Churg-Strauss Syndrome

**Synonyms:** allergic granulomatosis angiitis, granulomatous small-vessel vasculitis, eosinophilic granulomatosis with polyangiitis (EGPA)

A rare diffuse vasculitic disease affecting coronary, pulmonary, cerebral, abdominal visceral and skin circulations. The vasculitis affects small- and medium-sized arteries and veins and is associated with asthma.

The aetiology is unknown although autoimmune and genetic factors have been implicated. Drug-induced Churg-Strauss syndrome (CSS) has been reported. Drugs implicated have included mesalazine, propylthiouracil, methimazole, freebase cocaine and leukotriene receptor antagonists.

The American College of Rheumatology has identified six criteria for the diagnosis of CSS:

- Asthma (wheezing, expiratory rhonchi).
- Eosinophilia of more than 10% in peripheral blood.
- Paranasal sinusitis.
- Pulmonary infiltrates (may be transient).
- Histological confirmation of vasculitis with extravascular eosinophils.
- Mononeuritis multiplex or polyneuropathy.

The presence of four out of six of these features has a high specificity and sensitivity for the diagnosis of CSS.

**Epidemiology**

- Rare with incidence of about 1-2 per million people and prevalence about 10-15 per million people. The age at onset usually varies from 15-70 years, although patients as young as 9 have been reported.

**Presentation**

The presentation will depend on which systems are involved. In any patient with asthma and/or nasal polyposis, any new or worsening general or constitutional symptoms, including fever, joint pain, diffuse muscle pain, major involuntary weight loss, chest pain, palpitations or abdominal pain, may be the first signs of a vasculitis, including CSS.

The most prominent symptoms and signs include:

- Pulmonary: asthma, pneumonitis and haemoptysis.
- Upper respiratory tract: allergic rhinitis, paranasal sinusitis, nasal polyposis.
- Cardiac involvement is common. This includes heart failure, myocarditis and myocardial infarction.
- Skin: purpura, skin nodules, leukocytoclastic angiitis with palpable purpura, livedo reticularis, urticaria, necrotic bullae and digital ischaemia.
- Renal: glomerulonephritis, hypertension and advanced chronic kidney disease.
- Peripheral neuropathy: mononeuritis multiplex is the most frequent form. Less frequent symptoms include stroke and eye involvement.
- Gastrointestinal: vasculitis and bleeding, bowel ischaemia and perforation, appendicitis and pancreatitis.
- Cholestatic liver dysfunction has been reported.
- Malaise, fatigue, weight loss, fever, myalgia and arthralgia.
- Myositis following unaccustomed exercise has been reported.

**Differential diagnosis**

There are many possible differential diagnoses to consider but include:

- Other causes of systemic vasculitis:
  - Primary vasculitis - eg, polyarteritis nodosa, granulomatosis with polyangiitis (Wegener's granulomatosis).
  - Secondary vasculitis: a complication of a connective tissue disorder (eg, rheumatoid arthritis), infection, medication, or malignancy.

- Infections - eg, helminth/nematode.
- Primary eosinophilic syndrome.
- Malignancy - eg, leukaemias, lymphomas, myeloproliferative neoplasms, solid cancers (especially gastrointestinal, breast or lung).
- Myelodysplastic syndromes.
Investigations

- Antineutrophil cytoplasmic antibodies (ANCA): 30-40% of patients are perinuclear staining (p-ANCA) positive (antimyeloperoxidase antibodies). [10]
- Other likely findings include eosinophilia and anaemia on the FBC; elevated ESR and CRP; elevated serum creatinine; increased serum IgE levels, hypergammaglobulinaemia; proteinuria, microscopic haematuria and red blood cell casts in the urine.
- CXR: pulmonary opacities, transient pulmonary infiltrates, pleural effusions.
- Pulmonary CT scan: peripheral areas of parenchymal consolidation with ground-glass attenuation similar to chronic eosinophilic pneumonia.
- Bronchial lavage may yield eosinophilia.
- Biopsy: the characteristic changes, found especially in the lung, include small necrotising granulomas, as well as necrotising vasculitis involving small arteries and venules.
- Other investigations are indicated for the complications of the disease and specific organ system involvement.

Management [12]

- High-dose steroids are usually adequate for treatment.
- Cyclophosphamide is administered in patients with severe or life-threatening complications. Either azathioprine or methotrexate is also used.
- Other treatments include intravenous immune globulin, interferon-alpha and plasma exchange.
- Successful use of rituximab has been reported. [13]
- Oral tacrolimus in combination with methyprednisolone and cyclophosphamide was used successfully in the treatment of a child severely ill with CSS. [14]
- Gastrointestinal transplantation in a patient with severe gastrointestinal involvement has been reported. [15]

Complications

- 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. [16]

Prognosis

- Without treatment, the five-year survival rate is about 25%.
- However, patient outcomes have dramatically improved over a period of 20 years. Survival rates now exceed 90% at one year after diagnosis and 85% at five years. Delayed diagnosis and initiation of appropriate treatments can negatively affect overall prognosis and outcomes. [4]
- Relapses are not uncommon, [12]
- Diffuse organ involvement of CSS, especially cardiovascular and rare involvement of the CNS and renal system, suggests a poorer prognosis and can be fatal. [17]
- One review found that, compared with adult CSS patients, children had a predominance of cardiopulmonary disease, a lower rate of peripheral nerve involvement and a higher mortality. [18]

Further reading & references

- Vasculitis UK
  4. Information for doctors; Churg Strauss Syndrome Association