A 50-year-old man with eosinophilia and cardiomyopathy: need for endomyocardial biopsy?

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A 50-year-old man was admitted with a suspected acute coronary syndrome. The coronary angiogram, however, was normal. He was found to have a cardiomyopathy and eosinophilia. The diagnosis was established as a perimyocarditis secondary to the Churg–Strauss syndrome. An important question is whether an endomyocardial biopsy should have been performed.

Keywords Cardiomyopathy • Perimyocarditis • Eosinophilia • Churg Strauss Syndrome • Cardiac magnetic resonance imaging • Endomyocardial biopsy

A 50-year-old man presented with a 2-week history of chest discomfort, radiating to the arms and back. His symptoms worsened the day before admission, becoming more constant in nature.

The patient had previously been followed up at the out-patients clinic for pulmonary medicine for 6 years because of shortness of breath, increasing sputum production, and symptoms from the paranasal sinuses. He had been diagnosed with blood eosinophilia and an obstructive respiratory defect on spirometry. He had a good response to treatment with steroids. On one occasion, he had required admission and found to have bilateral infiltrates on chest X-ray and extensive eosinophilia on bronchoalveolar lavage. He again responded well to steroid treatment. He had been operated for a prolapsed disc at the level of L4/L5 and was known to suffer from hypertension, cataracts, and osteopenia, probably adverse effects of steroids.

The patient was observed in the coronary care unit with suspected acute coronary syndrome. He intermittently had severe chest pains, was sweaty, uneasy, and tachycardic above 100 b.p.m. Blood pressure was 130/90 mmHg. There were no clinical signs of heart failure or valvular disease.

Blood tests on admission were C-reactive protein: 49 mg/L, WBC: 16.2 × 10^9/L, CK-MB: 76.4 µg/L, Troponin T: 3.590 µg/L, Creatinine, electrolytes, glucose, and total cholesterol levels were all normal. Further tests revealed an eosinophil count of 8080 × 10^6/L. P-ANCA and C-ANCA were negative.

ECG showed dynamic ST-T changes in the form of both ST depressions and elevations (Supplementary data online, Figure S1A and B). A coronary angiogram, however, showed no signs of thrombosis or ruptured plaques.

Echocardiography showed hypo/kinesia of the intraventricular septum (IVS) and medial part of the inferior wall and an ejection fraction (EF) of 35%, E/E′ ratio of 9.3 indicating normal filling pressure, only small amounts of pericardial fluid, and a small mitral regurgitation. There was satisfactory function of the right heart with no evidence of pulmonary hypertension (Supplementary data online, Video S1A–C).

Cardiac magnetic resonance imaging (CMR) demonstrated several signs of myocardial affection: left ventricular (LV) enlargement and regional hypo-/akinesia of the IVS and inferior wall [end-diastolic volume (EDV) 245 mL, EF 47%] (trueFISP cine), antero-septal myocardial oedema in the IVS (T2 STIR), and relatively widespread regions of late enhancement (trueFISP PSIR), indicating fibrosis/necrosis. The distribution of late enhancement followed a circular subendocardial pattern in the LV, with additional transmural affection in parts of the septum corresponding to the
area of oedema, clearly differing from an ischaemic pattern (Figure 1A–H). No intraventricular thrombi were seen.

The most probable diagnosis, based on non-invasive evaluation, was Churg–Strauss syndrome (CSS).

The patient did well on treatment with high doses of oral steroids. The eosinophil count and inflammatory markers normalized within 6 days. He had episodes of frequent ventricular ectopics and some runs of self-limiting ventricular tachycardia which were asymptomatic. Treatment for heart failure was given along conventional lines with good effect.

After the acute episode had subsided, further treatment in liaison with the rheumatologists involved combining tapering doses of prednisolone with cyclophosphamide (CYC). Prospective trials have shown that patients with good prognostic factors should be treated with prednisolone and those with poor prognostic factors should also receive immunosuppressive therapy with CYC. The latter had to be stopped due to increasing liver enzymes and haematuria. The patient then continued with prednisolone in monotherapy, with a plan to introduce azathioprine as a steroid sparer once the liver enzymes normalized.

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The patient was closely followed up clinically and with echocardiography. During the first months, he felt well and echocardiography showed no areas of hypokinesia and an EF of 55% (Supplementary data online, Video S2A and B). $E/E'$ ratio was 9.6.

More than 2 years after the acute episode, the patient reported breathlessness on exertion and episodic swelling around the ankles. Echocardiography revealed dilatation of the LV and EF of 20% (Supplementary data online, Video S3A–C). $E/E'$ ratio was 21 indicating increased filling pressures. The eosinophil count was not elevated. CMR showed LV enlargement (EDV 370 mL) and a reduced EF of 20%. The regions of late enhancement persisted (Figure 1I–L).

Cardiomyopathy is a poor prognostic factor in CSS, giving a five factor score of 1, which has been reported to be associated with a 5-year survival rate of 69.4%.

Discussion

CSS is a necrotising vasculitis mainly of small vessels and a multisystem disorder, typically characterized by asthma, allergic rhinitis, and eosinophilia, first described in the 1950s. The American College of Rheumatologists (ACR) states that a diagnosis of CSS is probable with four or more of the following: asthma, eosinophilia > 10% on a differential count, neuropathy, pulmonary infiltrates (non-fixed), paranasal sinus abnormalities, and infiltration of eosinophils in extravascular areas.

An important question is whether there is indication for an endomyocardial biopsy (EMB)? The role of EMB has been
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controversial. It is an invasive test associated with complications, the most serious of which is perforation with pericardial tamponade and death. Furthermore, there is a considerable sampling error, variations in the interpretations even by experienced pathologists, and the Dallas histopathological criteria are being questioned as the gold standard for diagnosing myocarditis.9 Diagnostic, prognostic, and therapeutic benefits of EMB must be weighed up against the risks of the procedure.

The scientific statement from the American Heart Association, the American College of Cardiology, and the European Society of Cardiology identifies several clinical scenarios where EMB may be considered.7 The fourth scenario states that: ‘EMB is reasonable in the setting of unexplained heart failure associated with a dilated cardiomyopathy of any duration that is associated with suspected allergic reaction in addition to eosinophilia.’ Even though there was no strong suspicion of an allergic reaction, one might surely argue that there was a reasonable indication for performing an EMB in this setting of a dilated cardiomyopathy, most probably of short duration, and eosinophilia. A definite histological diagnosis would have been helpful.

On the other hand, the diagnosis of CSS is mainly a clinical one.8–10 The patient fulfilled four of the six criteria for the diagnosis of CSS from the ACR and fits well into the described three phases of the illness; first having sinusitis and asthma in his 40s, then eosinophilic lung infiltrates and subsequently serious cardiac involvement.9 His ANCA status was negative which is not unexpected with cardiac involvement.11 With the clinical diagnosis relatively certain, the importance of a diagnostic EMB is doubtful. In CSS with cardiac involvement, immediate and aggressive treatment is important since established cardiac disease is difficult to reverse.9 This took initial priority over establishing a histological diagnosis.

The patient initially did well on treatment with steroids. It was therefore unlikely that the result of an EMB would alter the patient’s management. Furthermore, the complete histological criteria often cannot be met, and the inflammatory infiltrate may be segmental, thereby leading to sampling errors. A CMR-guided EMB could, however, have increased the likelihood of a diagnostic result. In many hospitals, including our own, there is limited experience in performing and analysing EMBs. The complication rate is likely to be operator-dependent and the overall risks may therefore have outweighed the benefits.

Supplementary data
Supplementary data are available at European Journal of Echocardiography online.

Conflict of interest: none declared.

References