Case Reports

Myopericarditis in Churg-Strauss Syndrome

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Churg-Strauss syndrome is a disseminated vasculitis with multisystem involvement, characterized by necrotizing arteritis, eosinophilic infiltration, and extravascular granuloma formation. In as many as 60% of all cases, the heart may be affected. We describe a 30-year-old man in whom pericarditis was followed by the development of a large pericardial effusion, with evidence of impaired right and left ventricular function. The patient had a 5-year history of asthma. Early therapy with high-dose prednisolone and azathioprine led to resolution of the pericardial effusion and prevented a further reduction in biventricular function. ***(Texas Heart Institute Journal 1991;18:127-31)***

In 1951, Churg and Strauss[1] described 14 cases of disseminated vasculitis in patients with asthma. These patients had multisystem involvement with a histopathologic triad that comprised necrotizing arteritis, eosinophilic infiltration, and extravascular granuloma formation. The criteria for diagnosing Churg-Strauss syndrome include preceding asthma, eosinophilia (>1.5 x 10^9 L), and systemic vasculitis in at least 2 extrapulmonary organs;[2] however, all 3 of these criteria are met in only 13% of the cases.[3] Although cardiac involvement was commonly documented at postmortem examination in the original series,[1] and although heart failure is the most frequent cause of death,[3] cardiac involvement is rarely reported.[4]

We describe a case of Churg-Strauss syndrome in which both pericardial and myocardial involvement occurred acutely. Impairment of biventricular function was halted with early corticosteroid therapy.

Case Report

In October 1989, a 30-year-old man with a 6-week history of increasing exertional dyspnea and a nonproductive cough was admitted to another hospital for diagnostic assessment. Chest radiography disclosed mild pulmonary infiltrates in the lower lobes (Fig. 1A). Upon discharge, the patient was placed on antibiotic therapy, which proved unsuccessful; he was then given a 4-week course of prednisolone, in daily doses tapering from an initial dose of 30 mg daily. He continued to experience marked exertional dyspnea associated with an exercise tolerance of only 20 meters. He also reported malaise, generalized myalgia, lethargy, and occasional night sweats. Two months after presentation, he experienced sudden sharp precordial chest pain, which increased upon supination. The pain persisted for several days, and acute pericarditis was diagnosed. He then developed right-sided meralgia paresthetica and a productive cough, which necessitated readmission to the hospital in January of 1990.

Upon readmission, chest radiography showed a large, globular heart (Fig. 1B) and clear lung fields. Laboratory studies revealed peripheral blood eosinophilia (3.5 x 10^9 L), and cross-sectional echocardiography confirmed the presence of a large pericardial effusion. At pericardiocentesis, the aspirated fluid contained numerous eosinophils and had a protein content of 5.5 g L. Culture of the fluid (including a test for mycobacteria) was negative. The patient began to experience right-sided sciatic pain accompanied by lateral numbness of the right foot, so he was transferred to our institution for further studies.

At admission, enquiry confirmed a 5-year history of recurrent sinusitis and nasal polyposis. The patient reported no specific symptoms of atopy but did report documented asthma during the same 5-year period. He had emigrated to the United Kingdom from India in 1971, but had not recently traveled abroad. His family had

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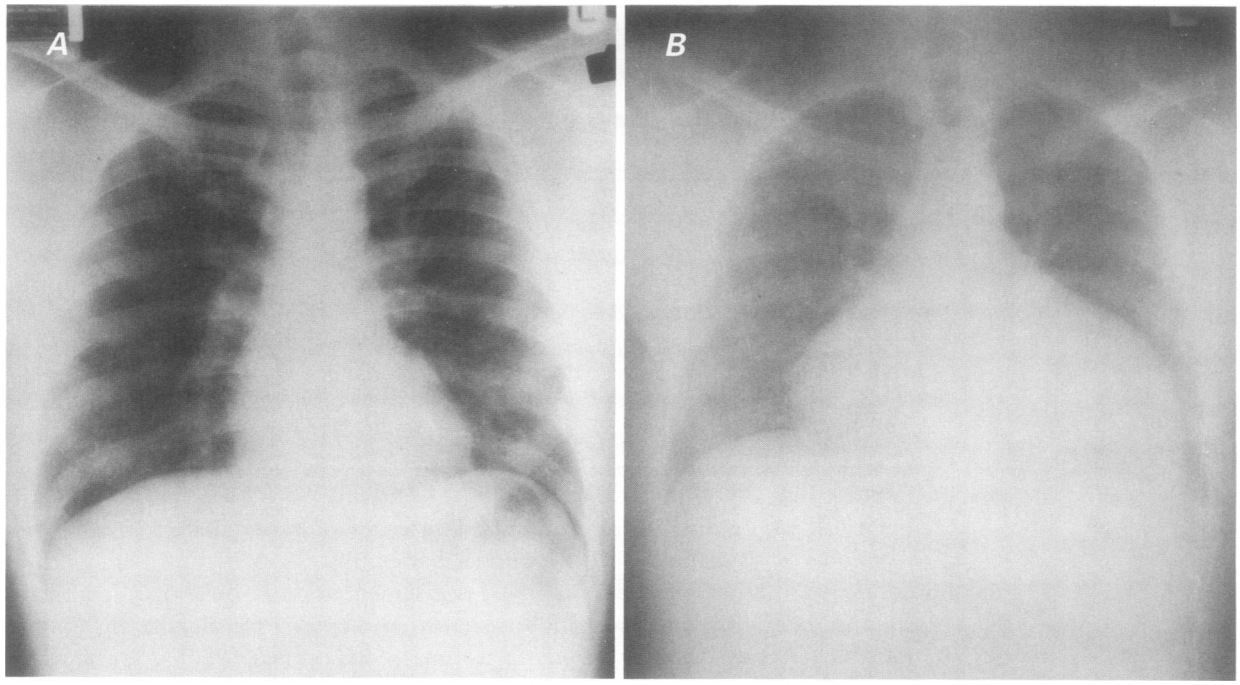

Fig. 1 *Chest radiographs showing* ***A****) normal cardiac size with mild pulmonary infiltrates and* ***B****) gross cardiomegaly.*

a history of rheumatoid arthritis. His medications included salbutamol and beclomethasone inhalers and dihydrocodeine. He was a nonsmoker.

On physical examination, the patient was mildly pyrexial but had no rashes or purpura. He had a normal, regular pulse without evidence of pulsus paradoxus. His jugular venous pressure was not elevated. The cardiac apex beat was diffuse and displaced laterally, and there was a soft 4th heart sound. Respiratory examination revealed no abnormalities. On the right side, the patient had grade 4/5 weakness of finger extension, hip extension, and plantar flexion and eversion, as well as an absent ankle jerk response. Light-touch sensation was reduced in the distal portion of the left ring finger and on the lateral border of the right foot. Dysesthesia was noted over the lateral right thigh, and the right leg could be raised to only a 30° angle.

Laboratory investigation revealed a total leukocyte count of 14.8 x 10^9/L, with an eosinophil count of 6.1 x 10^9/L; a hemoglobin of 12.3 g/dL; and a platelet count of 378 x 10^9/L. The erythrocyte sedimentation rate was 106 mm/hr according to the Westergren method, and the C-reactive protein level was 186 U/L (normal, <10 U/L). The IgE level was 165 U/L (normal, 0 to 122 U/L) and the IgG level was 21 U/L (normal, 5 to 16 U/L). The IgM, IgA, and complement levels were normal. Latex agglutination showed that the rheumatoid factor was positive to 1/80 (a nonspecific finding), but both antineutrophil cytoplasmic and antinuclear antibody assays yielded negative results. The patient's hepatitis B surface antigen status was negative. Coxsackievirus, *Legionella pneumophila*, *Mycoplasma pneumoniae*, and *Chlamydia psittaci* titers revealed no current or past infection. Immunoassays were negative for *Strongyloides* and microfilaria, and stool microscopy showed no abnormalities. Electrocardiography revealed anterolateral T-wave inversion, with no ST-segment changes. Pulmonary function tests confirmed an FEV_1/FVC ratio of 2.70/3.00 (90%) and a K_{CO} of 116% of predicted, suggesting the presence of a predominant restrictive defect. Computed tomography of the lumbar spine revealed a central L5/S1 disc protrusion that was calcified. Cross-sectional echocardiography disclosed a moderately large pericardial effusion and a slightly dilated left atrium (42 mm). The left ventricular dimensions were normal (left ventricular end-systolic diameter [LVESD] = 36 mm; left ventricular end-diastolic diameter [LVEDD] = 49 mm), but there was mild global hypokinesis (fractional shortening = 26.5%; normal, 29% to 37%) and evidence of diastolic right atrial and ventricular collapse (Fig. 2). Histologic examination of the previously resected nasal polyps confirmed widespread eosinophilic infiltration but showed no vasculitis.

Cardiac catheterization yielded the following pressure measurements: mean right atrial, 7 mmHg; right ventricular, 42/8 mmHg; pulmonary arterial, 42/16 mmHg; mean pulmonary artery wedge, 16 mmHg; and left ventricular, 110/24 mmHg. Angiography disclosed normal coronary arteries, but right and left ventriculography confirmed a global reduction in biventricular function. Histologic examination of right

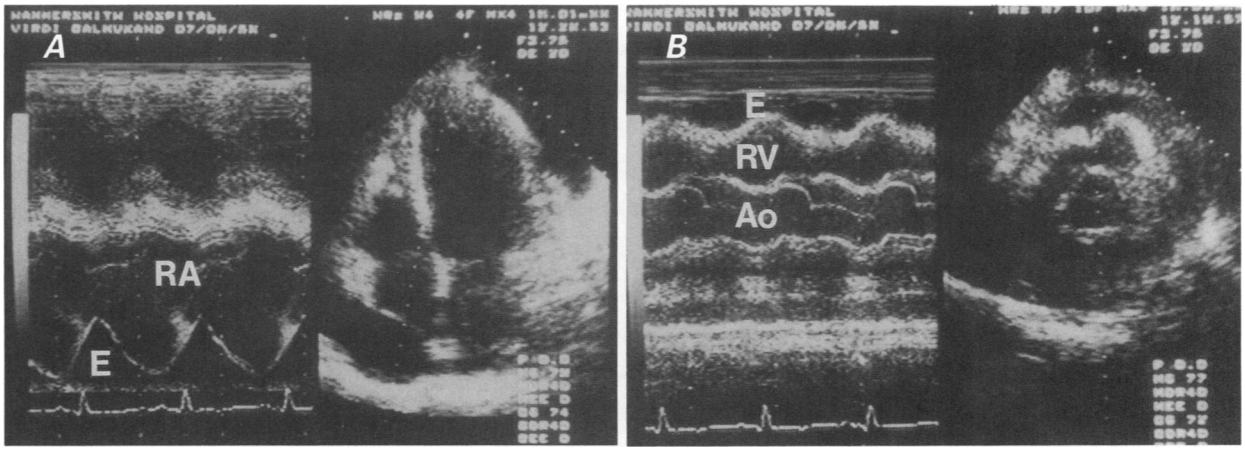

Fig. 2 *M-mode and cross-sectional echocardiograms revealing* ***A****) right atrial collapse during early systole in the apical 4-chamber view and* ***B****) right ventricular collapse during early diastole in the parasternal short-axis view. In the M-mode images, note the presence of a moderate pericardial effusion.*

Ao = aortic root; E = effusion; RA = right atrium; RV = right ventricle

ventricular biopsy specimens revealed a normal endocardium and mild interstitial myocardial fibrosis. The interstitium exhibited mild eosinophilic infiltration throughout (Fig. 3).

Churg-Strauss syndrome was diagnosed in light of the preceding history of asthma, as well as the eosinophilia, the clinical evidence of mononeuritis multiplex and eosinophilic myopericarditis, and the reduced myocardial function. Once therapy had been initiated with 60 mg of prednisolone per day, the patient had a decrease in dyspnea and an abatement of neurologic symptoms, concurrent with normalization of his eosinophil count, sedimentation rate, and C-reactive protein level. Ten days later, azathioprine (100 mg daily) was added because of the severity of the disease.

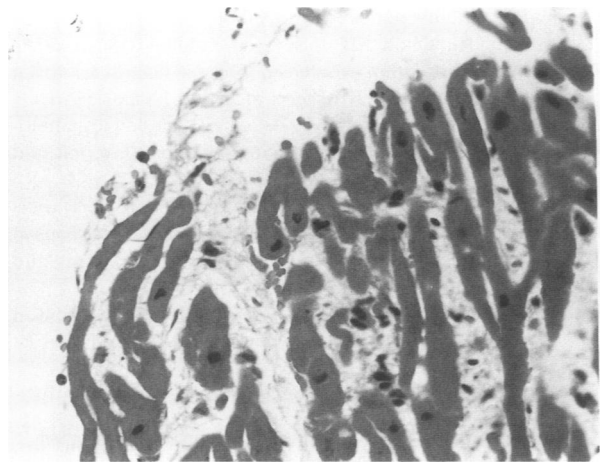

Fig. 3 *Histologic section of myocardium taken at right ventricular biopsy, showing mild eosinophilic infiltration and myocardial interstitial fibrosis. (H + E orig. x400)*

After 4 weeks of in-hospital treatment, the steroid dose was reduced to 40 mg. Repeat cross-sectional echocardiography revealed an LVESD of 39 mm and an LVEDD of 52 mm, with no change in the global left ventricular function (fractional shortening = 25%) or the size of the pericardial effusion.

Four weeks after hospital discharge, the patient returned for a follow-up study, which confirmed a resolution of his malaise, lethargy, and dyspnea, as well as an improvement in his neurologic and pulmonary status. Due to an increase in the sedimentation rate to 45 mm/hr, the azathioprine dosage was increased to 150 mg per day. Over the next 4 weeks, the patient's normal exercise tolerance was regained and maintained. Three months later, the prednisolone dosage was reduced to 30 mg per day, but the azathioprine dosage was not changed. Cross-sectional echocardiography confirmed fair biventricular function (LVESD = 41 mm; LVEDD = 54 mm; fractional shortening = 24.1%) and only a small posterior pericardial effusion.

Discussion

In the initial report describing Churg-Strauss syndrome, the epicardium was the most common site of granuloma formation (60% of all patients in the series).[1] Seventy percent had interstitial myocardial eosinophilic inflammation that ranged from an occasional focal infection to diffuse myocarditis. Myocardial fibrosis was common; the authors suggested that this phenomenon resulted from ischemia secondary to vasculitis or from scarring caused by inflammatory foci.[1] In describing the largest series reported to date, Chumbley and coworkers[3] did not mention cardiac involvement; but a later review of the English litera-

ture (with the addition of 6 new cases) found that cardiac failure had occurred in 47% and pericarditis in 32% of all cases, the former disorder accounting for 48% of the deaths.[2]

In recent years, the cardiac complications of Churg-Strauss syndrome have been studied more comprehensively. Cross-sectional echocardiography has shown increased myocardial echo intensity consistent with increased myocardial collagen content, in the absence of acute manifestations of the disease.[5] Moreover, in 1 series, mitral regurgitation was detected in 6 out of 12 patients, 2 of whom required mitral valve replacement. Regurgitation was attributed to direct papillary muscle fibrosis, in the presence of normal valve cusps. Because generalized myocardial fibrosis can remain subclinical,[5] it might be that myocarditis is rarely reported. In a recent case involving a patient who required heart transplantation, fibrinoid necrosis of small intramyocardial vessels was observed.[6] In the absence of vasculitis, however, foci of myocardial fibrosis and mild eosinophilic infiltration are all that were seen, as in the case we report here. Eosinophilic coronary arteritis may occur in the form of granulomatous vasculitis, often accompanied by granulomatous myocarditis,[7] and such arteritis has been reported as a limited form of the disease in the absence of systemic manifestations.[8]

In 2 cases diagnosed in life,[9] eosinophilic endomyocardial involvement in Churg-Strauss syndrome led to the development of an obliterative cardiomyopathy (as usually seen in the hypereosinophilic syndrome). This suggests a mechanism for ventricular impairment: there is a well-known association between eosinophilia and the endomyocardial disease encountered in the tropics, in Löffler's syndrome, and in endomyocardial fibrosis.[10] In temperate climates, eosinophilic endomyocardial disease usually appears as a feature of the idiopathic hypereosinophilic syndrome that occurs predominantly in men and often produces eosinophil counts as high as 100 x 10^9/L. This syndrome affects both ventricles; by passing through an acute necrotic and then a thrombotic stage, it leads to endomyocardial fibrosis.[10] There is good evidence that the eosinophils are responsible for tissue injury, particularly eosinophils in the degranulated form. Such eosinophils have an increased capacity for binding IgG,[11] as well as an enhanced capacity for causing cytotoxicity in vitro.[12] When incubated with isolated cardiac cells from rat hearts, eosinophil proteins such as cationic proteins, released upon degranulation, have induced sodium-pump stimulation and increased cellular respiration, both probable indications of cytotoxicity.[13] Infusions of human eosinophil granule proteins into rats have caused acute endocardial and myocardial necrosis in perivascular areas.[10] Although we have these reasons to believe that eosinophil cationic proteins may injure cardiac myocytes, the stimulus for degranulation remains unknown. Also unknown is why eosinophil-induced damage—if it does indeed occur in Churg-Strauss syndrome—commonly presents as myopericarditis, rather than as endomyocardial disease.

The combination of global myocardial dysfunction with a large pericardial effusion after acute pericarditis—indicative of widespread cardiac involvement—has been encountered once before in Churg-Strauss syndrome.[4] A vasculitic process, with eosinophilic infiltration, may be the usual mechanism for myocardial impairment. In our case, however, the dyspnea and exercise limitation was more likely caused by pulmonary infiltrates. Our patient had an abnormally high count of eosinophils throughout his myocardial interstitium, together with reduced biventricular function at echocardiography and angiography, in the absence of hemodynamic evidence of tamponade. As is usually seen,[2] there was no further deterioration in myocardial function after the patient responded well to high-dose corticosteroids, and his symptoms resolved. The strong potential for arresting progression of ventricular impairment underlines the need for early echocardiographic diagnosis, followed by cardiac catheterization, ventricular biopsy, and prompt, adequate treatment of myopericarditis. This approach can reduce the mortality associated with this rare syndrome.

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