An unusual cause of a recurrent painful rash

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Abstract

Churg-Strauss syndrome is an uncommon multisystem disease involving small and medium-sized arteries, capillaries, veins, and venules. It is characterised by the presence of asthma, hypereosinophilia, and evidence of vasculitis affecting a number of organs. It is important for acute physicians to recognise this condition as delayed diagnosis results in a higher morbidity and mortality. Here we describe a case of Churg-Strauss syndrome in a 41 year old woman presenting with a recurrent painful rash. The clinical manifestations and management of this condition are discussed.

Keywords

Churg-Strauss syndrome, asthma, rash.

Key Points

- Churg-Strauss syndrome should always be considered in patients presenting acutely with asthma, hypereosinophilia and clinical evidence of vasculitis.
- Perinuclear ANCA of anti-myeloperoxidase specificity is present in only 44-66% of patients with Churg-Strauss syndrome; a negative result should therefore not detract from a clinical suspicion.
- Consideration of the diagnosis of Churg-Stauss syndrome on the AMU enables early initiation of specialist treatment which may improve the outcome

Case report

A 41 year old woman was referred to the acute medical team with a recurrent, and persistent rash. The problem had started three months earlier following a miscarriage and initially began with a painful rash on her right thigh which resolved spontaneously. The patient had been seen in the dermatology outpatient clinic and patch testing had been arranged. The day before admission, she noticed a similar but more severe and progressive painful rash developing over her abdomen, back, arms and legs. In addition to the rash, she had also experienced nausea, vomiting, diarrhoea and, paraesthesia in her forearms and hands. She did not describe shortness of breath, cough, chest pain, joint or muscle aches/pains, weight loss, or fever and she had no recent travel history or exposure to unwell contacts. Her past medical history included asthma which was diagnosed 3 years earlier by her general practitioner (GP). This was normally well controlled with no previous hospital or ITU admissions. However, within the last 3 months she has experienced two exacerbations of her asthma, each successfully treated by her GP with a course of prednisolone. Her regular medication comprised seretide 50 micrograms twice a day and salbutamol inhaler when required.

On initial assessment, her blood pressure was 120/78, heart rate 72/min regular, respiratory rate 18/min, oxygen saturations 96% on air, and temperature of 36.7°C. A very extensive haemorrhagic necrotic rash with overlying blistering was found on her abdomen, lower back (Figure 1), arms (Figure 2), and legs. Examinations of the respiratory, cardiovascular and abdominal systems were unremarkable. Neurological examination revealed sensory disturbance in the distribution of the medial cutaneous nerve of both forearms and in the distribution of the median nerve in both hands. No weakness or muscle wasting was present. Reflexes were present and normal. No other finding was present on neurological examination.

Initial blood tests revealed a white cell count of $11.67x10^9$/L [4.0-$11.0x10^9$/L], eosinophil count of $3.03x10^9$/L [0.0-$0.5x10^9$/L] and a C reactive protein of >160 mg/L [0-8mg/L]. Blood tests were otherwise normal (including haemoglobin, platelets, clotting, urea and electrolytes, and liver function tests). Immunological testing was negative for antinuclear and antineutrophil cytoplasmic antibodies. Electrocardiogram revealed sinus rhythm at rate of 75/min whilst urinalysis was negative for blood, protein, leucocytes and nitrites. Chest x-ray was unremarkable. Her skin biopsy revealed a leucocytoclastic vasculitis with eosinophils. Echocardiogram showed a global left ventricular dysfunction with an ejection fraction of 17% whilst nerve conduction studies revealed a symmetrical sensorimotor axonal polyneuropathy

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Figure 1.

of the median nerve and medial cutaneous nerve of the forearms.

The combination of asthma, hypereosinophilia and histological evidence of eosinophilic vasculitis led to a diagnosis of Churg-Strauss syndrome. The patient was commenced on intravenous methylprednisolone, 1000mg daily for 3 days, followed by oral prednisolone. In addition, she was also commenced on cyclophosphamide 15mg/kg, carvedilol 3.125mg twice daily, ramipril 5mg daily and furosemide 40mg daily. Her skin lesions responded well and began to resolve at the time of discharge, 10 days after admission. A repeat echocardiogram showed an improved ejection fraction of 25%. At follow up 2 weeks after discharge, the patient had made a good recovery with her skin lesions and arm paraesthesia having resolved. She was continued on a tapered dose of prednisolone together with cyclophosphamide. Her cardiac medications were also continued.

Discussion

Churg-Strauss syndrome, also known as allergic granulomatous angiitis, was first described in 1951 by the pathologists Churg and Strauss and is characterised by asthma, hypereosinophilia, extravascular granuloma formation and necrotising vasculitis of multiple organ systems.[1] It is an uncommon disease with a mean annual incidence in England being approximately 2.4 per million inhabitants.[2] It affects males and females equally and most frequently occurs in those between the ages of 15 and 70 years old.[3]

Churg-Strauss syndrome consists typically of three phases, which may appear successively. The



Figure 2.

Box 1. Organ involvement in Churg-Strauss syndrome.[4]

Respiratory:
Asthma
Sinusitis
Allergic rhinitis
Nasal polyps
Neurological:
Mononeuritis multiplex
Symmetric/Asymmetric polyneuropathy
Cerebral haemorrhage and infarction
Cardiovascular:
Cardiomyopathy
Heart failure
Pericarditis
Myocardial infarction
Dermatologic:
Palpable purpura
Skin nodules
Urticarial rashes
Livedo reticularis
Gastrointestinal:
Gastroenteritis
Ischaemic bowel
Pancreatitis
Cholecystitis
Renal:
Proteinuria
Glomerulonephritis
Interstitial nephritis
Renal failure

prodromal phase is characterised by the presence of allergic disease (typically allergic rhinitis, allergic sinusitis, and asthma), which may last months to many years. This is followed by a second phase (eosinophilia-tissue infiltration phase) marked by the onset of peripheral blood and tissue eosinophilia, with chronic eosinophilic infiltration typically in the lung, skin and gastrointestinal tract. Spontaneous or

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treatment induced remission can occur at this stage, but recurrence is common. The third, vasculitic phase is defined by the presence of systemic necrotising vasculitis affecting a wide range of organs (Box 1).[4]

The most common presenting manifestation of Churg-Strauss syndrome is asthma, and is frequently associated with allergic rhinitis, sinusitis, and nasal polyps. In comparison to patients with common atopic asthma, asthmatic symptoms in Churg-Strauss syndrome typically develops at a later age, is more severe and requires more frequent use of corticosteroids to control symptoms.[4] In the case of our patient, asthma was relatively late in age of onset and the number of exacerbations the patient experienced increased as the vasculitic phase of Churg-Strauss syndrome began.

Cutaneous lesions are seen in about two thirds of patients suffering from Churg-Strauss syndrome, and may be the first manifestation of the condition.[5] The main dermatological manifestation is a palpable purpura of the lower limbs.[6] Other cutaneous manifestations that may be seen include subcutaneous nodules, livedo reticularis, urticaria, erythemato-bullous lesions and, as demonstrated by our patient, extensive ecchymoses and skin infarction.[7,8]

Neurological involvement is a common manifestation and occurs in approximately 75% of patients.[9] It usually manifests as a peripheral neuropathy in the form of a mononeuritis multiplex, most commonly involving the peroneal nerve. Untreated, this may progress to a symmetric or asymmetric polyneuropathy. In our patient, a symmetrical sensorimotor axonal polyneuropathy of the median nerve and medial cutaneous nerve of the forearm was present. Central nervous system involvement is less frequent (25%) but ranges from psychiatric disturbances to cerebral infarction, cerebral haemorrhage, epilepsy and coma.[9,10,11]

Approximately half of Churg-Strauss syndrome patients develop cardiovascular manifestations and its involvement often portends a worse prognosis.[12] The cardiac abnormalities in Churg-Strauss syndrome include congestive cardiac failure caused by a granulomatous eosinophilic infiltration of the myocardium, coronary vessel vasculitis, cardiomyopathy, and death.[13] Acute pericarditis, myocardial infarction, and pericardial effusions may also occur.[14] In this case, cardiac involvement was confirmed by the presence of global left ventricular dysfunction with an ejection fraction of 17% on echocardiogram. The 2005 American College of Cardiology/American Heart Association (ACC/AHA) guidelines recommend the use of an ACE inhibitor and a beta blocker in patients with asymptomatic left ventricular dysfunction.[15] An ejection fraction ≤ 40% has been defined as the threshold for initiating such treatment.[16] In accordance with these guidelines, we commenced our patient on ramipril and carvedilol. In addition, we also commenced our patient on furosemide.

Box 2. American College of Rheumatology 1990 criteria for classification of Churg-Strauss syndrome.[14]

- Patient is classified as having Churg-Strauss syndrome if at least four of these six criteria are positive:
- Asthma
- Eosinophilia > 10%
- Pulmonary infiltrates, non fixed
- Neuropathy, mono- or poly-
- Paranasal sinus abnormality
- Extravascular eosinophils (biopsy including vessels)

Although data on diuretic efficacy are limited, a meta-analysis of several small trials showed that use of diuretics were associated with a decreased mortality as well as a reduced admission for likelihood of worsening heart failure.[17]

To assist in the diagnosis of Churg-Strauss syndrome, the American College of Rheumatology has developed a useful set of diagnostic criteria (Box 2).[14] The presence of any four or more of the six diagnostic criteria allows a diagnosis of Churg-Strauss syndrome to be made with a specificity of 99.7% and a sensitivity of 85%.[14] In our patient, the diagnosis of Churg-Strauss syndrome was supported by the presence of asthma, peripheral blood eosinophilia > 10%, presence of symmetrical axonal polyneuropathy, and the presence of extravascular eosinophils from skin biopsy. It is of importance to note that anti-neutrophil cytoplasmic antibodies (ANCA) are not included in the diagnostic criteria for Churg-Strauss syndrome. ANCA are found in only 44 to 66 percent of patients with Churg-Strauss syndrome with the most common pattern being perinuclear (pANCA).[18] The presence of ANCA is neither specific nor sensitive for the diagnosis of Churg-Strauss syndrome and as a result is not often used as a diagnostic tool.[19] However, the clinical manifestations of Churg-Strauss syndrome may differ between ANCA positive and ANCA negative patients. For Churg-Strauss patients who are ANCA positive, the incidence of renal involvement, peripheral neuropathy, and biopsy proven vasculitis is higher, whereas those who are ANCA negative, as in our patient, have a higher incidence of heart disease and fever.[19]

Systemic glucocorticoid is the primary therapy for patients with Churg-Strauss syndrome. Treatment is typically initiated with oral prednisolone at a dose of 1mg/kg/day, and tapered progressively after 1 month over a 9-12 month period, according to the patient's clinical status, erythrocyte sedimentation rate and eosinophilia.[20,21] For those who present with acute multiorgan involvement, as seen in our patient, intravenous methyprednisolone (usually 1g daily for three days) is used for initial therapy, followed by oral prednisolone (1mg/kg/day).[22]

Systemic glucocorticoids alone are usually adequate for the treatment of Churg-Strauss syndrome. However, cyclophosphamide is typically added in patients who have failed to respond to

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glucocorticoid therapy or in those who present with fulminant multisystem disease.[23] The decision to add cyclophosphamide is often based on the severity of the disease in terms of the number of organs involved. The "five factors score" (FFS) is a commonly used scoring system used to help determine the need for cyclophosphamide and is based on the presence or absence of five clinical factors (Box 3).[24] An FFS score of 0 is given when none of the factors are present, a score of 1 if one factor is present and, a maximum score of 2 if two or more factors are present. Current recommendations suggest the addition of cyclophosphamide for patients with a FFS of 1 or more, particularly in the presence of cardiac or central nervous system involvement.[25,26] Our patient had an FFS of 1 with cardiac involvement, and as a consequence was given cyclophosphamide.

Box 3. "Five Factors Score" (FFS).[19]

- Cardiac involvement
- Gastrointestinal disease (bleeding, perforation, infarction, or pancreatitis)
- Renal insufficiency: plasma creatinine concentration > 1.58mg/dL [141 micromol/L]
- Proteinuria (> 1g/day)
- Central Nervous System involvement

Once remission is induced with prednisolone and cyclophosphamide, patients are typically switched to maintenance therapy with a less toxic immunosuppressive agent such as azathioprine or methotrexate together with a tapering dose of prednisolone. Maintenance therapy may need to be continued for an indefinite period.

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