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CLINICAL CASE/*CASO CLINICO*
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Eosinophilic granulomatosis with polyangiitis: a challenge for differential diagnosis

Granulomatosis eosinofílica con poliangitis: un desafío para el diagnóstico diferencial

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Abstract

Eosinophilic granulomatosis with polyangiitis (EGPA), previously known as Churg-Strauss syndrome, is a rare small and medium vessels vasculitis, consisting of asthma, migratory pulmonary infiltrates and eosinophilia. Its low occurrence makes it difficult to achieve an early diagnosis, and hence a directed treatment in order to control it and avoid complications. We report a 31 year-old man with refractary asthma, who developed arthritis and multiplex mononeuritis. Before EGPA´s diagnosis, he had just received asthma treatment (steroids, bronchodilators, antileukotriene and omalizumab); but once EGPA is confirmed and correct treatment was started, there was a remarkable clinical improvement.

Key words: Churg Strauss, Vasculitis, Allergic granulomatosis, Antineutrophil cytoplasmic antibody.

Resumen

La granulomatosis eosinofílica con poliangitis (EGPA), anteriormente conocida como síndrome de Churg-Strauss, es una vasculitis poco frecuente de vasos pequeños y medianos, que consiste en asma, infiltrados pulmonares migratorios y eosinofilia. Su baja aparición dificulta el diagnóstico precoz y, por lo tanto, un tratamiento dirigido para controlarlo y evitar complicaciones. Presentamos a un hombre de 31 años con asma refractaria, que desarrolló artritis y mononeuritis múltiple. Antes del diagnóstico de EGPA, acababa de recibir tratamiento para el asma (esteroides, broncodilatadores, antileucotrienos y omalizumab); pero una vez que se confirmó la EGPA y se inició el tratamiento correcto, hubo una mejoría clínica notable.

Palabras clave: Churg Strauss, vasculitis, granulomatosis alérgica, anticuerpo citoplasmático antineutrófilo.

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INTRODUCTION

In aggressive and rare diseases, a rapid diagnosis and therefore, a directed treatment improves substantially the prognosis of patients. EGPA requires for its diagnosis a high clinical suspicion, because the majority of cases can mimic diseases like asthma for several years. It is important to remark key points that allow medical doctors to have EGPA in mind, in order to achieve a timely treatment and prevent the progression of the disease that could be fatal.

CLINICAL CASE

A 31 year-old man was directed to the Rheumatologist for 4 months of swollen and tender joints in hands, elbows, shoulders and ankles; in addition to 30 minutes morning stiffness. He had also had frontal headache and hands paresthesias for 2 months.

The patient had a history of asthma, with poor response to treatment since he was 9 years old. He received prednisone, beclometasone, salbutamol, ipratropium bromide until 22 years of age, time when he started to use salmeterol/fluticasone plus montelukast, because of the uncontrolled asthma. Once the disease got worse in symptoms in spite of the described treatment, omalizumab was started.

Relevant exams showed: positive rheumatoid factor (100 UI/dL [reference<30 UI/dL); Blood eosinophils count: 7.830/mm^3 (representing 34% of total white blood cells); Erythrocyte sedimentation rate: 78 mm/hour (reference <30 mm/hour); and C-reactive protein: 12 mg/L (reference <3 mg/L). Antinuclear antibodies and extractable nuclear antigens antibodies were negative. C3 and C4 fractions were normal. Initially, the patient received a diagnosis of Rheumatoid arthritis (RA), and underwent therapy with metotrexate 15 mg per-week plus prednisone 5 mg/day without improvement.

For assurance reasons, the patient arrived to our center after 6 months of RA diagnosis. By that time, physical examination showed: normal respiratory sounds; hypothenar eminence atrophy in left hand with decreased muscular strength of flexors and extensors (Figure 1); left forearm and hand dysesthesias; and synovitis in elbows, wrists, and 2nd/3rd/4th metacarpophalangeal joints.

In summary, it is a case of a patient with uncontrolled asthma since childhood, arthritis, peripheral neuropathy, eosinophilia, positive rheumatoid factor and elevated acute phase reactants. Therefore, we asked for neurology consultation and some complementary studies.

An electromyogram test & nerve conduction study of upper extremities showed sensitive and motor neuropathy, with predominance of axonal involvement, more severe in the left ulnar nerve, basically related to multiple mononeuropathy. Magnetic resonance of the brain was normal, however it demonstrated pansinusitis. Chest tomography showed peribronchial enlargement, cylindrical bronchiectasis and subpleural emphysema (Figure 2).

6 months later, the patient developed purpuric skin lesions in feet, compatible with vasculitis (Figure 3). This last finding in addition to uncontrolled asthma, pansinusitis, eosinophilia and multiple mononeuropathy led to think about EGPA diagnosis. Antineutrophil cytoplasmic antibodies were weakly positives (ANCA-P titers 1:40). It was not possible to take specific antibodies (anti-proteinase 3 and anti-myeloperoxidase), and patient rejected a skin biopsy. In spite of low ANCA-P titers, ba-

sed on the context of clinical case, the antibodies were taken into account for EGPA diagnosis, highlighting that they are positive just in 40-60% of cases and they are not specific for EGPA. Omalizumab was suspended. It was ordered prednisone 50 mg/day plus cyclophosphamide 600 mg/m^2/month (6 doses).

Once the treatment started, patient improves arthritis, skin lesions, asthma symptoms and acute phase reactants. When clinical, radiological and para-clinical improvement was achieved, prednisone was lowered progressively 10 mg/week until 10 mg/day dose. Patient finished the 6 doses of cyclophosphamide successfully; and nowadays, he continues in medical control, without reactivation of EGPA, and persisting only with blood eosinophilia.

DISCUSSION

Churg-Sttrauss syndrome, since 2012 EGPA (1), is a medium and small vessels vasculitis, ANCA positive, with prevalence rate of 6,8 (IC95%: 1,8-17,3) per million-patients/year, and incidence of 0-14 cases per million-patients/year in asthmatic groups (2-4). In Colombia, there are cases reported in Cali, Bogotá, Medellín and Huila (5-8); but any in the Caribbean Coast. EGPA diagnostic criteria are listed in Table 1. EGPA affects mainly lungs and skin, but also kidney, heart, gastrointestinal tract and nervous system.

EGPA has 3 phases, not always distinguishable (9-12):

a) Prodromic: usually at 20-30 year-old, with allergic manifestations (rhinitis, dermatitis, asthma [present in 90% of EGPA]).

b) Eosinophilic: often after 30´s, with elevated eosinophils in blood (Eo>10% of total blood cells, or Eo count>500/mm^3) and organs like lungs. Eosinophilia may persist, even with disease control.

c) Vasculitic: appears after 8 to 10 years of symptoms onset. Here, 40% of patients debut with transitory pulmonary infiltrates (because of pulmonary vasculitis), asthma and eosinophilia. In this phase the mortality increases, due to necrotizing granulomatous vasculitis of multiple organs; and also leads to beginning of fever, arthritis, anorexia and weight loss.

Although bronchiectasis is more related to infections (tubeculosis, fungi), inflammatory pneumonitis, immunodeficiencies or systemic diseases (lupus, RA); in EGPA it is not known if bronchiectasis is produced by the disease or the immunosuppresion of its treatment. (13-14)

Regularly, it is difficult to achieve an adequate control in asthma related to EGPA. Asthma severity increases with the onset of the vasculitic phase, which suggests EGPA could be present. Corticosteroid for asthma can delay the beginning of vasculitic phase, which may suddenly appear with the decreasing or the suspension of corticosteroids.(15). There are data suggesting that EGPA could be an adverse effect of antileukotrienes, especially 3-12 months after its onset; however, there is not a proved causal relationship. This could be more related to the use of antileukotrienes for uncontrolled asthma (moment when is it possible to think in EGPA diagnosis) or with reducing of corticosteroids dose when antileukotrienes are started (which can precipitate the vasculitic phase onset). (16-18)

This clinical case shows the evolution of a male with asthma since childhood, with

EGPA diagnosis after 22 years. Difficult-to-treat asthma, pansinusitis, eosinophilia, pulmonary infiltrates, multiple mononeuropathy and cutaneous vasculitis in conjunction were the key points of EGPA diagnosis. Seropositive arthritis in EGPA is especially interesting, because it is not described in the review that was made for the case discussion.

EGPA should be suspected in late-onset or difficult-to-treat asthma, eosinophilia and neuropathy, remembering that the vasculitic phase may be delayed with corticosteroids for asthma; and may be facilitated after corticosteroids suspension or reduction. Early diagnosis leads to timely initiation of treatment that prevents progression to more severe stages.

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