA is most frequent when glomerulonephritis is present

Table 1: Definitions of AAV according to Chapel Hill Consensus Conference (CHCC) in 2012.

Clinical, laboratory and biopsy criteria	**SCORE**
Maximum eosinophil count ≥1×109/L	5
Obstructive airway diseas	3
Nasal polyps	3
Cytoplasmic antineutrophil cytoplasmic antibody (ANCA) or anti-Proteinase 3–ANCA positivity	-3
Extravascular eosinophilic predominant inflammation	2
Mononeuritis multiplex/motor neuropathy not due to Radiculopathy	1
Haematuria	-1
After excluding mimics of vasculitis, a patient with a diagnosis of small- or medium-vessel vasculitis could be classified as having EGPA if the cumulative score was ≥6 points.	

Table 2: ACR/EULAR Classification Criteria for EGPA

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