

Case Report

Severe Hypereosinophilia in an Asthmatic Young Female

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ABSTRACT

We present a case of a young asthmatic lady who presented with multiple systemic manifestations associated with severe eosinophilia. She proved to be a classical case

of Churg-Strauss syndrome. She was treated with corticosteroids only. She made a complete recovery and does not show any signs of relapse to date.

KEYWORDS: asthma, Churg-Strauss syndrome, hypereosinophilia, necrotizing vasculitis

INTRODUCTION

Churg-Strauss Syndrome (CSS) is a very rare systemic disease with clinico-pathological features that overlap with those of polyarteritis nodosa and Wegener's granulomatosis. It makes up to 20% of systematic vasculitis with an incidence of 30% of that estimated for Wegener's granulomatosis (5.3 per one million patients per year)^(1,2). It occurs almost exclusively in patients with asthma or history of allergy.

CASE REPORT

A 31-year-old Kuwaiti lady was admitted to our medical ward in March 2004 with a two weeks history of malaise, myalgia, neck pain and plantar fasciitis followed by one week history of productive cough and yellowish sputum. Soon after admission her cough improved while other symptoms persisted. Four days later she started developing skin lesions on her fingers, toes and elbows associated with arthralgia in addition to bilateral feet numbness. The patient was a known case of bronchial asthma, sinusitis and otitis media with several surgeries for the latter two conditions over the last eight years. Her asthma had gotten worse over the last three years with frequent exacerbations that needed short courses of steroid for control. Clinical examination initially was unremarkable but later showed vasculitic rash on previously mentioned areas.

Her investigations showed leukocytosis with severe eosinophilia (WBC = 16×10^9 , eosinophils count 8.7×10^9 , 53.8%), high erythrocyte sedimentation rate (ESR = 107 mm/h), C-reactive protein (CRP = 71.6 mg/l), rheumatoid factor (RF =

101 iu/ml), perinuclear antineutrophil cytoplasmic antibodies (P-ANCA = 63 u/ml), IgE level (2312 iu/ml), low albumin level (28 g/dl), proteinuria and microscopic hematuria. Her electrocardiogram showed sinus tachycardia with T wave inversion in leads V1 to V3 that normalized later on while her chest X-ray showed right upper lobe fibrosis and left lower lobe pneumonitis with mild pleural effusion. Her pulmonary function test showed moderately severe bronchial asthma as her forced expiratory volume in first second (FEV1) was 1.59 liters (51% of predicted), forced vital capacity (FVC) was 2.24 liters (62% of predicted), FEV1/FVC ratio was 71%, residual volume (RV) was 3.2 liters (219% of predicted) while her FEV1 after bronchodilators was 1.8 liter. Her lower limb nerve conduction study showed a picture of early sensory neuropathy. A high resolution computed tomography (HRCT) chest revealed scattered pulmonary infiltrations while her echocardiography was normal (Fig. 1). Skin lesion biopsy showed picture of leukocytoclastic vasculitis while her kidney biopsy revealed no abnormality. Finally, a video assisted thoracoscopic lung biopsy showed evidence of necrotizing vasculitis with intensive eosinophil infiltration with granuloma (Fig. 2).

Her other investigations (including hemoglobin level, platelets count, renal, liver and thyroid function test, stool for parasites, serum Troponin levels, antinuclear antibodies, cytoplasmic(c)ANCA and blood for aspergillus antibodies) were all normal.

The diagnosis of CSS was made and she was started on prednisolone 60 mg daily. She showed immediate dramatic response with disappearance

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Fig. 1: High resolution CT chest shows scattered peripheral pulmonary infiltrations

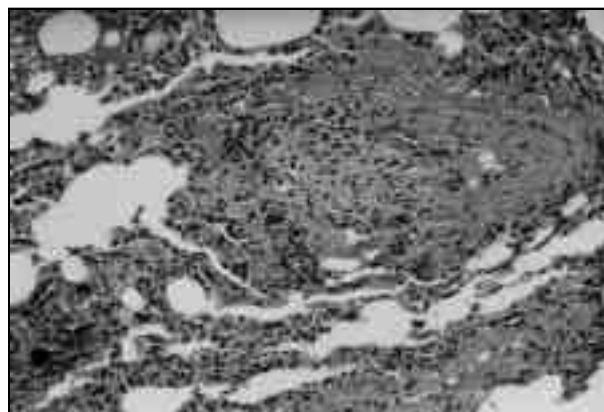


Fig. 2: Section from lung biopsy shows evidence of necrotizing vasculitis with intense eosinophil infiltration

of all symptoms, normalization of eosinophil count, ESR and HRCT chest picture. She remained in remission while her prednisolone dose was tapered over the next 16 months and then discontinued. Currently she is under close follow-up clinically, biochemically and radiologically for any possible relapse.

DISCUSSION

CSS is a necrotizing systemic vasculitis, which involves small vessels and is distinguished by asthma, hypereosinophilia and extra-vascular granuloma^[1]. Its prevalence varies in the general population with a frequency of 2.4 - 6.8 per one million patients per year. It is global in distribution with no significant gender predilection. It occurs in all age groups but is most common in third to fifth decade of life^[3,4]. The exact etiology is still unknown but allergic or immuno-pathogenesis was suggested^[2,3]. CSS was also described in association with macrolides and leukotrine receptors antagonists although evidence points clearly to steroids withdrawal unmasking the disease^[3-6]. Clinically it has three distinct consecutive phases: (1) prodromal phase that may persist for many years consisting of asthma often preceded by allergic rhinitis, which is often the first evidence of disease, (2) second phase of marked peripheral eosinophilia with tissue infiltration and (3) life-threatening vasculitis phase. Because of this, it may be difficult for non-specialists to recognize the disorder^[1,2]. Asthma usually precedes the development of vasculitis by period of weeks to years (0 to 30 years with an average of 6 years); it is often progressively severe and requires steroids for adequate control^[1,3].

The disease most frequently involves the lungs (100%), nerves (75%), skin (81%), heart (37.5%) and gastro-intestinal system. The pulmonary involvement is universal and manifests as transient pulmonary infiltration that antedate vasculitis in 40% cases^[2,7].

Peripheral nerve involvement is typical of mononeuritis multiplex while cranial nerve palsies are infrequent and when the former is seen in asthmatic patient with eosinophilia the diagnosis of CSS is almost certain^[2,4]. Skin lesions can occur in any form but palpable purpura is the most frequent form^[2,7]. Cardiac and gastro-intestinal involvement are the two major causes of morbidity and mortality with the former being responsible for 48% of deaths in one series^[1,2,7]. On the other hand, renal involvement which is a major and serious feature in other types of vasculitis occurs only in 20% of cases, commonly as mild hematuria with albuminuria and focal segmental glomerulonephritis while renal failure occurs in only 9% of cases^[3,7]. Laboratory features including high ESR, CRP and IGE level are non-specific while severe peripheral eosinophilia is the hallmark of CSS. ANCA, mainly perinuclear on the other hand is only positive in 50 to 75% of cases and so can be a valuable adjunct in supporting the diagnosis^[1,7].

Radiologically 27 to 93% of cases will show abnormality on chest radiograph (72% - non-segmental air space disease, 40% - transient Löffler's pneumonia, 67% - patchy multifocal peripheral consolidation) while thin section CT, which is abnormal in 88% to 100% of cases often shows subpleural consolidation with lobular distribution, centrilobular perivascular densities, and bronchial wall thickening^[2].

Although CSS can be readily diagnosed on clinical grounds, histological confirmation should always be sought whenever possible by biopsy of any involved organ to confirm the presence of an eosinophilic infiltration or vasculitis^[2-4]. In our case, although the patient had a classical presentation of CSS and the skin biopsy showed evidence of vasculitis which was enough to make diagnosis, open lung biopsy (which is not needed for all cases) was still done mainly to rule out other types of necrotizing vasculitis that have different prognoses

and response to treatment.

Accurate diagnosis remains problematic as none of the features are pathognomonic and because asthma itself might be associated with sinusitis and pulmonary infiltration^[3,4]. For this reason, in 1990 the American College of Rheumatology developed six criteria, four or more of which are required for diagnosis. Although they were not designed for this purpose, they are still widely used (sensitivity and specificity of 85 and 99% respectively). They includes asthma, eosinophilia > 10%, neuropathy, non-fixed pulmonary infiltration, paranasal sinus abnormality and biopsy containing extravascular eosinophil infiltration^[7].

Treatment remains an unresolved problem given the rarity of the disease with no established protocol whose efficacy has been documented in trials^[1]. 40% of cases are treated with steroids alone for 12-18 months while immune suppressive agents are added only in life-threatening conditions such as severe CNS, cardiac and gastro-intestinal involvement or in those cases who do not respond adequately to steroids^[4,7]. Some authors recommend routine use of cyclophosphamide in all cases although this did not show improvement in 10 year survival rate and increased the rate of infection by 10%^[3-4]. Use of plasmapheresis alone did not offer additional benefit whereas when it was combined with intravenous immunoglobulin therapy a benefit was demonstrated in several case reports^[8]. Moreover, preliminary observations suggest efficiency of high dose alpha interferon in treating patients with incomplete response to steroids or infection complications^[9].

Overall, remission in CSS is 81 to 92% with a relapse rate of 26 to 28%. It could be 40% in first year but is much rare afterwards. The blood eosinophil count is the only sensitive indicator for activity or relapse as relapses are always preceded by an increase in the count^[4,7,9]. The overall prognosis is good with low mortality rate compared to other forms of vasculitis^[10].

In conclusion, recognition of CSS as separate disease entity is important because of its distinctive natural history, frequent rapid response to treatment and good prognosis that suggests a pathogenic mechanism different in nature and degree from other forms of vasculitis^[3]. All of the available classifications and definitions have obvious limitations especially in mild and limited disease or those who have already started steroid therapy. The difficulties highlight our need for better understanding of the underlying pathogenesis for purpose of diagnosis and other therapeutic interventions for some of the patients as currently case reports are plentiful but without evidence support.

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