Case Reports

Aortic Valvulitis in a Patient With Wegener's Granulomatosis

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WEGENER'S GRANULOMATOSIS was characterized as a clinical syndrome by Wegener in 1936.[1] Manifested by granulomatous vasculitis of the upper and lower respiratory tracts and by glomerulonephritis, Wegener's granulomatosis is frequently associated with vasculitis involving other organs. Clinically evident cardiac disease is uncommon. In this report we describe the case of a patient with Wegener's granulomatosis who presented with acute aortic insufficiency requiring surgical replacement. The histologic examination of the native valve revealed changes consistent with Wegener's granulomatosis.

Report of a Case

The patient, a 77-year-old woman, was transferred to the University of California, San Francisco (UCSF), Medical Center in early November 1987 for worsening dyspnea, pulmonary infiltrates, and cavitary lesions of the lung. She had had a right upper lobectomy for removal of a solitary cavitary lesion in November 1986, which on pathologic examination was diagnosed as a lung abscess. The patient was well until early October 1987 when she noted dyspnea on exertion and a cough productive of blood-streaked mucus. She had a long history of sinus problems that had recently worsened with several episodes of bleeding from her left nostril. Her dyspnea became more severe, and paroxysmal nocturnal dyspnea and orthopnea developed. She had also recently noted a rash on her legs and hands. A chest x-ray film revealed bilateral infiltrates and cavitary lesions of the lung.

In late October on admission to another hospital, she had bibasilar rales in her lungs; no gallop or murmur was heard. She had petechiae and purpura on the dorsum of her feet and the periungual areas of her hands. Arterial blood gas determinations made while the patient was receiving six liters of oxygen by mask revealed a pH of 7.44, a partial carbon dioxide pressure of 32 mm of mercury, and a partial oxygen pressure of 65 mm of mercury. Fine needle aspiration of a cavitary lesion was reported to show caseous necrosis, and treatment with isoniazid and rifampin was begun for presumed tuberculosis. The patient's respiratory status continued to deteriorate, and she was transferred to UCSF for further evaluation.

On admission, the patient's blood pressure was 130/40 mm of mercury, her pulse was 120 per minute, and temperature 37°C (98.6°F). There were many raised purpura on the dorsum of her feet and several raised, firm, tender, pustular nodules on the periungual areas of her fingers. She had scleritis of her right eye. There was clinical evidence of congestive heart failure, including rales in the lower half of her lung fields, a jugular venous pressure of 10 cm of water, and a summation gallop with a grade II/VI systolic murmur at the base and a grade I/VI blowing diastolic murmur at the left sternal border. In addition, there was 4+ pitting pedal edema up to the knees.

Laboratory studies elicited the following values: hematocrit 0.28, leukocyte count 13.2×10^9 per liter, blood urea nitrogen 23.2 mmol per liter of urea (65 mg per dl [normal, 3.0 to 6.5 mmol per liter]), creatinine 132 μmol per liter (1.5 mg per dl [normal, 50 to 110 μmol per liter]), prothrombin time 13.4 seconds, albumin 26 grams per liter (2.6 grams per dl), C3 1 gram per liter (100 mg per dl), C4 0.24 grams per liter (23.8 mg per dl), and CH_{50} 0.034 U per liter (34.0 units per ml). A urinalysis showed 0.3 grams per liter protein by dipstick, 40 leukocytes per high-power field, and 10 erythrocytes per high-power field; no casts were seen. On a chest roentgenogram she had worsening diffuse hazy densities and cavitations bilaterally. An electrocardiogram showed sinus tachycardia, normal intervals, and nonspecific ST segment and T-wave abnormalities in the inferolateral leads.

Five sets of blood cultures were done, and all were negative for pathogens. Culture of specimens of pustular lesion on the hand and of sputum elicited no pathogens. Empiric antibiotic therapy was begun for presumed bacterial endocarditis. An echocardiogram showed severe aortic insufficiency with mild left ventricular dilatation. The left ventricular contractile function was moderately decreased. There was moderate mitral regurgitation and a suggestion of a small vegetation (less than 5 mm) on the posterior leaflet of the mitral valve.

The patient's congestive heart failure continued to worsen, and she was taken to the operating room on the second hospital day for a valve replacement. On gross inspection, the right and left coronary cusps of the aortic valve appeared normal but the noncoronary cusp was red and thickened. The anterior leaflet of the mitral valve was slightly thickened, and the posterior leaflet was normal. No vegetations were seen. The aortic valve was excised, and a Carpentier-Edwards porcine prosthesis was placed.

On pathologic examination, the aortic valve showed myxomatous change and degeneration of collagen consistent with collagen vascular disease (Figure 1). The inflammatory response was insignificant, and there was no evidence of bacterial endocarditis. Culture of a specimen of the aortic valve and a swab of the mitral valve was negative for bacteria. A review of a specimen of the pulmonary lesion removed in 1986 showed necrotizing granulomatous inflammation and arteritis consistent with Wegener's granulomatosis. A review of a skin biopsy specimen of a purpuric lesion on the patient's elbow a day before transfer showed vasculitis and extravascular granulomatous changes, also consistent with Wegener's granulomatosis.

Postoperatively the patient had renal insufficiency with a peak blood urea nitrogen level of 39.3 mmol per liter of urea

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(110 mg per dl) and a creatinine level of 371 μmol per liter (4.2 mg per dl). A urinalysis showed pyuria and hematuria. Following the diagnosis of Wegener's granulomatosis, she received an intravenous pulse dose of 800 mg cyclophosphamide, and a regimen of methylprednisolone sodium succinate, 60 mg a day, was begun. The patient's condition gradually improved, and she was discharged to a rehabilitation facility six weeks after admission on a regimen of cyclophosphamide, 75 mg per day, and prednisone, 60 mg per day, with considerable resolution of her pulmonary and skin lesions.

Comment

This case fulfills the clinicopathologic criteria for Wegener's granulomatosis described by Godman and Churg,[2] although the patient's clinical course was somewhat protracted.[3] The initial manifestation of her disease was a cavitary lung lesion that was removed and misinterpreted as a lung abscess. Even though immunosuppressive therapy was not given, nearly a year passed before she was seen again with extensive pulmonary, ocular, dermatologic, and aortic valve involvement. In addition, the renal failure that developed postoperatively was presumably due to glomerulonephritis, although no renal biopsy was done to confirm this.

Although Wegener's granulomatosis is a systemic disorder, clinical evidence of cardiac involvement is uncommon. Involvement of the heart has been reported in 30% of patients at autopsy.[4] In a recent report of 85 patients being observed for Wegener's granulomatosis at the National Institutes of Health, 12% had clinical evidence of cardiac involvement, usually of the pericardium and myocardium.[5] Involvement of the heart valves is rare and generally noted at autopsy.

We think this is the first reported case of pathologically documented involvement of the aortic valve in association with Wegener's granulomatosis. While myxomatous alteration of a valve is common and not always associated with underlying disease, degeneration of collagen representing early fibrinoid change is seen primarily in the collagen vascular diseases. Inflammation and fibrinoid necrosis of the mitral valve have been reported in six patients with Wegener's granulomatosis at autopsy.[2,6-9] Two cases of presumed aortic valve involvement in Wegener's granulomatosis have been reported. Gerbracht and co-workers reported the case of a 20-year-old man who suffered a myocardial infarction five days after immunosuppressive therapy was begun following an initial diagnosis of Wegener's granulomatosis.[10] An echocardiogram showed increased reflectance of the noncoronary cusp of the aortic valve, which returned to normal over two months with treatment. Dabbagh and associates reported the case of a 16-year-old boy in whom aortic insufficiency developed, detected by examination and echocardiogram during the third week of immunosuppression treatment of Wegener's granulomatosis.[11]

In summary, although aortic valvular involvement in Wegener's granulomatosis is rare, this case shows that it does occur and may be severe enough to require emergent surgical intervention. The pathologic changes in the valve leaflets, while not specific, are unusual and suggest the presence of a collagen vascular disease.

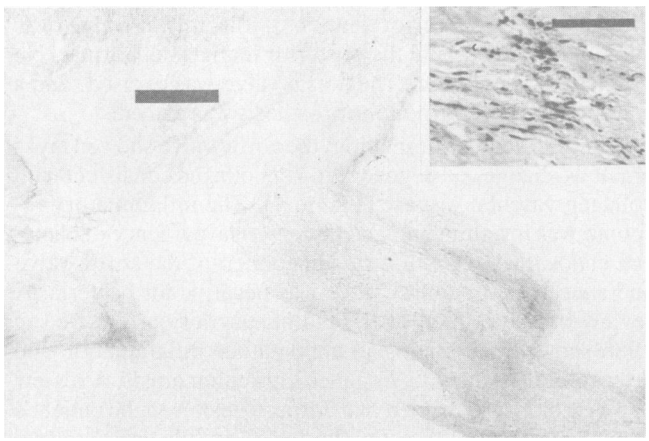

Figure 1.—On histologic examination, a specimen of the aortic valve shows myxomatous degeneration (hematoxylin and eosin; original magnification × 10, scale = 1 mm). **Inset,** There is focal necrosis of collagen (hematoxylin and eosin; original magnification × 100, scale = 0.1 mm).

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Intestinal Pseudo-obstruction Related to Using Verapamil

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VERAPAMIL has become increasingly popular for treating supraventricular tachycardia, angina pectoris, and hypertension.[1-3] Gastrointestinal adverse effects of using verapamil include constipation and nausea.[4] The constipation is frequently substantial enough to warrant discontinuing the medication and using an alternative. We report a case of intestinal pseudo-obstruction apparently aggravated by the use of verapamil for supraventricular tachycardia. This adverse effect appears to be a logical extension of the drug's action.

Report of a Case

The patient, a 73-year-old woman, was admitted to hospital in May 1988 because for two weeks she had had right

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