CASE REPORT

# Churg-Strauss Syndrome: A Series of Two Cases

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## ABSTRACT

Churg-Strauss syndrome (CSS) is a multisystem vasculitic disease, which can involve the upper and the lower airways, peripheral nerves, and presents as a characteristic peripheral blood and tissue eosinophilia. We report two cases of CSS.

**Keywords:** Vasculitis, peripheral nerve, eosinophilia

Churg-Strauss syndrome (CSS) is a systemic vasculitis characterized by the presence of asthma, hypereosinophilia, and necrotizing vasculitis with extravascular eosinophilic granulomas. Three phases have been described in the natural history of the disease (rhinitis, asthma, vasculitis), although they do not always occur successively. The American College of Rheumatology has proposed 6 criteria for CSS classification, 4 being necessary for CSS to be diagnosed with 85% sensitivity and 99.7% specificity: Asthma, eosinophilia >10%, paranasal sinusitis, pulmonary infiltrate, histologic proof of vasculitis, and mononeuritis multiplex. Although not a criterion for the diagnosis, the presence of antineutrophil cytoplasmic autoantibodies (ANCA) is now established as being associated with it. CSS has to be distinguished from other conditions associated with peripheral blood eosinophilia and pulmonary infiltrates some of which are given in below.

**Etiology known:**

- Allergic bronchopulmonary aspergillosis (ABPA)
- Parasitic infestations
- Drug reactions
- Eosinophila – Myalgia syndrome

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**Idiopathic:**

- Loeffler's syndrome
- Acute eosinophilic pneumonia
- Chronic eosinophilic pneumonia
- Allergic granulomatosis of CSS
- Hypereosinophilic syndrome.

## FIRST CASE REPORT

A 35-year-old male came to our hospital with history of episodic breathlessness and wheezing suggestive of asthma, rhinitis, sinusitis and itching all over body since 6 months. He had been prescribed antihistaminics by a general practitioner outside which he had been taking since 6 months without any relief in symptoms. On examination patient had bilateral scattered rhonchi in chest and on routine investigations, he was found to have a peripheral blood eosinophilia of 57% (total counts were 14,100 of which 8,400 were eosinophils), bilateral pulmonary infiltrates and X-ray paranasal sinuses (PNS) view was suggestive of right maxillary sinusitis. An high-resolution computed tomography (HRCT) was done which confirmed bilateral pulmonary reticular infiltrates without evidence of bronchiectasis. Stool culture for ova cyst was negative. Patient did not have any evidence of vasculitis or neuropathy and was not affordable for perineuclear ANCA (p-ANCA) but since 4 out 6 essential criteria for diagnosis of CSS were present a probable diagnosis of CSS was made and patient was put on oral corticosteroids (prednisolone 40 mg once a day) and inhaled steroids 800 µg/day. After 4 weeks, patient's symptoms improved. Breathlessness and cough was reduced with no rhonchi in chest and reduced itching over body with chest X-ray showing clearing of pulmonary infiltrates. Patient was put on tapering dose of steroids and is awaiting second follow-up after 2 months.

## SECOND CASE REPORT

A 32-year-old male came to our hospital with complaints of breathlessness and cough since 6 months, rhinitis and sinusitis since 6 months and weakness in his left lower foot and left hand since about 1 month. On examination patient had bilateral maxillary sinus tenderness and chest examination revealed bilateral rhonchi. Central nervous system (CNS) examination revealed left sided foot drop with left wrist drop. On laboratory investigations patient had 52% eosinophilia (with total count being 18,000 and eosinophil count 9,360/cumm). Chest X-ray showed bilateral pulmonary infiltrates and X-ray PNS showed bilateral maxillary sinusitis. EMG showed reduced nerve conduction velocities in left radial nerve and left common peroneal nerves respectively, suggestive of mononeuritis multiplex. An HRCT was done which showed bilateral pulmonary infiltrates. Stool culture for ova/cyst was negative and ruled out any parasitic infection. Patient did not have any evidence of vasculitis and was not affordable for p-ANCA. A probable diagnosis of CSS was kept as 5 out of 6 essential criteria required for CSS were present. Patient was put on oral and inhaled corticosteroids (oral prednisolone 40 mg/day and beclomethasone 800 µg daily). Patient was reviewed after 1 month and showed improvement. Breathlessness and cough was reduced with no rhonchi in chest. Chest X-ray showed clearing of pulmonary infiltrates with reduced haziness in PNS X-ray.

## DISCUSSION

### History

Jacob Churg and Strauss from the Division of Pathology at Mount Sinai Hospital in New York were the first to publish a series of 13 autopsy cases with the clinical symptoms of severe asthma, fever and hypereosinophilia, accompanied by vascular embarrassment in various organ systems, in 1951.

### Incidence

CSS is slightly more common in males than in females. The age at onset varies from 15-70 years, with a mean age of approximately 38 years.

### Clinical features

- Constitutional symptoms (70%) – malaise, fatigue, flu like symptoms, weight loss
- Asthma (97%)
- Paranasal sinusitis (61%)
- Allergic rhinitis (40%)
- Pulmonary symptoms like cough and hemoptysis (37%)

**Table 1**

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|---|
| Asthma |
| Eosinophilia >10% |
| Paranasal sinusitis |
| Pulmonary infiltrates |
| Mononeuritis multiplex |
| Histologic evidence of vasculitis |

- Arthralgias (40%)
- Skin manifestations (49%)
- Purpura – skin nodules, urticarial rash, necrotic bullae, digital ischemia
- Cardiac manifestations (40%)
- Gastrointestinal symptoms (31%)
- Mononeuritis multiplex (77%).

**ARA Criteria:** Atleast 4 out of 6 criteria are needed to make a diagnosis of CSS with 85% sensitivity and 97.7 % specificity. These criteria are:

CSS is distinguished from other systemic vasculitides by the presence of asthma. Involvement of the myocardium, peripheral nerves, gastrointestinal tract, and skin is common. p-ANCA, present in most patients, should be considered as a major diagnostic criterion but have not proven useful for follow-up purposes.

**Pathophysiologically:** CSS is characterized by activated circulating eosinophilis and a nonspecific elevation of immunoglobulin E (IgE) levels in 75% of patients. ANCA can be detected in 38-50% of the patients. Lanham and colleagues divided the clinical course of the disease into three, usually successive phases: The prodromic phase (Phase 1; asthma and often allergic manifestations), followed by Phase 2, resulting from eosinophilic infiltration into tissues, particularly the lung, myocardium and/or gastrointestinal tract with or without granulomas, and the systemic phase (or Phase 3), with the development of necrotizing vasculitis, usually occurring after 3-4 years of asthma, and affecting the skin, peripheral nerves and kidneys in particular.

Retrospective studies suggest that patients with ANCA-positive CSS differ clinically significantly from those without ANCAs. While ANCA-negative patients have higher rates of cardiac involvement, pericarditis and cardiomyopathy, pleural effusion, fever and livedo, ANCA-positive patients have more renal involvement, sinusitis, peripheral neuropathy and purpura. Most importantly, mortality rates and relapse rates at 3-5 years were similar regardless of ANCA status at diagnosis.

Prognosis of CSS has improved dramatically since the introduction of corticosteroids and, when indicated, immunosuppressants. Remission is usually achieved rapidly in more than 80%, while relapses may occur in 15-43% of patients. The overall 5-year survival rate is about 90%, while 75% of the deaths are directly attributable to vasculitis, with cardiac involvement being the primary cause.

### Poor Prognostic Factors

**Table 2**

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| Proteinuria (>1 g/d) |
| Renal functional impairment (creatinine >140 µmol/L) |
| Cardiomyopathy |
| Gastrointestinal tract involvement and |
| Central nervous system involvement |

### Treatment

**Table 3**

| Treatment options | Comments |
|---|---|
| Corticosteroids | Prednisolone and methylprednisolone for severe forms. |
| | Impossible to discontinue them due to residual asthma |
| Immunosuppressants (cyclophosphamide, azathioprine and mycophenolate) | Major life-threatening organ involvement, steroid-resistant eosinophilia. Required in <20% cases |
| Infliximab | Steroid-dependent CSS |
| Interferon-α | Aggressive forms of CSS |
| Plasmapheresis | Used as adjuvant therapy to steroids and cyclophosphamide. Not of proven benefit |
| Newer therapies | Interleukin 5 antagonists like Mepolizumab which can be used as a steroid sparing agent |

## CONCLUSION

The CSS 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. The recognition of CSS as a separate disease entity is important, because its distinctive natural history, its frequent rapid response to treatment, and its good overall prognosis suggest pathogenic mechanisms that differ either in nature or in degree compared with other forms of necrotizing vasculitis.

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