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CHURG-STRAUSS SYNDROME: A RARE CASE REPORT AND A BRIEF REVIEW OF LITERATURE

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Abstract

Churg-Strauss syndrome (CSS) is a rare primary, non-inheritable, non-transmissible systemic disease, which occurs in patient with history of bronchial asthma. CSS is an eosinophil-associated, small vessel granulomatous vasculitis, characterized by late onset asthma, upper airway disease, eosinophilia, and clinical manifestations of systemic vasculitis. We report a rare case of Churg-Strauss syndrome. A 48-year-old male diagnosed case of bronchial asthma presented with history of progressive dyspnoea, fever, productive cough. He responds rapidly to corticosteroids.

Introduction

Churg-Strauss syndrome was first described in 1951 by churg and strauss[1]. Churg-Strauss syndrome (CSS) is a vasculitis of medium to small sized arteries and veins. The incidence is approximately 2.5 cases per 100,000 adults per year[2]. CSS was first described in 13 patients with deadly asthma who had the combination symptoms of asthma amd eosinophilia, rhinosinusitis and signs of vasculitis in the heart, pericardium, the nervous and gastroenteric symptoms[3]. It is characterized by a triad of clinical signs: asthma, hypereosinophilia and necrotizing vasculitis. Usually the patient's age range is between 20 and 40 years, and both men and women are equally affected[4]. It is important to recognize the disease and be aware of underdiagnosis because of emphasis on pathologic evidence. Here, we report a rare case of Churg-Strauss syndrome in the absence of other known factors.

Case report

A 48-year-old male presented with one month history of progressive dyspnoea, productive cough, fever of 102^0 F, wheeze despite antibiotic therapy. He had been diagnosed with bronchial asthma over 20 years before admission and he was on regular treatment with bronchodilators. He was a life long non-smoker. 2 days prior to admission, in addition to increased shortness of breath, blood streaks were present in his sputum and he developed gradual paresthesia in his lower legs.

On clinical examination, the patient was averagely built with a weight of 60kgs. Patient was conscious, oriented, febrile and was in respiratory distress with respiratory rate of 36 /min, pulse rate of 1110 /min, blood pressure of 140/90 mm of Hg. He had coarse crackles and generalized rhonchi and wheeze in the lung bases. The level of SPO2 upon admission was 74% and increased to 91% with administration of 6 liters of 40% oxygen via venturi mask. Our patient's hemodynamics were stable except for tachypnoea. Physical examination revealed skin nodules, urticarial rash and necrotic bullae over both lower limb. We suspected of Churg-Strauss syndrome with history of bronchial asthma.

Laboratory evaluation revealed a white cell count of 22,000 /mm^3 with 23% eosinophils with no anemia and the platelet count was 215,000 /mm^3. Erythrocyte sedimentation rate (ESR) was 28mm/h (N:0-10) with an absolute eosinophil count of 520 (N: <350 cells/mcL) and low albumin level (1.6 g/dl). C reactive protein (CRP) of 96 (N:

<10). Liver and renal function tests, blood coagulation studies and electrolytes were within normal limits. Urinalysis was normal. As we suspect of CSS and blood was send for perinuclear anti neutrophil cytoplasmic antibody (p ANCA) which turn to be positive. ECG showed heart rate of 110 beats/min in addition to specific findings of sinus tachycardia. Minimal myocardial fluid on ECHO found. Chest X-ray showed transient, patcht, nonsegmented areas of consolidation with bilateral basal infiltrates. Skin biopsy of lesion revealed focal, necrotizing vasculitis.
Clinical suspicious of Churg-Strauss syndrome was confirmed. We treated him with antibiotics, intravenous corticosteroids (methyl-prednisone) for 3 days as a pulse and then at a dose of 60 mg per day, i.e. 1 mg/kg/day. After 3 days of treatment , temperature normalized and dyspnoea diminished. After 15 days of therapy, skin lesions regressed. Then, prednisone dose was titrated according to the level of blood eosinophil. After 3 month treatment, the patient reported no signs or symptoms of the disease. Patient continues oral corticosteroid therapy at a dose of 10 mg of prednisone per day. Patient improved in 2 weeks with a given treatment and was discharged and under regular follow-up. We hereby describe a rare case report of Churg-Strauss syndrome with history of bronchial asthma.

Discussion

Churg-Strauss syndrome is an eosinophil-associated, small vessel granulomatous vasculitis, characterized by late onset asthma, upper airways disease, eosinophilia, and clinical manifestations of systemic vasculitis[5].
Churg and Strauss in their original 1956 article outlined three pathologic features associated with the disease: an eosinophilic tissue infiltration, granuloma formation, and a necrotizing vasculitis involving small and medium-sized vessels[6]. Lanham *et al*[7] . Proposed a combined clinical and pathologic diagnostic scheme (Table 1) and although the validity and accuracy of this schem has never been assessed objectively, it has nonetheless been widely used.
More recently, the American Rheumatology Association has proposed alternative diagnostic criteria for CSS[8]. The presence of at least four of six findings (Table 1) was diagnostic of Churg Strauss, with a sensitivity of 85% and a specificity of 99.7% within the source population[9].
The 1994 Chapel Hill consensus conference further defined CSS as an "eosinophil-rich and granulomatous inflammation involving the respiratory tract, and necrotizing vasculitis affecting small to medium sized vessels, and associated with asthma and eosinophilia"[10].

Table 1. Diagnostic criteria for the Churg Strauss syndrome

Lanham's criteria[7] :
asthma
peak peripheral blood eosinophil count > 1.5 * 10^6 /cc
systemic vasculitis involving two or more extrapulmonary organs.
ARA criteria[8, 9] (requires four of the following six findings)
asthma
eosinophilia >10% in blood
mono or polyneuropathy
migratoty or transient pulmonary opacities
paranasal sinus abnormality
extravascular eosinophils at biopsy
(ARA : American Rheumatology Association)

CSS is global in its distribution and has no significant gender predilection. It occurs in all age groups. The mean (95% confidence interval) annual incidence of CSS in northern England between 1988 and 1994 was 2.4 (0.9 to 5.3) per million population[11]. In a retrospective study from Norway, the estimated prevalence of CSS was 1.3 per 100,000 population[12].
Drug-induced Churg-Strauss syndrome (CSS) has been reported. Drugs implicated have included mesalazine, propylthiouracil, methimazole, freebase cocaine and leukotriene receptor antagonists[13].
CSS is unknown in origin. Suggestions are allergic or immune mediated. Etiology is considered to be autoimmune due to allergic symptoms, immune
Complex mediation 48% are (ANCA, antineutrophil cytoplasmic antibody) positive, increased T-cell mediated immunity, elevated immunoglobulin E

(IgE) levels and rheumatoid factor[14] . Also superantigen theory proposes that
Due to SAg, vascular wall destruction by autoreative T-cells may occur or autoreactive B-cells may form antibodies involved in formation of vasculitis[15].
The central feature of CSS is an eosinophil-associated small vessel vasculopathy Tai *et al*[16]. were able to demonstrate that activated eosinophils and eosinophil degranulation products were present within both vessel walls and granulomata
The pathophysiology of eosinophil-mediated disease has recently been reviewed elsewhere From the viewpoint of CSS, it is noteworthy that activated eosinophils are able to induce vascular endothelial cell activation[17].
Allergic rhinitis is often the first evidence of disease and occurs in up to 70% of cases[18] . It is frequently severe and may be associated with nasal polyposis, obstruction, and recurrent sinusitis, Asthma usually precedes the development of vasculitis by a period of weeks to years ; it is often progressively severe and eventually requires oral steroids for adequate control[19]. Gastrointestinal tract infiltration may present as eosinophilic gastroenteritisSystemic disease features during the vasculitic phase include weight loss, anemia, and fever. Rash occurs in up to 70% of cases[20]. Skin lesions are the most common extra-pulmonary finding in the course of the disease. The main types of skin lesions reported include erythematous maculopapules resembling erythema multiform, hemorrhagic lesions ranging from petechiae to extensive ecchymosis, often associated with wheals, necrosis and ulceration, and cutaneous and subcutaneous nodules that are usually deep-seated and tender with a predilection for the scalp and temple region[21].
Pulmonary involvement represents a vasculitic process with a varying degree of eosinophilic infiltration. It may be associated with progressive dyspnea, alveolar hemorrhage , pleurisy, and the development of eosinophil-rich pleural transudates[22]. Cardiac involvement is a common, although often late, manifestation of the disease. Acute pericarditis may occur in up to one-third of cases and may be associated with pericardial effusion. Cardiac tamponade may develop and should be considered before initiating aggressive fluid removal with dialysis. Myocarditis may lead to postinflammatory fibrosis and congestive cardiac failure, while coronary vasculitis may result in ischemic heart disease[23] .
Gastrointestinal involvement is common and often severe, resulting in abdominal pain, ascites, diarrhea, and/or hematochezia. It resulted in 8% of the deaths reviewed by Lanham in his literature review[7] . Involvement of vasa nervorum results in a mononeuritis multiplex and was found in 72% of cases in Guillevin's series and most commonly involved the common peroneal (84%) and the ulnar (55%) nerves[19] . Cerebral vasculitis may predispose to hemorrhagic cerebrovascular events, especially in association with uncontrolled hypertension.
Traditionally, renal involvement in CSS has been reported as being mild. In Churg and Strauss' original report, they comment that mild hematuria and albuminuria were commonly present. Chumbley reported that the incidence of renal involvement was 20%.
Lanham *et al*[7]., in his literature review, found 49% of cases to have mild or moderate renal involvement and renal failure in 9%.
Typical laboratory findings in CSS include a normochromic normocytic anemia, leukocytosis, and an acute-phase response with elevated erythrocyte sedimentation rate and C-reactive mprotein levels. Approximately one-half to two-thirds of reported patients with CSS are ANCA-positive[24].
According to Reid et al[25] and Della Rosa et al[26] positive ANCA may be found in 39 to 59% of patients with CSS. Sable-Fourtassou et al[27] found the predominance of glomerulonephritis and peripheral neuropathy among positive ANVA patients, and more frequent cardiac involvement, and fever, among ANCA negative patients.
Histological diagnosis is by demonstration of vasculitis that is necrotizing, tissue infiltration with eosinophils and extra-vascular granulomas are found in a few cases[28]. The most common radiographic pulmonary manifestations of Churg-Strauss syndrome consist of bilateral and transient non-segmental areas of consolidation, without any predilection for any pulmonary region, resembling Loeffler's syndrome, or may be predominantly peripheral (50% of cases), resembling chronic eosinophilic pneumonia or organizing pneumonia[29]. high-resolution computed tomography, the most common findings include subpleural ground glass opacities or consolidations with lobular distribution, centrilobular nodules, bronchial wall thickening, and interlobular septal thickening. Less common findings include hyperinsufflation, hilar or mediastinal lymph node enlargement, pleural or pericardiac effusion, and also small or large nodular opacities which rarely cavitate[30].
The differential diagnosis includes Wegener's granulomatosis, drug reaction, Bronchogenic granulomatosis, fungal and parasitic infections, and malignancy.

Included in the differential diagnosis are immune mediated diseases such as idiopathic thrombocytopenic purpura, cryoglobulenemia, and collagen vascular
Diseases.
CSS frequently responds rapidly to corticosteroids (4). Corticosteroids suppress gene transcription of various cytokines, and inhibit the prolongation of eosinophil survival in extravascular tissues[31]. Treatment regularly is with prednisone starting at 40-60mg a day and the occasional addition of cyclophosphamide or azathioprine with the purpose to limit the disease or
Spare steroids[32]. In case of fulminant disease or multi-organ involvement, parenteral corticosteroid such as methylprednisolone is used. If response to mentioned treatment is not seen, parenteral immunoglobulin is administered. Newly experimental medications for unresponsive cases are mycophenolate mofetil and tumor necrosis factor (TNF)-a blockers (such as etanercept and infliximab). Treatment is continued at least one month after remission. Uncommon but presented as case report has been also cardiac function improvement (ejection fraction increased from 28 to 67%) after a year of
corticosteroid therapy[33].
In particular, in steroid-sensitive patients, the potential long-term complications of cyclophosphamide may negate any additional benefits of its use. Interferon-a is also a potent inhibitor of eosinophil effector functions34 . It has recently been reported to achieve control in four patients with aggressive disease, two of whom had achieved an incomplete remission after treatment with steroids and cyclophosphamide . Azathioprine , cyclosporine , and immunoglobulin infusions have also been used in an adjuvant setting in CSS, although their role in disease treatment remains uncertain[35].
CHURG et al[36]. have previously reported the appearance of Churg-Strauss
syndrome in steroid-dependent asthmatics whose corticosteroids were decreased or eliminated.
Oral tacrolimus in combination with methylprednisolone and cyclophosphamide was used successfully in the treatment of a child severely ill with CSS[37]. Gastrointestinal transplantation in a patient with severe gastrointestinal involvement has been Reported[38].
Complications of vasculitis depend on the specific organ system involvement.
Cardiac and neurological complications are particularly serious and are more likely in patients with a delayed diagnosis[39].
Although the overall prognosis is good, and treatment with prednisone alone or in combination with immunosuppressive drugs is usually successful, severe asthma typically persists. Without treatment, the five-year survival rate is about 25%. With treatment, the one-year survival rate is 90% and the five-year survival rate is 62%[40].
It is important to diagnose the disease as it is frequent and requires immediate attention.
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Conclusion

The Churg Strauss Syndrome is an eosinophil-associated small vessel vasculitis. Although its pathogenesis may be distinctive and the association with severe late-onset asthma typical, the clinical features during the vasculitic phase widely overlap with those of the other forms of necrotizing vasculitis, and no single clinical or histologic feature is pathognomic of the condition.

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