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Case report

Acute myocardial infarction as Eosinophilic granulomatosis with polyangiitis (formerly Churg Strauss syndrome) initial presentation

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ABSTRACT

Eosinophilic granulomatosis with polyangiitis is a rare primary vasculitic disease characterized by hypereosinophilia, late onset asthma and extravascular eosinophil granulomas. We report a case presented initially with acute myocardial infarction which later only proceed with asthma, skin manifestations and peripheral neuropathy. Laboratory parameters showed hypereosinohpilia with negative perinuclear pattern of antineutrophil cytoplasmic autoantibodies (p-ANCA). Skin biopsy showed leucocytoclastic vasculitis with eosinophilic infiltration while coronary angiography was normal. The patient's symptoms improved with IV methylprednisolone, pulse cyclophosphamide and azathioprine.

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Infarto agudo do miocárdio como apresentação inicial de granulomatose eosinofílica com poliangiite (anteriormente, síndrome de Churg Strauss)

Palavras-chave:
Síndrome de Churg Strauss
Granulomatose eosinofílica com poliangiite
Hipereosinofilia
Asma
Infarto do miocárdio

RESUMO

A granulomatose eosinofílica com poliangiite é uma vasculite primária rara, caracterizada por hipereosinofilia, asma de surgimento tardio e granulomas eosinofílicos extravasculares. Relatamos um caso apresentado inicialmente com infarto do miocárdio e que, ulteriormente, teve prosseguimento apenas com asma, manifestações cutâneas e neuropatia periférica. Os parâmetros laboratoriais revelaram hipereosinofilia com um padrão perinuclear negativo de autoanticorpos citoplásmicos antineutrófilos (p-ANCA). A biópsia de pele demonstrou vasculite leucocitoclástica com infiltração eosinofílica, diante de uma

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angiografia coronária normal. Os sintomas do paciente melhoraram com metilprednisolona IV, pulsoterapia com ciclofosfamida e azatioprina.

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Introduction

Eosinophilic granulomatosis with polyangitis (EGPA), or previously better known as Churg Strauss Syndrome (CSS), is a rare disorder with an annual incidence of 2.7 cases per million.[1] It is characterized by hypereosinophilia, late onset asthma and extravascular eosinophil granulomas. This was first described by Churg and Strass in 1951.[2] EGPA is variable in its manifestations, which may range from skin lesions, asthma, non-erosive arthritis to life threatening conditions, such as cardiac disease, severe gastrointestinal and peripheral nervous system involvement. Cardiac involvement is a leading cause of mortality, accounting for 48% of deaths in EGPA.[3]

The 1990 American College of Rheumatology (ACR) classification criteria for EGPA required the presence of four or more of the following six criteria for making the diagnosis: asthma, eosinophilia (>10% of leukocytes by differential cell count), mononeuritis multiplex or polyneuropathy, pulmonary infiltrates (may be transient, paranasal sinusitis and histological proof of vasculitis with extravascular eosinophils).[4] The recently published 2012 Revised International Chapel Hill Consensus Conference (CHCC) Nomenclature of Vasculitides stated EGPA as an antineutrophil cytoplasmic antibodies (ANCA) associated vasculitides with eosinophil-rich and necrotizing granulomatous inflammation often involving the respiratory tract, and necrotizing vasculitis predominantly affecting small to medium vessels, and associated with asthma and eosinophilia.[5]

We report a 50-year-old man presented with inferior myocardial infarction who later developed skin manifestations, exacerbation of bronchial asthma and disabling peripheral neuropathy.

Case report

A 50-year-old male was presented at our emergency department with severe chest pain and shortness of breath for 2 days. His past medical history revealed hypercholesterolemia with no previous hospitalizations. The 12-lead electrocardiogram (ECG) showed a sinus rhythm and ST-segment elevation in the inferior leads. Echocardiography revealed a good left ventricular systolic function with ejection fraction of 78% with no regional wall motion abnormality. Laboratory assessment showed raised CKMB 148 U/L (normal < 25 U/L) and LDH 2,047 U/L (normal 200-480 U/L). Due to late presentation, he was not thrombolyzed. He was prepared for percutaneous cardiac intervention (PCI), but he refused. He was discharged with medications for coronary artery disease.

Two weeks later, he developed multiple painful nodular lesions over his soles and hands associated with intermittent fever. Further questioning revealed that he had been suffering from dry cough for 1 year for which he did not seek any treatment. There was no allergic rhinitis or any symptoms that might suggest asthma. However, he still experienced chest discomfort since discharged 2 weeks ago.

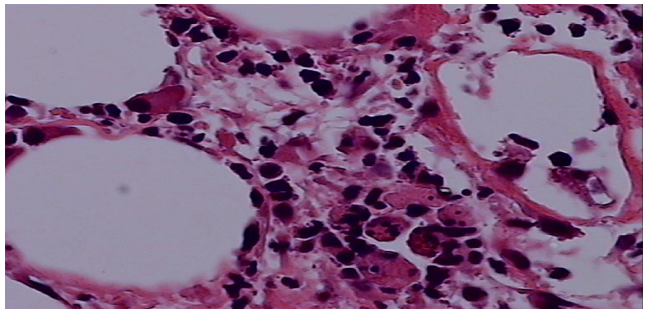

Figure 1 – Skin biopsy of this patient which shows lymphocytic and eosinophilic infiltrations consistent with leukocytoclastic vasculitis.

Chest radiograph was normal. Repeated echocardiographs showed global hypokinesia with poor left ventricular systolic function of 35%. Laboratory analyses showed an increase white blood cell count (14,900/μL) with predominance of eosinophils (33%), LDH 863 U/L, raised erythrocyte sedimentation rate (52 mm/h), CRP (125 U/L) and positive rheumatoid factor. Immunological markers, such as antinuclear antibody, perinuclear and classic ANCA, extractable nuclear antigen were all negative. A skin biopsy was performed and showed dense neutrophilic and lymphocytic infiltrations with eosinophilic vasculitic changes (Fig. 1). He only fulfilled 2 out of the 6 of the ACR classification criteria with no history of asthma or sinusits. However, he was given prednisolone 60 mg (1 mg/kg), and his skin lesions improved. This time he agreed on undergoing coronary angiography, which showed no evidence of atheroma on coronary luminogram.

Four months later, he presented with exacerbation of bronchial asthma with nocturnal cough. There were no new skin lesions or chest pain. His symptoms improved with nebulizers and a short course of prednisolone 30 mg (0.5 mg/kg) for 5 days.

During the follow-up, 6 months later, his complaint of Raynaud's phenomenon and numbness over both his lower limbs with more prominent over the right foot. This was proceeded with right foot dorsiflexion weakness. The physical examination revealed right foot drop, vasculitic lesions over the palms and a nodule with necrotizing surface over the right hand. Laboratory findings showed raised white cell counts 22.2 with eosionophils (78.8%), ESR 32 mm/h and CRP 64 U/L. Electromyography and nerve conduction studies were consistent with sensorimotor polyneuropathy.

He was given IV methylprednisolone 500 mg daily for three days followed by 60 mg of oral prednisolone (1 mg/kg) and

amlodipine 5 mg daily. After the completion of IV methylprednisolone, monthly intravenous cyclophosphamide was administered for 6 months. The patient responded well to the treatment, with improvement of the symptoms After the completion of the pulse cyclophosphamide, he was added on azathioprine 25 mg daily.

Throughout the 8 years follow-up, there was no relapse after initiation of the immunosuppressive treatments. However, the patient still experience some residual neurological deficit of the right foot. Otherwise, the laboratory parameters and echocardiography were all normal.

Discussion

EGPA is a multisystem vasculitic disorder which involve medium to small sized muscular arteries and veins. It is typically manifested in 3 consecutive phases. The prodromal phase consists of allergic manifestations. The second phase involves tissue eosinophilia infiltration and blood eosinophilia. This is followed by vasculitic systemic manifestations.[6] However, this patient had a different sequence in which acute myocardial infarction was the initial presentation and asthmatic symptoms only appeared later.

EGPA may affect the myocardium, valves, coronary arteries and pericardium. This will lead to structural and functional impairment.[7] Eosinophils infiltrate the myocardium and release toxic inflammatory mediators which lead to arrhythmias and systolic dysfunction.[8] Cardiac involvement is the major cause of mortality in EGPA with poor outcomes, but it is fully reversible as occurred in this patient.[9] However, both 1990 ACR classification criteria and the new revised CHCC nomenclature do not emphasize on cardiac symptoms.

Peripheral nerve involvement is the most frequent vasculitic manifestation of EGPA.[10] Most patients responded well with immunosuppressive therapy, however some residual symptoms might persist as in this case.[11] Other organs involvement includes cutaneous lesions, lungs (asthma, nasal polyps), kidney and gastrointestinal involvement.

Laboratory parameters were non-specific, which included raised ESR, CRP and eosionophil counts.

Anti-MPO perinuclear ANCA (p-ANCA) can be found in only 30%-40% of patients with EGPA.[12] Most patients with positive ANCA had glomerulonephritis, peripheral neuropathy and vasculitis in biopsy.[13] It was negative in our patient. Indeed, few literatures had reported that EGPA with heart involvement are mainly ANCA negative.[13,14] Persistent hypereosinophilia alone does not exclude other diagnosis such as hypereosinophilic syndromes. However, the presences of other clinical manifestations help to reach the diagnosis.

The five-factor score was developed by the French Vasculitis Study Group to predict the risk of death in EGPA. This includes, reduced renal function (creatinine > 1.58 mg/dL or 140 μmoL/L), proteinuria (> 1 g/24 h), gastrointestinal hemorrhage, infarction or pancreatitis, involvement of the central nervous system and cardiomyopathy. Presence of any one of these have 5-year mortality of 26%, while 2 or more with 46% mortality.[15]

Currently, there is no established protocol for treatment of EGPA. The type of treatment mainly based on the severity of the disease. Minor manifestations, such as asthma or cutaneous manifestations can be treated with corticosteroids alone. Life threatening multisystem involvement (acute coronary syndrome, severe peripheral polyneuropathy or severe gastrointestinal involvement) required combination therapy of glucocorticoids and cyclophosphamide. In this patient, he was given 3 consecutive days of intravenous methylprednisolone (500 mg/m^2) followed by monthly pulse of IV cyclophosphamide (750 mg/m^2) for 6 months.

There was a delay in reaching the diagnosis in this patient as asthmatic symptoms only become apparent after 5 months of the initial presentations. It took approximately 10 months for the disease to evolve from acute myocardial infarction, cutaneous lesions and exacerbation of asthma to peripheral neuropathy.

Reports show that 45% of the relapses occurred during the first year of therapy, and it occur either very soon or long after the clinical remission.[16] So far, there was no relapse after 8 years of follow up.

Conclusions

EGPA is a multisystem disease, and to obtain the diagnosis can be challenging. High suspicion for EGPA should be raised especially in young patients who presented with acute coronary syndrome without any risk factors associated with history of asthma and peripheral eosinophilia of more than 10%.

Conflicts of interest

The authors declare no conflicts of interest.

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