Granulomatous mitral valve obstruction

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Acquired non-rheumatic valvular mitral valve obstruction is extremely rare. A case of mitral valve obstruction is described which resulted from a granulomatous mass replacing the valve cusps. The problems in diagnosis and probable aetiology are discussed.

Acquired non-rheumatic valvular obstruction involving the mitral leaflets is extremely rare. Obstruction to left ventricular inflow may be caused by tumours and other masses in the left atrium which prolapse through the mitral orifice during ventricular diastole. All these are rare and include left atrial myxomas and malignant neoplasm as well as fungal masses and ball thrombi. We describe a case of non-rheumatic granulomatous mitral valvular obstruction with associated pulmonary lesions and discuss both the diagnostic problems and probable aetiology.

Case report

The patient, a 42-year-old Grenadan woman, was first seen in the chest clinic at Hammersmith Hospital in 1967 because of persistent hoarseness. At that time the chest radiograph was normal and a Heaf tuberculin test negative. However, cultures from two laryngeal swabs grew an atypical scotochromogenic mycobacterium of doubtful significance. Annual chest radiographs were taken and in 1972 first showed the development of bilateral apical opacities. In 1972 the patient had an uneventful eighth and twin pregnancy. She had at no time had rheumatic fever or contact with tuberculosis.

When she was initially examined in March 1974 the only significant cardiovascular abnormality was a soft pansystolic murmur. When admitted to hospital in May 1974 she had developed florid signs of pulmonary hypertension with early right ventricular failure, and showed an increased 'a' wave in the venous pulse in the neck, parasternal heave, and delayed accentuated pulmonary component of the second heart sound. The pansystolic murmur was still present and in addition there was now a dull opening snap but no mid-diastolic murmur. The electrocardiogram had also changed from normal in March to show right ventricular hypertrophy, which later became more distinct (Fig. 1). Serial chest radiographs from 1972 showed the development of pul-

monary venous hypertension and left atrial enlargement together with the bilateral apical opacities.

The haemoglobin was 11.4 g/dl; WBC 8000 (63% lymphocytes); ESR (Westergren) 80 mm in one hour. Protein electrophoresis showed a pronounced increase in gammaglobulin and immunoglobulins IgG 3360, IgM 206, IgA 484 mg/100 ml. Tests of thyroid and adrenal function were normal. Mantoux test was negative 1:10 000. Multiple cultures of sputum, urine, gastric aspirate, bone marrow, and laryngeal swabs were negative for mycobacteria. An echocardiogram (Fig. 2) showed a mobile yet stenotic mitral valve. However, in several views multiple echoes may be seen between the abnormally moving posterior echo, which is separated from the anterior cusp even in systole. Cardiac catheterization confirmed that there was pronounced pulmonary arterial and venous hypertension. Pressures were: pulmonary artery 60/30 mmHg (8/4 kPa); pulmonary wedge (mean) 26 mmHg (3.5 kPa); left ventricle 110/9 mmHg (14.6/1.2 kPa) with an indirect mitral valve gradient of 16 mmHg (2.1 kPa) at end diastole. The left ventriculogram showed mild mitral regurgitation with unusual trapping of contrast medium behind the mitral valve cusps. In retrospect, the pulmonary arterial follow-through injection shows a filling defect in the position of the mitral valve (Fig. 3).

Antituberculosis chemotherapy was instituted because of the x-ray appearances of apical tuberculosis, and it was decided to replace the mitral valve. However, while waiting for surgery the patient was readmitted in acute pulmonary oedema. On 16 December 1974 a mitral valve replacement was carried out by Mr. Brian Pickering. The left atrium was opened transversely. The mitral valve leaflets could not be recognized. In their place was a smooth, tumour-like mass some 2 cm thick and forming two lumps 3 cm long not bounded by the mitral ring but extending to the aorta and left pulmonary veins. It was covered with apparently normal endothelium, and attached to the underside were normal chordae and papillary muscles. The mass was excised and a 30-mm Starr-Edwards valve inserted. There was some difficulty in attaching the valve ring securely as several stitches had to pass through abnormal tissue.

FIG. 1 *Electrocardiograms (A) March 1974, (B) November 1974, showing rapid development of left atrial and right ventricular hypertrophy.*

The tissue removed at cardiectomy consisted of two large fragments, measuring $4 \times 3 \times 1.5$ and $3 \times 2.5 \times 1.5$ cm, and a number of smaller pieces of papillary muscle, chordae, and fibrous tissue (Fig. 4). The large fragments were firm, with glistening, slightly bosselated superior surfaces, and gradually merged with the chordae at the free margins of the valve cusps. The chordae did not appear thickened or shortened and there was no fibrosis of the papillary muscle tips. The cut surface of the large fragments presented a mottled yellowish grey appearance with a translucent rim on the superior surface. No verrucae were evident on the valve cusps nor was there calcification in the tissue. Microscopy of the valve showed complete replacement of normal architecture by coalescent granulomata containing a central zone of necrosis surrounded by palisaded histiocytes, with scattered giant cells and a mantle of lymphocytes (Fig. 5). In the more fibrous 'endocardial' zone many typical Anitschkow myocytes were evident (Fig. 6) together with histiocytic cells containing SSD- and ZN-positive material. No residual elastica of the valve could be identified. Interestingly, the reticulin framework persisted in the areas of necrosis. Staining of the tissue by various methods failed to show any evidence of mycobacteria, spirochaetes, rickettsia, fungi, or more commonplace organisms.

After surgery the patient initially made a good recovery but a soft systolic murmur became audible before discharge. While at convalescence she became very dyspnoeic and developed severe congestive cardiac failure. A loud pansystolic murmur was noted. Left ventricular angiography showed dehiscence of the mitral

FIG. 2 *Echocardiogram of mitral valve area showing structure with two interfaces separated in both diastole and systole.*

valve ring with a paraprosthetic regurgitant jet and gross reflux of contrast medium into the left atrium. On 14 February 1975 the mitral prosthesis was explored and the posterior, inferior border of the mitral valve ring found to be loose. The mitral valve ring was buttressed with Teflon and the prosthesis resutured. She has since made an excellent recovery and currently is being treated with antituberculous chemotherapy. Subsequent Mantoux reactions (1:100), skin tests for atypical mycobacteria (*M. kansas*, *M. battey*, and *M. scrofulaceum*), and a Kveim test were negative.

Discussion

The diagnostic problems posed by this case are of particular interest. There were strong reasons for doubting that the patient had simple rheumatic mitral valve stenosis. At the age of 42 she had rapidly developed symptoms and signs of severe pulmonary hypertension over the course of a few months yet had uneventfully survived a twin pregnancy only two years previously. There was also good evidence of systemic disease (WBC, ESR, immunoglobulins). To our surprise, angio-

FIG. 3 Pulmonary arteriogram PA view. L atrial and ventricular phase showing filling defect in position of mitral valve.

graphy showed no evidence of a left atrial myxoma and the echocardiogram was thought to be compatible with valvular mitral stenosis. Retrospectively, it is apparent that both investigations

provided clues to the real nature of the valvular obstruction.

Granulomatous lesions of the endocardium are recorded in both tuberculosis and sarcoidosis. True tuberculous endocarditis is excessively rare (Mark, 1938; Davie, 1936; Baker, 1935), but tuberculomas have been reported to obstruct blood flow in the right atrium (Eisenmenger, 1900) and pulmonary outflow tract (Raws *et al.*, 1968). Sarcoidosis usually affects only the myocardium but endocardial vegetations of the aortic and mitral valves have been reported (Faivre *et al.*, 1956). There have been no reports of endocardial sarcoidosis obstructing blood flow or producing valvular stenosis. Mitral regurgitation consequent on papillary muscle involvement has been described in a patient with myocardial sarcoidosis (Raftery, Oakley, and Goodwin, 1966).

In the present case the associated pulmonary lesions and granulomatous replacement of the mitral valve cusps make either tuberculosis (typical or atypical) or sarcoidosis must likely. The preservation of an endocardial layer excludes an endocarditic process such as described in the patient with sarcoidosis (Faivre *et al.*, 1956), or tuberculous endocarditis (Mark, 1938). Sarcoidosis is favoured by the preservation of the reticulin pattern in the central necrotic zones of the endocardial layer together with the persistently negative tuberculin tests, despite the absence of a positive Kveim reaction. An atypical mycobacterium could possibly cause similar features, and as such an organism was

FIG. 4 Excised mitral valve ring, tumours, chordae, and papillary muscles.

FIG. 5 Left: Low power view of granuloma. N=central necrosis; H=palisaded histiocytes; L=lymphocytic surround. (H. and E. $\times 50$.) Right: Constituent cells of granuloma. Lymphocytes, histiocytes, and multinucleate giant cells. (H. and E. $\times 500$.)

FIG. 6 Amitschkow 'myocytes' in subendocardial region of valve cusps. (H and E. $\times 625$.)

isolated in 1967 (though a scotochromogen) this aetiology must remain a distinct possibility.

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Addendum

Since this report was submitted, follow-up chest x-rays have shown the development of fine nodular shadowing throughout both lung fields. These changes have occurred while the patient was on full antituberculous chemotherapy and are consistent with a diagnosis of sarcoidosis.

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