AN UNUSUAL CAUSE OF MYO-PERICARDITIS: A CASE REPORT

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A 40 year old female presented to the acute admissions unit in May 2010 with shortness of breath, wheeze, productive cough, and fever. She has a past medical history of asthma diagnosed at the age of 25, reasonably controlled, nasal polyps and a family history of factor V Leiden deficiency. Physical examination was unremarkable apart from crackles at the right base. Investigations showed a normal white cell count and C reactive protein (CRP). The D-dimers were negative. Chest X Ray showed patchy linear opacities seen at the lung bases consistent with atelectasis. The patient was treated for infective exacerbation of asthma. The patient was reviewed by the respiratory team who optimised the asthma management by adding seretide and monteleukast. The patient was discharged with outpatient referral to the allergy clinic. The patient had a high resolution computer tomography (HRCT) scan of the chest as an outpatient which did not show any focal parenchymal lesions, or features of aspergillosis. Blood test in the allergy clinic showed negative ANA and ANCA. ESR was 12. Specific IgE aspergillus was 0.10 kUA/L (<0.35), specific IgE silver birch was 0.01 kUA/L (<0.35), total IgE 55 kU/L (0-81).

Figure 1. The chest X-Ray on the first admission.
The patient was admitted to hospital in September 2010 with a three week history of productive cough, shortness of breath on exertion and nausea. Physical examination on this admission revealed scattered wheeze throughout the chest and mild tenderness in the right upper quadrant. Observations were stable with oxygen saturations being 99% on air. Investigations showed a CRP of 30.1. Haemoglobin was 11.8. WCC was 19.76, neutrophils were 8.72, eosinophil count was raised at 8.38. D-dimers were 751. Liver function tests were normal apart from a raised gamma-glutamyl transferase at 192. The Troponin I test was raised at 0.35. ANA and ANCA were negative. Urine analysis showed no protein, erythrocytes, leucocytes, casts, or bacterial growth. Chest X-Ray is shown in Figure 1 above.

The patient underwent a computer tomography pulmonary angiogram [Figure 2] in view of recent long haul flight, which did not show any pulmonary emboli; however, it showed bilateral pleural effusions as well as pericardial effusion. There were also features of focal airspace disease and interstitial oedema. The patient was treated for a lower respiratory tract infection. The chest pain was attributed to pericarditis. The blood test prior to discharge showed an improved white cell count, with a neutrophilia of 7.76 and eosinophilia of 5.34.

Figure 2. Computer tomography pulmonary angiogram.

The patient was readmitted 10 days later with increasing chest pain which was relieved by sitting forward. The ECG showed new changes including T wave inversion in the anterior leads and ST segment elevation in the inferior leads. The white cell count was 20.40, eosinophil count was 5.24 and neutrophils were 12.05. ESR was 18. Troponin I was 0.15.

In view of the positive troponin I and new ECG changes the patient underwent an urgent angiogram, which showed normal smooth coronary arteries.
The viral serology for B. burgdorferi, CMV, EBV, Hepatitis A, B, and C were all negative. Thyroid function test was normal, as were the liver function test and bone profile. LDH was 671. Serum protein electrophoresis was normal with negative urine Bence-Jones protein.

Echocardiogram [Figure 3] showed global hypokinesis more pronounced at the septum. The overall left ventricular systolic function was mild to moderately impaired. The ejection fraction was 46 %. There was moderate mitral regurgitation and mild tricuspid regurgitation. The echocardiogram also demonstrated a small rim of pericardial effusion.

![Echocardiogram showing a small rim of pericardial effusion.](image)

The cardiologist’s impression was progression to myopericarditis. The patient was commenced on colchicine, angiotensin converting enzyme inhibitor, spironolactone and nebivolol. The patient was discharged with outpatient echocardiogram and cardiology follow-up.

The patient re-presented two weeks later with five day history of watery diarrhoea with no blood, right loin pain and poor appetite. There was mild epigastric tenderness. The examination was otherwise unremarkable.

Investigations showed a white cell count of 24.02, neutrophils of 10.01 and eosinophils of 11.07. The blood film showed mild anisocytosis (+). The CRP was 71. Renal function was normal. Liver function tests were normal apart from a raised gamma GT at 318 and ALP at 199. Troponin I was 0.25. ANA and ANCA were negative. Rheumatoid factor was greater than 100. Complement C3 was 1.37 and C4 0.30. Stool and urine cultures were negative. The ECG showed new T wave changes which were thought to be due to pericarditis. The diarrhoea was attributed to colchicine, which was stopped.

The patient was readmitted a few days later with continuing diarrhoea, facial rash and epigastric pain. The patient had low grade pyrexia at 37.8 °C.
Clinical examination showed mild epigastric tenderness. There was also an erythematous maculopapular rash on the left side of the forehead.

After discussion with the rheumatology team, the patient was started on intra-venous methylprednisolone due to the concern of eosinophilic myocarditis. Chest X-ray on this admission is shown in figure 4.

Figure 4. Chest X-ray showing a large pericardial effusion.

The echocardiogram [Figure 5] showed a large global pericardial effusion. The left ventricle was mildly dilated with moderately impaired systolic and diastolic function. The mitral and tricuspid regurgitations were as reported in previous echocardiogram.

Figure 5. The echocardiogram above shows a large global pericardial effusion.
The patient was seen by the dermatology team who arranged a skin biopsy, which showed mild hyperkeratosis with very mild perivascular lymphohistiocytic infiltrate in the superficial and interstitial dermis. There were no definite granulomas or eosinophils seen in the skin biopsy. The changes were non specific and may have been modified by treatment with steroids.

A haematological opinion was sought with regards to the eosinophilia. The haematology team queried Churg-Strauss syndrome and advised FISH testing for FIP1L1 mutation in order to distinguish Churg-Strauss syndrome from other haematological causes of eosinophilia. The white cell count was 29.10, neutrophils 11.35, eosinophils 14.84. There were no blasts, myelocytes, metamyelocytes, or promyelocytes. ESR was 39. CRP was 146.4.

A repeat echocardiogram [Figure 6] after commencing steroids showed a non dilated left ventricle with no hypertrophy of the walls. The global systolic function was mild to moderately impaired. The ejection fraction was reported as 45 %. There was mild pericardial effusion (1.2cm) with no significant respiratory variation.

Figure 6. Echocardiogram after commencement of steroids showing a mild pericardial effusion.

The patient underwent a cardiac MRI, which showed a dilated left ventricle with moderately impaired overall function. The right ventricle was normal. The pericardium appeared normal with a mild rim of pericardial effusion. There was extensive subendocardial/transmural fibrosis affecting all three coronary territories and papillary muscle with some evidence of some septal acute inflammation at mid-cavity level. Overall, in the context of unobstructed coronaries, the findings were in keeping with cardiac
involvement from Churg-Strauss. A HRCT of the chest was requested by the respiratory team, in order to assist in distinguishing between hypereosinophilic syndrome and Churg-Strauss syndrome. The HRCT did not show any pericardial effusion, mediastinal lymphadenopathy, consolidation, nodules, or ground glass appearance.

A repeat echocardiogram [Figure 7] prior to discharge showed no pericardial effusion. The systolic function was globally moderately impaired and the ejection fraction was 45%.

![Figure 7. Echocardiogram showing no pericardial effusion.](image)

The patient responded well to the steroids and was discharged. The patient has been commenced on cyclophosphamide infusions as an outpatient.

**DISCUSSION**

Churg-Strauss syndrome (CSS) is a rare small vessel vasculitis characterised by asthma, lung/tissue infiltrates, extravascular necrotising granulomas, and eosinophilia. Its annual incidence has been reported to be 6.8 per million inhabitants [1]. Antineutrophil Cytoplasmic Antibodies (ANCA) are positive in 38% of the patients. ANCA negative patients develop heart disease and fever. Whereas, the presence of ANCA is associated with renal involvement, peripheral neuropathy, and biopsy-proven vasculitis [2].

The prevalence of cardiac involvement in CSS ranges between 45% to 62% [3,4]. Cardiac disease is one of the five-factor score (FFS) prognostic items in Churg-Strauss and is a major contributor to death. Cardiac pathology may be associated with the involvement of the endocardium, myocardium, and pericardium. Cases have been reported of massive pericardial effusions or tamponade being the first manifestation of cardiac involvement in CSS.
Other cardiac involvements in CSS include angina pectoris, myocardial infarction, heart failure, presyncope, and sudden death [7].

Endomyocardial disease may represent the most severe form of cardiac involvement and may be associated with reduced cardiac function at presentation. CSS patients with pericardial effusion but preserved left ventricular systolic function have an excellent outcome and maintain cardiac function [3].

Cardiac magnetic resonance imaging (MRI) is a helpful investigative tool in diagnosing cardiac involvement in CSS, and should be performed at an early stage, because cardiac manifestations are predictive factors of poor prognosis [8].

Colchicine has been effectively used in the treatment of several inflammatory conditions, such as gout, familial Mediterranean fever, Behçet syndrome, and also in recurrent pericarditis. Colchicine is safe and useful in recurrent pericarditis, although less evidence supports its use in acute pericarditis [9]. A study showed that colchicine, when used in the treatment of first episode of recurrent pericarditis, significantly decreased the recurrence rate and symptom persistence [10].

In our patient the symptoms persisted and the pericardial effusion worsened after commencing colchicine. It indicates that colchicine alone was not adequate to treat recurrent pericarditis in our case. A favourable outcome has been shown after introduction of combined therapy with prednisolone and cyclophosphamide [8].

There has been some concern that leucotriene receptor antagonists (LTRA) used in the treatment of asthma, may lead to the onset of CSS. A case cross-over study showed that monteleukast use, a leucotriene receptor antagonist used in the treatment of asthma, was associated with a 4.5-fold higher risk of CSS onset within 3 months of use. There are conflicting views regarding the association between LTRA and CSS, and several hypotheses have been proposed. A possibility is that LTRA therapy may lead to a reduction in corticosteroid use, unmasking underlying CSS. Another hypothesis is that LTRA may have been prescribed in severe asthma, which might have been an early prodromal phase of CSS, leading to full expression of the disease. However, studies have shown that LTRA are a suspect medication [11].

CSS can clinically resemble other diagnoses, including idiopathic hypereosinophilic syndrome (HES), lymphocytic, or myeloproliferative HES, chronic eosinophilic leukaemia and other eosinophilic myeloid neoplasms. Patients, in particular those who are ANCA negative and/or without histologically proven vasculitis, should undergo testing to detect Fip1-like1 (FIP1L1) platelet-derived growth factor receptor-[alpha] (PDGFRA) gene fusion, to detect myeloid neoplasms associated with eosinophilia and abnormalities of PDGFRA, platelet-derived growth factor receptor [beta] (PDGFRB), or fibroblast growth factor receptor 1 (FGFR1).
Other hyper eosinophilic syndromes that overlap with CSS, such as lymphocytic-HES, can be detected by analysing T-cell subset cytokine profiles, including eosinophilopoietic (IL-3 and granulocyte-macrophage colony-stimulating factor) and/or Th2 type cytokines (IL-4, IL-5, IL-13), measurement of serum tryptase, and cytogenetic analysis focusing on imatinib targeted tyrosine kinases. Myeloproliferative neoplasms can be detected by bone marrow examination and Janus kinase 2 gene (JAK2 V617F) mutation screening [12]. However, it may be technically difficult to exclude an overlap between some of these entities, especially lymphocytic-HES or idiopathic-HES and CSS.

REFERENCES


