CASE REVIEW: CYCLOPHOSPHAMIDE THERAPY IN CHURG-STRAUSS SYNDROME

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SUMMARY

This report describes a 35- year old male patient known to have bronchial asthma since 16 years, lastly he presented with arthralgia, cutaneous vasculitis, pulmonary infiltration and polyneuropathy. The patient was diagnosed as having Churg-Strauss syndrome according to the pathological, clinical and blood works results which together fulfills the criteria of ACR (American College of Rheumatology). Successful treatment was achieved with cyclophosphamide.

INTRODUCTION

Churg-Strauss syndrome (CSS) is a rare diffuse vasculitis that is almost invariably accompanied by severe asthma 1. This syndrome was first described by Churg and Strauss in 1951 (two pathologists) as allergic granulomatosis and angiitis, a clinicopathologic entity in which necrotizing vasculitis, tissue infiltration by eosinophils and extravascular granulomas were present 2.

Lanham et al. 3 emphasized the distinct clinical presentation rather than the pathologic findings based on series of 16 patients and the review of another 138 reported in the literature. They identified three phases of the disease. The aprodromal period, which last for years (over 30 years), consists of manifestations of allergic rhinitis and nasal polyposis. It is frequently followed by asthma. The second phase of the disease is characterized by the onset of peripheral blood and tissue eosinophilia producing a picture similar to Loffler syndrome, chronic eosinophilic pneumonia, or eosinophilic gastroenteritis. The eosinophilic infiltrative disease may remit and recur over the years before the systemic vasculitis appears and defines the third phase of the disease 3, although these three phase do not necessarily have to follow one another in this order 4.
In 1990, The American College of Rheumatology (ACR) developed criteria for epidemiologic and therapeutic studies: I- Asthma, II- Peripheral blood eosinophilia >10% on differential WBC count, III- Mononeuropathy (including multiplex) or polyneuropathy, IV- Nonfixed pulmonary infiltrates on radiology, V- Paranasal sinus involvement, VI- Biopsy specimen showing vaculitis with extravascular eosinophils. These ACR criteria provide adequate sensitivity, specificity, and statistically significant discriminating ability to permit classification of the disease. These ACR criteria were developed by comparing 20 patients with CSS and 787 patients with other forms of vasculitis; the presence of four or more criteria yielded a sensitivity of 85% and specificity of 99.7%.5

CASE REPORT

On 24 June 2001, we admitted a 35 years old Saudi male to the Rheumatology Department in Assir Central Hospital with severe bronchial asthma and polyarthralgia, his is known to have bronchial asthma for 16 years, treated with monthly intramuscular long acting steroid for 14 years then shifted to inhaled steroid and bronchodilators with reasonable control of his symptoms for the last 2 years.

Two months ago the patient developed cough with occasional heamoptysis, progressive shortness of breath and wheezes. His medication was no more effective; and he had frequent visits to the emergency department in peripheral hospitals. He also suffered from frontal headache, joint pain without swelling involving wrists, knees, ankles. At the same time he started to have burning sensations in the soles of his feet, numbness over the lateral part of the right thigh, severe pain and numbness of the right thumb and the lateral three and half fingers of the right hand. One week before admission to the hospital he developed painful skin blister over the inner aspect of the right thigh and multiple painful purpuric skin eruption on the palm of both hands. He had no urinary or gastrointestinal symptoms. He had no fever but he lost around 5 Kg of his weight over 2 months.

On examination the patient was looking ill, tachypnic but not cyanosed. His blood pressure was 130/80 mm hg with regular pulse 100/min, respiratory rate 26/min with normal temperature (37 C°). Chest examination revealed diffuse bilateral expiratory ronchi, and signs of moderate bilateral pleural effusion. Cardiovascular and abdominal examinations were normal with normal JVP level. Neurological examination showed normal cranial nerves. Wasting of the right thenar muscle and weakness in flexion, abduction and opposition movements of the right thumb (power 3/5). Hypoesthesia along the distribution of right median and right lateral cutaneous nerve of the thigh. On his skin there were
tender erythematous blistering lesion over the inner side of the right thigh and painful purpuric eruption on the palm of both hands.

The results of his investigations were: ESR 68 mmhg, CBC: WBCs 8000/ul (41% eosinophil, 40% neutrophill, 17% lymphocytes and 2% monocytes), Hb 15.8g/dl, Plt 290000/ul. Normal blood chemistry including renal function tests and serum electrolytes. Normal urine analysis with normal 24/h urinary protein excretion (88mg/24h). Sputum examination and cultures including for acid fast bacilli were negative.

Immunological panel: positive rheumatoid factor, negative results for antinuclear antibodies, perinuclear and cytoplasmic antineutrophil cytoplasmic antibodies (p-ANCA and c-ANCA).

Pleural fluid was exudative with WBCs count 2600c/hpf (58% lymphocytes, 39% neutrophill, 3% monocytes), RBC 50c/hpf and no growth on the culture/sensitivity plates.

Echocardiography revealed normal size left ventricle with good function (EF >55%), mild pericardial effusion, valves were normal.

Radiographic evaluation of the chest (figure 1) showed moderate amount of bilateral pleural effusion associated with underlying partial atelectasis, mainly in the medial segment of the right lobe. The subtended bronchus is patent with no evidences of mediastinal adenopathy.

CT para-nasal sinuses showed soft tissue opacification of both maxillary and sphenoid sinuses with an fluid-air level in maxillary sinuses bilaterally. Associated haziness of ethemoid cells is noted with no obvious bony destruction was detected.

Skin biopsy (figure 2) showed ulceration of epidermis, the medium and small vessels of superficial and deep dermis showed features of necrotizing vasculitis, thrombosis, fibrinoid deposits with eosinophilic infiltration. Dermal infiltration by eosinophils and extravascular eosinophilic granuloma. The subcutaneous fat shows septal necrosis. The histological features are consistent with allergic granulomatosis (Churg-Strauss Syndrome).

According to the clinical, radiological and pathological results the patient was diagnosed as Churg-Strauss syndrome and accordingly treatment with pulse methyl predinosolone (1 gram intravenously for three successive days) was started followed by oral corticosteroid (1mg/kg/day). The patients showed unsatisfactory improvement especially his polyneuritis and vasculitic manifestation. So, single dose of pulse cyclophosphamide (10mg/kg. IV) Was given 2 weeks later followed by oral cyclophosphamide (2mg/kg/day) which resulted in marked improvement of his symptoms with reduction in peripheral blood eosinophilia as noticed during his regular
follow up in outpatient rheumatology clinic. After 3 months of treatment, gradual tapering of corticosteroid and cyclophosphamide was discontinued after 6 months. Continuous follow up showed complete clinical recovery without relapse for the last three years.

Figure. (1): Plain X-ray of the chest shows bilateral pleural effusion with pneumonic consolidation of middle lobe.

Figure. (2): Shows feature of necrotizing vasculitis of small and medium sized vessels with fibrinod deposits and eosinophilic infiltration.
DISCUSSION

Churg-Strauss syndrome (CSS) is a rare disease and the diagnosis of CSS can be difficult because the syndrome may arise at first as a common association between asthma and allergic rhinitis and asthma itself may be associated with sinusitis, occasional pulmonary infiltrates (e.g., mucous plugging, atelectasis or intermittent infection). Anyhow, the diagnosis of CSS is made on the basis of clinical features and confirmed by the pathological study. Patients are usually middle-aged and have a history of asthma that has been present for several years. In addition to, allergic rhinitis and eosinophilia, the appearance of systemic illness characterized by mononeuritis multiplex, pulmonary infiltrates, cardiomyopathy, and calf pain or cramps should lead the physician to consider the diagnosis of CSS.

Although asthma is the single best discriminator in the classification scheme, it often abates with the onset of vasculitis. Pulmonary infiltrates are a central feature of CSS and commonly include transient patchy infiltrates, nodular infiltrate without cavitation, and diffuse interstitial disease. Less common radiographic abnormalities are hilar adenopathy and pleural effusions which frequently contain large numbers of eosinophils.

Cutaneous and subcutaneous lesions, so-called Churg-Strauss granulomas, develop in more than two thirds of patients with CSS and include palpable purpura, subcutaneous nodules, erythematous papules and macules, vesicles and bullae, cutaneous infarction, livido reticularis, urticaria, ulceration, and facial edema. Although the various skin lesions are nonspecific, and 50% of such lesions occur in a variety of systemic diseases other than CSS, identification of such skin findings, accompanying other clinical features of the disease, may lead to an early diagnosis of CSS and, with treatment, prevent irreversible tissue damage.

Before the use of corticosteroids, CSS was thought to be uniformly fatal, the majority of death occurring as a result of congestive heart failure or myocardial infarction. Corticosteroids are the first line of therapy with initial dose of 40 to 60 mg/day and dramatic response have been reported with the use of intravenous cyclophosphamide and pulse methylprednisolone. The duration of required treatment for vasculitis appear to be less than one year and remission of vasculitis occur in most case, but the length and regimen of therapy needs to be individualized and continuous observation for CSS patients to avoid any hidden vasculitic complication or relapse, which may need further treatment by intravenous immunoglobulin associated with plasmapheresis in addition to the standard treatment (prednisolone and cyclophosphamide).
Conclusion:

Although patients with CSS respond well to corticosteroids, the addition of immunosuppressive treatment such as cyclophosphamide is recommended and the decision to use immunosuppressive should be based on the severity of the disease as higher mortality strongly associated with cardiac, gastrointestinal and renal involvement or severe polyneuropathy or inadequate response to corticosteroid.

REFERENCES


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