CASE REPORT

Is this an exacerbation of asthma? A cautionary tale

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Dr Bharat Sidhu,
b.sidhu2@hotmail.com**SUMMARY**

Asthma exacerbations are a fairly common presentation to emergency departments. However, a careful history, clinical examination and interpretation of investigations may uncover a more serious pathology. We present an interesting case of a 44-year-old man with symptoms suggestive of an asthma exacerbation, who was found to have Churg-Strauss vasculitis/eosinophilic granulomatosis with polyangitis. He had clinical features of a vasculitis, ECG changes and a troponin T level of 7562 ng/L. Renal biopsy confirmed Churg-Strauss vasculitis. Cardiac involvement in Churg-Strauss Syndrome (CSS) is one of the leading causes of mortality. We describe the successful diagnosis and management of a patient with CSS.

BACKGROUND

This patient was seen by three different medical practitioners and was diagnosed as having an exacerbation of asthma. It was almost 1 week prior a diagnosis of Churg-Strauss vasculitis/eosinophilic granulomatosis with polyangitis (EPGA) was conducted. In this case, a detailed history and examination was enough to raise a suspicion of an underlying vasculitis. Furthermore, close interpretation of investigations would have prompted the need for further investigation. In this case report we detail the clinical signs, successful diagnosis and management of having Churg-Strauss vasculitis/EPGA. We hope it provides medical education on this condition as well encouraging medical practitioners to further investigate asthma patients with atypical features.

CASE PRESENTATION

A 44-year-old man who worked as an engineer, presented to our hospital with symptoms of progressively worsening shortness of breath over a period of 6 days. He was known to have a history of mild asthma with minimal symptoms and occasional use of inhalers prior to his hospital visit. His medical history included asthma diagnosed in childhood, nasal polyps and episodes of epistaxis for which he required surgery and also a history of obstructive sleep apnoea. He was a non-smoker with no family members having premature coronary artery disease. He had no recent travel history. He had presented to another hospital a week earlier with the same symptoms; however, they were less severe and he was given a course of antibiotics for a suspected lower respiratory tract infection causing an asthma exacerbation.

His symptoms continued to worsen and he then presented to our hospital with chest tightness, shortness of breath, myalgia, swelling of both his

feet and ankles. His chest discomfort was pleuritic in nature. He also developed a cough with haemoptysis. Exercise tolerance had reduced to several yards and was limited by shortness of breath on exertion over 1 week prior to being admitted.

On presentation his blood pressure was 110/80 mm Hg, pulse 110/min and regular, respiratory rate was 30 breaths/min. Heart sounds were audible with no additional sounds. There was no chest wall tenderness with bilateral crackles on auscultation of his chest and mild expiratory wheeze. He had mild non-pitting pedal oedema. His jugular venous pressure was raised at 2 cm. Abdomen was soft and non-tender with no palpable masses. There were vasculitic lesions on his distal interphalangeal joints with splinter haemorrhages on both hands. He had no lymphadenopathy. There were no focal neurological signs even though he did describe some paraesthesia in his upper and lower limbs. A urine dip showed 4+ protein and 2+ blood.

INVESTIGATIONS

Blood tests (below) showed renal impairment, hyponatremia, eosinophilia and a very high troponin T level.

		Normal range
Na ⁺ (mmol/L)	126	133–146
K ⁺ (mmol/L)	4.9	3.6–5.3
Urea (mmol/L)	19.6	2.5–7.5
Creatine (μmol/L)	169	60–115
eGFR (mL/min 1.73 m ²)	39	60–115
Bicarbonate (mmol/L)	15	22–29
Creatine kinase (μ/L)	211	0–160
LDH (μ/L)	621	0–580
Troponin T (ng/L)	7562	<13
WCC (l)	10.32×10 ⁹	4–11×10 ⁹
Hb (g/L)	11.7	133–180
Platelets (l)	538×10 ⁹	140–400×10 ⁹
Eosinophils (l)	12.8×10 ⁹	0.02–0.5×10 ⁹

eGFR, estimated-glomerular filtration rate; Hb, haemoglobin; LDH, lactate dehydrogenase, WCC, white cell count.

Coagulation profile was normal. Urine creatine 8497, urine protein 0.54, urine protein: creatine 0.56. Urine protein creatine ratio 64. Perinuclear: antineutrophil cytoplasmic antibody was positive.

An ECG was carried out and showed sinus tachycardia, ST segment elevation in leads III and aVF but normal lead II, poor R wave progression anteriorly and right axis deviation (figure 1). His chest X-ray (figure 2) showed right basal consolidation with a small right-sided pleural effusion.

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Figure 1 ECG showing ST elevation in leads III and aVF.

Echocardiogram showed severely impaired left ventricular systolic function with a 4–6 mm left mural wall thrombus and raised right heart pressures.

TREATMENT

In summary, this 43-year-old man with worsening shortness of breath and chest tightness had acute renal failure, a markedly raised troponin, ST elevation, hypereosinophilia and vasculitic skin changes with a history of asthma. Our working diagnosis at this point was a possible acute coronary syndrome (ACS) and associated renal impairment most likely secondary to small vessel vasculitis.

He was given ACS treatment, nebulised salbutamol and ipratropium bromide, analgesia and intravenous fluids. The patient was discussed with the local renal unit and was accepted for urgent transfer for haemofiltration. The renal team started him on methylprednisolone 500 mg intravenous twice a day and sodium bicarbonate. Subsequently he was started on oral prednisolone 50 mg once daily. A vascular catheter was inserted and he was plasma exchanged.

Clinical suspicion now pointed to a diagnosis of Churg-Strauss Syndrome (CSS) with myocardial involvement secondary to vasculitis. He was consented for a kidney biopsy of his left kidney. Biopsy results showed crescentic glomerulonephritis and eosinophilic infiltrates confirming CSS (see figure 3). He had five cycles of plasma exchange and was then started on cyclophosphamide 150 mg once daily and loaded with warfarin.

This patient had a previous CT of the head (figure 4) that showed extensive opacification of the maxillary antra bilaterally with some destruction/loss of the medial walls. The middle turbinates were absent. There was extensive opacification of the ethmoid, frontal and sphenoid sinuses bilaterally in keeping with extensive inflammatory disease of the nasal and paranasal

Figure 2 Chest X-ray with right lower zone changes.

Figure 3 Histological sections of two left kidney demonstrating eosinophilic infiltrates with crescents.

sinuses. These inflammatory changes, although rare, can be an early sign suggestive of CSS vasculitis.¹

OUTCOME AND FOLLOW-UP

The patient's symptoms improved dramatically, with normalisation of renal function and clinically he became asymptomatic on the third day of admission. He was in hospital for a total of 8 days before being discharged home.

He was followed up in the outpatient's clinic a month later. He had recovered very well and was tolerating the cyclophosphamide as well as prednisolone without side effects. His cyclophosphamide was converted to azathioprine at 3 months and his steroid dose was weaned down to 10 mg once a day, which he will continue for at least 1 year. A repeat echocardiogram showed no residual thrombus; however, his left ventricular systolic function remained impaired. Since going home he has been systemically well with no cardiac, respiratory or renal symptoms. His peripheral oedema has subsided and the skin lesions have resolved.

DISCUSSION

CSS is a rare multisystemic clinical syndrome first described by Churg and Strauss in 1951. They defined the syndrome as a necrotising vasculitis of medium-to-small sized veins and arteries associated with eosinophilic infiltration in and around the vessels and adjacent tissues.^{2,3} Recently there has been a gradual re-naming of the syndrome to EGPA. Cardiac involvement is a common manifestation and a leading cause of mortality. Presentation can be acute and can also mimic ACS.⁴

CSS has been defined by Lanham *et al* and recently (1990) by the American College of Rheumatology (ACR) as described as in box 1. The patient in this case report presented with all three criteria consistent with Lanham's diagnostic classification of CSS.

Figure 4 Extensive opacification of the ethmoid, frontal and sphenoid sinuses. There is also right periorbital soft tissue swelling.

Box 1

Lanham's criteria:

1. Asthma
2. Peak peripheral blood eosinophil count $>1.5 \times 10^6/\text{cc}$
3. Systemic vasculitis involving two or more extrapulmonary organs

*ACR criteria*⁶:

1. Asthma
2. Eosinophilia $>10\%$
3. Neuropathy
4. Non-fixed pulmonary infiltrates
5. Paranasal sinus abnormality
6. Extravascular eosinophils

Patients with CSS present with a series of three clinical phases. The initial phase of asthma and rhinitis are the most common clinical manifestations. Tissue eosinophilia and pulmonary infiltrations are components of the second clinical phase and the last phase involves multiple organ systems, such as the heart, upper airway, skin, renal, lung, gastrointestinal and peripheral nervous system.⁵ The patient in this report demonstrated all three clinical phases.

The clinical presentation can, however, be varied. The most common presenting symptoms of CSS suggested by one retrospective study include weakness, fatigue, cough, dyspnoea, myalgia, angioedema, rash, fever and rhinitis.⁷ Cutaneous lesions are present in about two-thirds of patients. CSS mainly affects adults with a mean age of about 40–45.⁸

Cardiovascular disease occurs in about 50% of patients with CSS and the clinical spectrum of cardiac involvement ranges from patients being asymptomatic, having acute and/or constrictive pericarditis, restrictive or dilated cardiomyopathy, intracavity thrombi, abnormalities in ECGs and sudden death.⁹ Eosinophilic infiltration of the myocardium and coronary vessel vasculitis are the most common lesions leading to coronary disease and congestive cardiac failure.⁸

The diagnosis of CSS is mainly a clinical one.¹⁰ Confirmation of cardiac involvement may require further investigation. Markers that are routinely used to assess for myocardial involvement such as creatine kinase MB and troponin can be early sensitive indications of myocardial damage in CSS.⁴ Echocardiography may be normal or may show impairment of contractility, thickening of the ventricular wall and the presence of intracardiac thrombi or pericardial effusion. A coronary angiogram is more accurate than MR angiogram for detection of vasculitis; however, an angiogram can have false-negative results.⁹ Cardiac MRI may confirm myocardial necrosis, inflammation or thrombosis.⁴ For an absolute definitive diagnosis an endomyocardial biopsy can be considered. It is an invasive test with serious complications such as perforation and pericardial tamponade. The benefits of these investigations, particularly a biopsy, must be weighed up against the potential risks and also whether it would change overall management.¹⁰

Two papers demonstrated that an emergency coronary angiography in CSS showed normal epicardial coronary arteries.^{4 11} The need for a coronary angiogram in CSS should only be

pursued for ongoing cardiac ischaemic symptoms. The patient in our case report was treated for vasculitis and responded well with a gradual reduction in troponin and eosinophils.

Treatment of CSS with corticosteroids usually results in rapid resolution, mainly by reducing the length of survival of eosinophils in the tissues. If there is inadequate control of the disease with steroids alone, then cyclophosphamide may be used.⁶

Learning points

- ▶ Patients, particularly those with a history of asthma, presenting with shortness of breath should always be investigated thoroughly.
- ▶ Detailed history and clinical examination alone may be enough to raise suspicion of an underlying vasculitis; however, a raised eosinophil count should prompt further investigation.
- ▶ In this case the patient's symptoms and clinical features worsened over the course of a week, with an acute deterioration in renal function and coronary artery vasculitis. Early recognition and initiation of treatment is imperative.
- ▶ High troponin T levels can be due to non-arteriosclerotic pathologies as highlighted in this case report.
- ▶ The first line therapy for Churg-Strauss Syndrome (CSS) is corticosteroids. Where there is advanced involvement of organs in the form of necrotising vasculitis then corticosteroids may be combined with cyclophosphamide and even plasma exchange as demonstrated in this case. This does not improve survival, but controls relapses of CSS.

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