

Case Report

Asthma and Churg–Strauss syndrome*

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ABSTRACT

We report the case of a 25-year-old woman with Churg–Strauss syndrome, the symptoms of which had first appeared soon after she began taking oral contraceptive at the age of sixteen. The clinical profile evolved rapidly to severe persistent asthma, nasal polyposis, perennial obstructive rhinitis, eosinophilia (peripheral/tissue) and mononeuritis. Churg–Strauss syndrome is the type of disease that demands early detection, accurate diagnosis, aggressive treatment and periodic monitoring. It should be considered in the differential diagnosis of moderate and severe persistent asthma. The case reported calls attention to possibility that there is a hormonal component and that the disease can present early onset.

Keywords: Asthma; Churg–Strauss syndrome; Eosinophilia; Nasal polyps; Vasculitis; Case reports [publication type]

INTRODUCTION

In 1866, Kussmaul and Maier first identified polyarteritis nodosa in their description of a case of vasculitis involving the large elastic arteries and characterized by the formation of macroscopic aneurysms. In the 1930s, Wegener's granulomatosis, a necrotizing vasculitis that affects the small blood vessels and is accompanied by impaired renal function, was discovered. Twenty years later, based on post-mortem observations, Churg and Strauss

described a triad consisting of the combination of allergic granulomatosis, allergic angiitis and polyarteritis nodosa.⁽¹⁾ The discovery of this triad was fundamental for the establishment of Churg–Strauss syndrome (CSS) as a distinct form of vasculitis, although the diagnosis can now be made based on clinical or pathological criteria. Due to the great variability in nomenclature, the Chapel Hill Consensus Conference on the Nomenclature of

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Systemic Vasculitis, held in 1994, classified the disease as a form of small blood vessel vasculitis.⁽²⁾ Despite the fact that none of these classifications included the test for antineutrophil cytoplasmic antibodies, it is of note that approximately 70% of cases test positive for these antibodies.

Being more common in adults, CSS principally appears in the fourth or fifth decades of life. Asthma can precede systemic vasculitis by up to 30 years. A shorter interval between the onset of asthma and vasculitis suggests a poor prognosis. It is common for CSS symptoms and signs to appear after a reduction in the dosage of a systemic corticosteroid. The diagnosis is made based on a combination of clinical characteristics and laboratory test results, the essential components being asthma, eosinophilia and systemic necrotizing vasculitis. The appearance of multiple mononeuritis, palpable purpura, transitory pulmonary infiltrates and cardiomegaly (with or without cardiac insufficiency) should raise strong suspicion of CSS. Less common symptoms are abdominal pain, diarrhea, proteinuria/hematuria, progressive lymphadenopathy and chronic sinusitis.

The pathogenesis of CSS has not been fully clarified, but it likely involves auto-immune mechanisms in which leukocytes and endothelial cells play a role. Recently, an alteration in the CD95 ligand-mediated apoptosis of lymphocytes and eosinophils was observed. In addition, an increase in the serum levels of cationic eosinophilic proteins and soluble thrombomodulin, which are responsible for endothelial cell lesions, has been reported. An increase in the level of soluble IL-2 receptor suggests T-cell activation.⁽³⁾ It has also been suggested that CSS is induced by drugs such as zafirlukast, montelukast, zileuton, fluticasone, salmeterol, macrolide antibiotics, estrogens, cocaine, paroxetine and carbamazepine. These drugs might act through pseudoallergic/hypersensitivity or idiosyncratic mechanisms.^(1,3-4) It should be stated that the aforementioned drugs do not have a common chemical structure, thereby making it difficult to provide a single explanation of the pathogenesis of CSS. It has not yet been established whether using corticosteroids to treat asthma masks CSS symptoms and postpones the onset of vasculitis, or whether the condition would be aggressive independent of the use of corticosteroids.⁽⁵⁾ Some

of the effects that estrogens have on the immune system have already been identified.⁽⁶⁾

CASE DESCRIPTION

A 25-year-old white female began taking oral contraceptives at the age of sixteen and presented symptoms compatible with obstructive rhinitis and persistent asthma three months thereafter. She continued taking the oral contraceptives for six months and then stopped doing so because she believed it was related to her respiratory condition. She became pregnant three months later. During the pregnancy, her asthma worsened even with the use of corticosteroids. This resulted in the patient being admitted several times and led her to suspect the inefficacy of the corticosteroids. From the onset of her respiratory symptoms, she used injectable corticosteroids (which have a prolonged effect) for two years without any medical oversight, discontinuing their use immediately after giving birth. The moderate asthma and perennial obstructive rhinitis persisted. However, at approximately eight months postpartum, she developed cutaneous pallor in the extremities upon contact with cold water. This was accompanied by subsequent abdominal pain, vomiting, diarrhea (containing mucus, pus and blood) and significant weight loss. These symptoms required that the patient be admitted to various hospitals for prolonged periods. Nevertheless, there was no report of pulmonary infiltrates.

After her admittance to the Clementino Fraga Filho University Hospital, she complained of leg cramps, followed by progressive and serrated paresthesia in her arms and legs, constituting a clinical profile consistent with multiple mononeuritis. The complementary exams revealed the following: 25% eosinophils ($2300/\text{mm}^3$); high erythrocyte sedimentation rate (63 mm/h); platelet count, $540,000/\text{mm}^3$; immunoglobulin E, 166 U; 25.8% globulin (1.7 g). Immediate skin tests with inhaled antigens, including *Aspergillus fumigatus*, were negative. The baseline spirometry results were normal. The methacholine bronchoprovocation test was not performed, since there had already been a significant drop in forced expiratory volume in one second after inhalation of saline solution, which is compatible with important bronchial hyperresponsiveness. The biopsy of the sural nerve



Figure 1 - Computed tomography of the paranasal sinuses. Near-total opacity with material of the soft parts of the frontal sinus and right sphenoidal sinus, as well as of ethmoidal cells, the right maxillary sinus and nasal cavities. Bilateral darkening of the osteomeatal complex

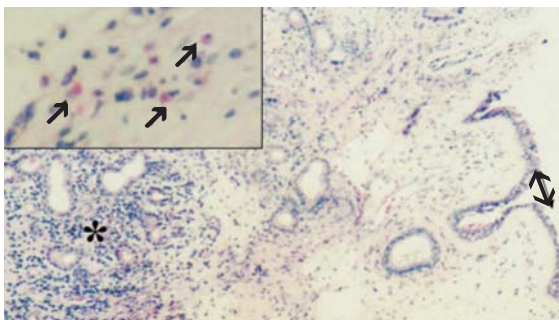


Figure 2 - Biopsy of the nasal polyp. Inflammatory nasal polyp covered with respiratory epithelium (double arrows) composed of conjunctive edematous tissue permeated by mixed inflammatory infiltrates(*). An enlarged photograph (inset) shows eosinophils (arrows)

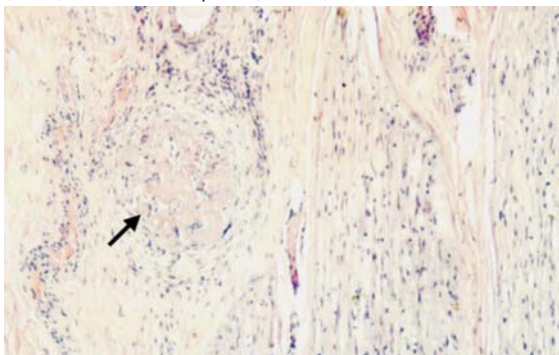


Figure 3 - Biopsy of the sural nerve. Biopsy of the sural nerve showing necrotizing vasculitis with deposits of fibrin in the epineural vessel (arrow) - H&E, x100

revealed severe axonal neuropathy, with necrotizing vasculitis but without granulomas (Figure 1). The patient then developed chronic sinus disease (Figure 2) and nasal polyposis (Figure 3). She had not had asthma or rhinitis during her childhood and adolescence, although there was a family history of atopia. The combination of asthma, rhinosinusitis, nasal polyposis, eosinophilia and vasculitis met the criteria for CSS.

She then received a six-month course of pulse therapy with cyclophosphamide (500 mg) and a corticosteroid (1 gEV/day). The patient also received meperidine, amitriptyline and carbamazepine, in conjunction with an inhaled oral corticosteroid (30 mg/day), for an additional year. Currently, the patient is asymptomatic. However, she has a residual neural manifestation and limited finger movement, together with a low degree obstructive pattern seen in her spirometry results, positivity of the bronchodilator test (with normalization) and mild obstructive rhinitis. She uses inhaled corticosteroids.

DISCUSSION

Early detection, a precise diagnosis, aggressive treatment and periodic monitoring are required in cases of CSS. It is fundamental to suspect this condition in patients with moderate or severe asthma who frequently take oral corticosteroids and who present peripheral eosinophilia. The phenomenon generally occurs after the discontinuation of systemic corticosteroids.

The case presented here is noteworthy in that it involves a young patient presenting early symptoms of rhinitis and difficult-to-control asthma after taking oral contraceptives, accompanied by a worsening of the condition during pregnancy. She developed a rare set of gastrointestinal symptoms, characterized by impaired absorption and accompanied by rapid-onset vasculitis, which implies a worse prognosis. It has yet to be fully clarified whether CSS constitutes an aggressive disease regardless of the use of corticosteroids, or whether, during their use in the treatment of asthma, corticosteroids mask CSS symptoms. There is considerable discussion regarding the pathophysiological aspects of CSS and the need for controlled prospective studies in order to increase knowledge of the drugs related to its onset.

Treating asthma with high-dose inhaled corticosteroids and oral corticosteroids might reduce the frequency of vasculitis in susceptible populations. It is difficult to identify a specific population that is at a high risk for this rare syndrome.⁽¹⁾ Sex hormones could be considered potential determinants of asthma severity. Additional studies are needed in order to learn more about the pathological mechanisms involved in the interaction between asthma and sex hormones.^(3,6) In view of the lack of controlled studies in the literature and based on the clinical evolution of the case reported here, the combination of symptoms appearing after the patient had begun taking oral contraceptives, as recounted by the patient herself, leads to the suspicion that oral contraceptives are a trigger factor for CSS.

In cases of CSS, systemic corticosteroids can

be started in the initial phase of the treatment. When the patient presents vasculitis, a one-year course of corticosteroids and cyclophosphamide (2 mg/kg/day oral) is recommended. Methotrexate (15-25 mg, once a week) can also be used. Cyclophosphamide acts by inhibiting T cells, B cells, and macrophages. The side effects include leukopenia and hemorrhagic cystitis. There is a relationship between efficacious treatment and a reduction in blood eosinophilia. The levels of immunoglobulins and antineutrophil cytoplasmic antibodies also decrease. Alternative treatments include the use of trimethoprim/sulfamethoxazole, as well as pulse therapy with cyclophosphamide, interferon and intravenous immunoglobulin. Experimental treatment using the combination of a tumor necrosis factor antagonist and a monoclonal tumor necrosis factor antibody has been tested.

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