

Churg Strauss Syndrome: a Review

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Abstract

Background: Churg Strauss syndrome is a medical condition of unknown aetiology characterized by asthma, eosinophilia and finally vasculitis involving small vessels in the limbs and nasal sinuses and the lungs. The purpose of this review is to highlight the natural history of this condition, the pathogenesis, clinical features and treatment modalities available and the prognosis.

Methods: Literature on the subject was reviewed using manual library search, articles in journals, internet search and conference abstracts.

Result: Churg Strauss syndrome has been reported to be predominantly common in middle aged individuals in their middle age of life with a history of new onset or worsened asthma. The condition has a male predisposition. Prior to the advent of steroid therapy this condition invariably leads to death, but since the introduction of prednisolone therapy and other immunosuppressive therapy, the outlook has improved for sufferers and long term survival has been seen.

Conclusion: Suspicion of this condition should be based on a good history, physical examination and laboratory investigations and diagnosis based on the criteria that has been drawn by the American College of Rheumatology.

Keywords: Asthma, Churg Strauss syndrome, Eosinophilia, Vasculitis.

Date Accepted for Publication: 11th March 2010

NigerJMed 2010: 136 - 139

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Introduction

Churg Strauss syndrome is an extremely rare condition which results from vasculitis of vessels. The inflammation leads to systemic organ damage chief among them being the skin, lungs, kidneys, nerves, nasal sinuses, joints, intestinal tract and the heart¹. There is almost always a history of asthma and allergic rhinitis². The inflammation is accompanied by peripheral blood eosinophilia and tissue invasion by eosinophils. These changes are seen along

with granulomatous lesions that appears as vasculitis on tissue biopsy. The vasculitis can present either as weakening of the blood vessels leading to formation of aneurysm and bleeding or to narrowing of vessels to the point of obliterating such vessels with resultant blockage and organ damage.

Although CSS is a rare disease, it is however often seen in clinical practice. Misdiagnosis is due to the clinician failure to have a high index of suspicion. This has resulted in many high profile patients seeking treatment overseas.

Historical perspective

This condition was first described by Dr Jacob and Dr Lotte Strauss³ in 1951. They described it as a syndrome consisting of asthma, eosinophilia, fever and an accompanying vasculitis involving several organ systems. CSS shares several clinical and pathological features with another type of vasculitis known as polyarteritis nodosa (PAN)⁴. Churg and Strauss were able to identify that this clinical entity differs from PAN by the presence of granulomas and peripheral blood eosinophilia. CSS is also known as allergic granulomatosis⁵.

Etiology/pathogenesis

The cause of CSS is unknown. It is not a form of malignant condition nor is it contagious. There is no evidence that CSS is contagious nor for a familiar inheritance⁶. Evidence from the laboratory has shown that the immune system plays a key role in the pathogenesis⁷. An over reactive immune system due to an unknown stimulus results in immense production of eosinophils. The granule content of the eosinophils finally leads to vasculitis which leads to damage of blood vessels⁸. Recent finding has linked the CSS to the presence of the antineutrophilic cytoplasmic antibody (ANCP) and the characteristic vasculitis⁷. However the association with asthma and eosinophilia remains unexplained⁹.

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Epidemiology

CSS can occur in all age groups from childhood to the elderly. The average age of patients at the time of diagnosis is between 35-50 years old. There is a male predominance in this disorder⁶.

Clinical features

The typical patient with CSS presents with asthma in 100% of patients. Asthma symptoms may begin long before the onset of vasculitis which may be many years before any other symptom of CSS arising⁸. Other early symptoms and signs include nasal polyps and allergic rhinitis in 61% of patients. There may be anorexia with loss of weight, fever and myalgias in 50-70% of cases. The next stage is the finding of an increase number of eosinophils in the blood usually > 15% and sometimes in excess of 60%. The final diagnosis in the disease process is the development of vasculitis which involves the skin, nose, lungs, nerves and kidneys and other organs¹. Involvement of the nerve may result in the devastating medical condition known as mononeuritis multiplex which induces severe tingling sensation, numbness, shooting pains and muscle wasting/ power loss in the hands or feet in 78% of patients¹⁰.

Morphological changes

The changes affecting various organs in CSS usually include the nose, lungs, skin kidney, gastrointestinal tract, heart and the nerves¹². In the nose, sinusitis including allergic rhinitis and nasal polyps are the main findings⁸. Figure 1 below shows the changes that occur on the septum of the nose.

In the lungs, pulmonary infiltrates are seen in 1/3rd of patients. Bleeding into the lungs is occasionally seen, while diffuse interstitial lung disease is rare¹³. Pleural effusions are seen in a third of cases. The effusions may be exudative and may contain a significant number of eosinophils¹⁴.

Skin changes including rashes and palpable purpura and nodules above and below the skin are the main picture seen often at sites of pressure such as the elbows and this is evident in about 50% of cases. There are palpable purpuras in 29% of patients while skin nodules and urticarias are found in 29% and 8% respectively in affected individuals¹⁵. Figure 2 below shows the skin changes at the elbow.

In the kidneys, glomerulonephritis and hypertension are the main changes seen and they are found in about 25% of individuals. In most cases these affection appears to be mild¹⁶.

The gastrointestinal tract is characterized by vasculitic lesions which are occasionally found while granulomas are sometimes seen in the spleen¹⁷. In the heart vasculitic lesion can lead to congestive heart failure or heart failure⁸. Involvement of the nerves are usually confined to peripheral nervous system and results in pain, numbness or tingling in the extremities (neuropathy/ mononeuritis multiplex)¹⁰.

Laboratory investigations

In addition to a good and detailed history a careful physical examination will be able to elicit some of the changes involving various organ systems. Full blood counts will reveal an increase in the eosinophil count (see figure 3 below), all other cells may remain normal or within limit. Chest x ray and other imaging technique may help to show other changes in the lung¹⁸. Nerve conduction studies and tissue biopsy from skin, lung and nerve may contribute to the diagnosis¹⁷. The ESR is invariably increased in 90% of individuals and may be accompanied with mild anaemia. Majority of patients with CSS appears to have positive antineutrophil cytoplasmic antibody (ANCA)⁷. An increased level of IgE is indicative of disease severity⁶.

Diagnosis

In order to arrive at a diagnosis, the American College of Rheumatology has established certain criteria that must be satisfied before classifying anybody as having CSS. These criteria are designed to differentiate CSS patients from those having other forms of vasculitis for example PAN. Not all patients meet all the criteria. Some may have only 2 or 3 of the criteria and they may be classified as having CSS. In order to avoid this pitfall, the American College of Rheumatology selected 6 disease features to help in making a diagnosis and differentiating CSS from other vasculitides. In order to make a diagnosis a patient must have at least 4 of the following criteria¹⁹:

1. Asthma
2. Eosinophilia > 10% of differential WBC count
3. Mononeuropathy
4. Transient pulmonary infiltrates on chest x ray
5. Paranasal sinus abnormalities
6. Biopsy of a vessel containing extravascular eosinophils

Treatment and prognosis

Treatment depends on severity symptoms and the involvement of organ damage. In patients with mild disease, systemic corticosteroid may be sufficient²⁰. When major organs are involved with necrotizing

vasculitis, cytotoxic therapy must be undertaken with cyclophosphamide as the drug of choice, although there are data that appear to suggest that the use of high dose intravenous steroid therapy may result in remission in more than 90% of patients. Relapse can occur in 26% of patients and even with aggressive treatment death has been described in 25% of patients²¹. The cause of death in most patients with CSS was vasculitis related primarily, affecting the cardiac and mesenteric vessels²¹.

In general, CSS usually respond to prednisolone. Initially high doses of oral prednisolone are given in order to produce remission as quickly as possible. This will entail giving a start dose of 40-60 mg daily in divided doses for a period of about a month and then tapering the dose in the subsequent month depending on the response of this initial dose. Other immunosuppressive drugs which may help in the control of this condition include Azathioprine, Cellcept, Methotrexate or Cyclophosphamide either as single dose or in combination²². In addition to the regimen above, intravenous steroid such as methylprednisolone and plasmapheresis may be used in patients that did not respond to prednisolone or other immunosuppressive regimen²⁰.

Prior to the advent of prednisolone, CSS was often a fatal disease the majority of patients dying from rampant uncontrolled disease. With present therapy constitutional symptoms begin to recede quickly with gradual improvement in cardiac and renal functions as well as improvement in the pain that results from peripheral involvement. The course of therapy may last for 1-2 years, although the length and type of treatment depend on the severity of disease and organ involved. The patient's response to treatment and continuation of disease control during lowering of prednisolone dose are the primary determinate on how long therapy is continued. Laboratory monitoring of blood tests is very helpful in gauging the activities of disease. Some of the most useful laboratory tests are the erythrocyte sedimentation rate and the WBC count and differentials.

However the five year survival ranges from 62-79% with mortality strongly associated with cardiac, gastrointestinal and renal involvement⁵. Nevertheless, after treatment with corticosteroids, relapses are frequent in 25% of cases even after recovering from vasculitis most patients (95%) still have asthma requiring corticosteroid therapy²⁰.

Conclusion

With the advent of prednisolone CSS, which in the past carried a dismal prognosis has now been brought under

control. However the benefits of steroid and other immunosuppressive therapy will not mean much if a proper diagnosis is not reached before the onset of organ damage. Therefore it is incumbent on physicians to have a high index of suspicion when the physical examination and the white cell count are suggestive of CSS and to institute early treatment.



Figure 1 showing ulceration of the nasal septum



Figure 2 showing a granulomatous lesion on the elbow.

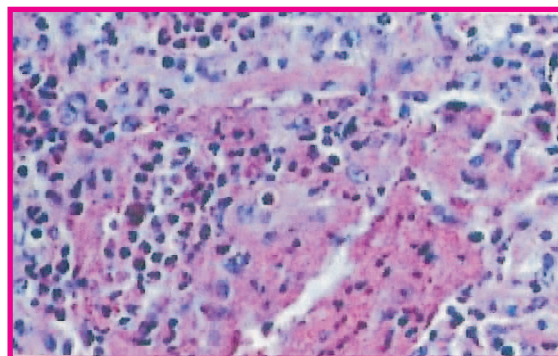


Figure 3 showing the peripheral blood with eosinophilia

References

1. Montano A. Churg Strauss syndrome. Program and abstract of the 58th annual meeting of the American College of Allergy, Asthma and Immunology. Nov 3 8, 2000: Seattle, Washington.
2. Masi AT, Hunder GG, Lie JT, Michel BA, Bloch DA et al. the American College for the classification of Churg Strauss syndrome (Allergic granulomatosis and Angiitis). *Arthritis Rheum* 1990; 33: 1094 1100.
3. Churg Strauss Syndrome. Program and abstract of the 58th annual meeting of the American College of Allergy, Asthma and immunology NOV 3 8, 2000: Seattle Washington.
4. Fredrick J, Schoen FJ, Ramzi SC. Blood vessels. Robin's pathological basis of disease. Contran RS, Kumar V, Collins T. 6th edition, Philadelphia, WB Saunders, 1999 page 493 541.
5. Ramakrishna G, Midthurn DE. Churg Strauss syndrome. *Ann Allergy, Asthma and Immunol* 2001, 86: 603 613.
6. Pagnoux C, Guilpan P, Guillerin L. Churg Strauss syndrome. *Curr Opin Rheumatol* 2007; 19: 25 32.
7. Sable Fourtassou R, Cohen P, Maher A. Antinutrophilic cytoplasmic antibodies and the Churg Strauss syndrome. *Ann Intern Med* 2005; 143: 632 638.
8. Schwarz MI, Brown KK. Small vessel vasculitis of the lungs. *Thorax* 2000, 55: 502 51.
9. Noth AT, Streck ME, Leff AR. Churg Strauss syndrome. *Lance* 2003; 361: 587 594.
10. Hashida G, Kan A, Inoue S, Abe K. Rehabilitation method for Churg Strauss syndrome from early stage: considering functional prognosis of mononeuritis multiplex. *No To Shinkei* 2006; 58(5): 425 9.
11. Lanhan JG, Elken KB, Pusey CD, Hughes GR. Systemic vasculitis with asthma and eosinophilia: A clinical appraisal to Churg Strauss syndrome. *Baltimore J Med* 1984; 63: 65 81.
12. Bacciu A, Bacciu S, Mercante G. Ear, Nose and Throat manifestation of Churg Strauss syndrome. *Acta Otolaryngol* 2006; 126: 503 509.
13. Conron M, Huw LCB. Churg Strauss syndrome. *Thorax* 2000; 55: 870 877.
14. Chen KR, Sakamoto M, Ikemoto K, Abe R, Shimizu A. Granulomatous arteritis in cutaneous lesions of Churg Strauss syndrome. *J Cutan Pathol* 2007; 34(4): 330 337.
15. Guilevin L, Cohen P, Gayraud. Churg Strauss syndrome, clinical study and long term follow up of 96 patients. *Baltimore J Med* 1999; 78: 26 37.
16. Oh MJ, Lee JY, Kwon NH, Choi DC. Churg Strauss syndrome: the clinical features and long term follow up of 17 patients. *Korean J Med Sci* 2001; 21: 265 271.
17. Pela G, Tirabassi G, Patoneri P. Cardiac involvement in the Churg Strauss syndrome. *Am J Cardiol* 2006; 97: 1519 1524
18. Masi AT, Hunder GG, Lee JT. The American College of Rheumatol 1990 criteria for the classification of Churg Strauss syndrome. *Arthritis Rheum* 1990; 3: 1094 1100.
19. Yael W. Intravenous immunoglobulin with plasmapheresis improves outcome of Churg Strauss syndrome therapy. *Ann Rheum Dis* 2004; 63: 1649 1653.
20. Solans R, Bosch JA, Perez Bocanegra C, Selva A, Huguet P et al. Churg Strauss syndrome: outcome and long term follow up of 32 patients. *Rheumatology (Oxford)* 2001; 40: 763 771.
21. Lhote F. Churg Strauss syndrome. *Presse Med* 2007; 36(5 Pt 2): 875 889.