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Prominent pericardial and myocardial lesions in the Churg-Strauss syndrome (allergic granulomatosis and angiitis)

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The Churg-Strauss syndrome is a rare multisystem disease of unknown cause characterised by asthma, appreciable blood and tissue eosinophilia, angiitis, and necrotising granulomas.[1] The clinical features are protean but cardiac lesions received little emphasis in the largest clinical series of patients so far reported.[2] We report three patients with the Churg-Strauss syndrome who had prominent pericardial and myocardial lesions and also some previously undescribed clinical features.

Case reports

CASE 1

A 33 year old non-smoking woman, who had suffered for 11 years from mild asthma controlled with inhaled salbutamol, developed a painful rash, pericarditic chest pain, shortness of breath, left pleuritic pain, polymyalgia, and emotional lability. There was no family history of allergy. On examination she was febrile and had splinter haemorrhages, a raised, confluent, purplish rash on both arms, bilateral ankle oedema, and scattered wheezes.

When she was transferred to the Brompton Hospital, her rash was fading but she had developed weakness and anaesthesia in the distribution of her left popliteal and right radial nerves and the right dorsalis pedis, and both posterior tibial pulses were impalpable. The chest radiograph showed cardiomegaly, a left pleural effusion, and bilateral basal shadowing. The haemoglobin concentration was 9·0 g/dl, eosinophil count $15{\cdot}2 \times 10^9$/1, and erythrocyte sedimentation rate (ESR) 39 mm in the first hour. The serum IgE was 1300 IU/ml (normal 5-150 IU/ml) and circulating immune complexes containing IgG and IgA were detected. No autoantibodies or aspergillus precipitins were detected. Stool and serological tests for parasites gave negative results. Skin test responses to a standard range of 32 common environmental allergens were negative. Electrocardiographic and echocardiographic features were compatible with a pericardial effusion. An open pericardial biopsy showed infiltration by eosinophils, vasculitis, and giant cell granulomas. The pericardial fluid contained 7×10^9/1 eosinophils.

The patient was treated initially with 60 mg of prednisolone a day, the dose being reduced over four months to 20 mg on alternate days. She was then symptom free, all pulses were palpable, and the neuropathy had almost totally resolved. She has remained well for over 18 months, maintained on alternate day prednisolone, with no haematological or immunological abnormalities.

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CASE 2

A 32 year old man presented with a history of anorexia, weight loss, fever, intermittent joint pains, and continuous retrosternal chest pain. At 17 years of age he had developed asthma; for the last two years his only treatment had been choline theophyllinate and inhaled beclomethasone dipropionate.

On examination, the pulse was 120 beats/min, blood pressure 90/60 mm Hg, and jugular venous pressure raised 6 cm; and there was a gallop rhythm. There were bilateral wheezes and crackles in the lungs. The chest radiograph showed cardiomegaly. The haemoglobin concentration was 11·7 g/dl, white cell count $11{\cdot}4 \times 10^9$/1, and absolute eosinophil count $4{\cdot}7 \times 10^9$/1. The ESR was 104 mm in the first hour. Stool and serological tests for parasites gave negative results. Autoantibodies and aspergillus precipitins were not detected. Serum IgE was normal. Skin test responses to a standard range of 32 common environmental allergens were negative. Tests of renal function gave normal results. Liver enzyme levels were raised and a liver biopsy showed a focal non-necrotising granuloma with occasional eosinophils.

Electrocardiographic and echocardiographic features were compatible with a pericardial effusion. Right heart catheterisation showed normal pressure (including pulmonary artery wedge pressure) and an angiogram showed normal cardiac function. Open pericardial biopsy showed that the pericardium was thickened by fibrosis and densely infiltrated with eosinophils, and contained prominent necrotising epithelioid and giant cell granulomas. The pericardial fluid was sterile and contained no eosinophils. The patient improved with diuretic treatment but still had a raised ESR and blood eosinophil count on discharge.

Two months later he was readmitted in cardiac failure. His full blood count and ESR were now normal. Electrocardiograms showed left axis deviation and poor R wave progression. A chest radiograph showed cardiomegaly with upper lobe blood diversion and bilateral pleural effusions. Pericardial effusion was not indicated by echocardiography. Cardiac catheterisation showed a raised right ventricular pressure of 55/18 mm Hg and a raised left ventricular end diastolic pressure of 22 mm Hg. Pressure tracings did not suggest restrictive heart disease. Angiograms showed dilated and poorly functioning ventricles with mild incompetence of both mitral and tricuspid vales. There was no evidence of fibrosis or thrombosis. Right ventricular endomyocardial biopsy specimens were normal. The patient was given anticoagulant treatment and increased doses of diuretics and vasodilators with good effect.

A year later he was admitted with severe asthma. There was no eosinophilia; serum IgE was 280 IU/ml (normal

5–150 IU/ml). The asthma improved with prednisolone and bronchodilator treatment. He was maintained on these drugs in addition to his previous treatment, and remained well for 18 months. He then developed a rash while taking prednisolone 15 mg/day. Circulating immune complexes containing complement fraction Clq, IgG, and IgA were detected. Skin biopsy showed a small vessel angiitis with considerable lymphocyte and neutrophil polymorphonuclear infiltration. The rash resolved after the addition of azathioprine (100 mg/day) to the medication.

CASE 3

A woman developed hay fever, nasal polyps, and asthma (non-atopic) in 1972 when 35 years of age. Later that year she developed widespread bilateral shadows on the chest radiograph and had an eosinophil count of $9{\cdot}5 \times 10^9/1$, haemoglobin concentration of 9·9 g/dl, and ESR of 112 mm in the first hour, for which no cause was found. There was no family history of atopy. The patient was treated with a course of hydrocortisone and improved.

Similar episodes occurred in 1973, 1974, 1975, 1976, and 1979. Additional features noted at these times included joint pains, pericarditis, epigastric pain, cervical lymphadenitis, paraesthesiae down the outer aspect of the left arm and a serum IgE concentration of 840 IU/ml. Prednisolone produced clinical improvement on each occasion.

In February 1981, while taking prednisolone 4 mg/day, she developed a tender submandibular swelling, further lung shadows, and eosinophilia. In June 1981 she transferred to the Brompton Hospital after the development of pleuritis and pericarditis. Splinter haemorrhages were present under the nails and the left posterior tibial and the right dorsalis pedis pulses were absent. Renal and hepatic function tests were normal. No autoantibodies or aspergillus precipitins were detected. Circulating immune complexes containing Clq, IgM, and IgA were found. The electrocardiographic and echocardiographic findings were consistent with a pericardial effusion. A pleural biopsy showed eosinophilic infiltration and granulomas.

The dose of prednisolone was increased and after two months the patient was symptom free, all her pulses were palpable, the pericardial and pleural effusions had resolved, and the ESR and the eosinophil count were normal. She has remained well on alternate day prednisolone.

Discussion

In the original description of allergic granulomatosis and angiitis,[1] the heart was frequently found to be affected at necropsy, but there was little reference to myocardial disease and none to pericardial disease in the clinical series of 30 patients reported by Chumbley *et al*.[2] Similarly, the 1980 WHO/ISFC Task Force on the definition of cardiomyopathies did not include allergic granulomatosis as a cause of heart muscle disease.[3] All of our patients had pericardial disease and the second patient also had myocardial disease. The latter resulted in cardiac dilatation and had to be distinguished from idiopathic congestive cardiomyopathy[3] and idiopathic hypereosinophilic endomyocardial disease.[4] The former lacks the eosinophilia, asthma, and vasculitis of the Churg-Strauss syndrome, whereas in the latter there is characteristically a restrictive cardiac defect associated with a prolonged eosinophilia of unknown cause.

In addition to myocardial and pericardial disease, our patients also had hepatic, pulmonary, pleural, lymph node, peripheral nerve, muscle, joint, and skin lesions and anaemia, thus illustrating the multisystem disease which may occur in the Churg-Strauss syndrome. The submandibular gland enlargement and transient vascular lesions with loss of peripheral pulses that occurred in two of our patients do not appear to have been reported previously in this disease. The emotional lability of our first patient, which improved after treatment, may perhaps reflect additional central nervous system disease.

The major pathological lesions of the Churg-Strauss syndrome may not be present together and a single biopsy may fail to show all the characteristic features.[1] By itself, an arteritis is not diagnostic, but necrotising granulomas with intense eosinophilic infiltration in a patient with asthma and blood eosinophilia provide strong evidence of the Churg-Strauss syndrome and distinguish the condition from polyarteritis nodosa.

Asthma and eosinophils suggest allergy, but the atopic state of patients with Churg-Strauss syndrome has seldom been clarified and no specific allergen has been identified. None of our cases had positive immediate responses to hypersensitivity tests or a family history of allergy. Raised serum IgE concentrations have been reported[2 5] and in two of our patients the level was raised when the disease was active and fell with treatment, but in our second case the reverse occurred. The extent of increase in IgE was moderate by comparison with the very high blood eosinophil count. The clinical relevance of the high IgE concentrations is uncertain. Circulating immune complexes were detected and eosinophils may have a role in immune complex clearance;[6] immune complexes have, however, been detected in other types of vasculitis.[7]

A diagnosis of Churg-Strauss syndrome should be considered in any asthmatic patient who develops evidence of cardiac disease (or other multisystem disease) and a high ESR or a high eosinophil count. Specific treatment is required and will differ from treatment for asthma with unrelated cardiac disease—for example, idiopathic cardiomyopathy. Favourable responses to corticosteroids,[2] azathioprine,[2] combinations of corticosteroid and azathioprine,[8] and cyclophosphamide[7] have been described in the Churg-Strauss syndrome and a five year survival of 62% after the start of treatment has been reported.[2] Continuous treatment is usually required to prevent relapse.

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