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Mitral stenosis in Whipple's disease

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Rose, Alan G (1978). *Thorax*, **33**, 500–503. **Mitral stenosis in Whipple's disease.** A patient who died of Whipple's disease had moderate mitral stenosis with large firm yellow vegetations on the contact area of the mitral leaflets. Light microscopy showed PAS positive macrophages within the thickened cusps and overlying vegetations. Negative images of rod-shaped bodies were visible in the cytoplasm of the histiocytes. No Aschoff bodies were seen, and there was no history of rheumatic fever. The findings in this patient lend support to the concept that chronic rheumatic type valvar deformity may result from a persistent intrinsic infectious agent.

Although pericarditis is present in more than two-thirds of patients with Whipple's disease, verrucous endocarditis in about one-third, and sudden death occurs in 20%, cardiac involvement has attracted little attention. Few reports (Sieracki and Fine, 1959; Enzinger and Helwig, 1963; James and Haubrich, 1975; McAllister and Fenoglio, 1975; Lie and Davis, 1976) document the cardiac pathology in Whipple's disease in detail. The favourable prognosis of Whipple's disease with antibiotic treatment has reduced the opportunity for examining the cardiac pathology in this disease. The paucity of pathological descriptions of the cardiac alterations in Whipple's disease prompts me to document the findings at necropsy in the heart of a patient with Whipple's disease. Furthermore, this patient supports the concept that disease other than rheumatic fever may lead to diffuse thickening and fibrosis of the mitral valve leaflets and chordae tendineae.

Case report

The patient, a 52-year-old man, presented in 1963 with a three-year history of malaise, anorexia, loss of weight, and diarrhoea. A laparotomy had been performed a few years before at another hospital, but no diagnosis had been made. There was no history of rheumatic fever.

Examination showed an emaciated man with a blood pressure of 95/60 mmHg. No heart murmurs were heard, and examination of the other systems showed no abnormality. Mild bilateral supraclavicular lymphadenopathy was noted. The haemoglobin was 10·5 g/dl, the sedimentation rate 50 mm in the first hour (Westergren), and urine analysis results were normal.

Biopsy of a supraclavicular lymph node showed large collections of foamy macrophages that contained PAS-positive oval and rod-shaped bodies within their cytoplasm. The appearances were those of Whipple's disease. A jejunal biopsy result was also positive for Whipple's disease. Biopsy of the liver showed no abnormality. A xylose tolerance test result was normal, and there was no excess of fat in the stool. Serum albumin was 28 g/l and serum globulin 26 g/l.

The patient's condition improved on general supportive treatment and a gluten-free and low fat diet. (The value of antibiotics in treating Whipple's disease had not been widely recognised in 1963.) No steroids were given. The patient was discharged much improved after several months in hospital. Several months later he was readmitted because of severe diarrhoea and abdominal pain. Death occurred suddenly soon after admission.

At necropsy the patient was greatly emaciated and had diffuse moderate lymphadenopathy. The small bowel showed the typical changes of Whipple's disease. The pericardial sac contained 300 ml of straw-coloured fluid, the heart weighed 276 g and showed signs of brown atrophy. The mitral valve (fig 1) admitted only one finger and had a ring circumference of 7 cm. Commissural fusion was present. The chordae tendineae were thickened and fibrosed with some fusion. In the contact area of the cusps there were numerous confluent firm yellow vegetations. A single similar vegetation was present on the septal leaflet of the tricuspid valve, which appeared otherwise normal.

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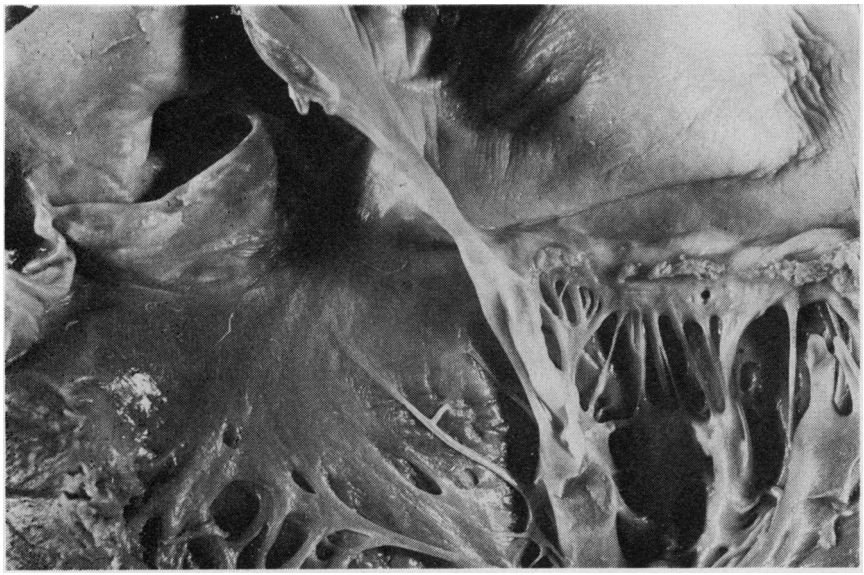

Fig 1 *Close-up view of mitral and aortic valve cusps. Mitral cusps and chordae are thickened, and chordal fusion is seen. Vegetations are seen along contact area of mitral valve.*

The aortic and pulmonary valves looked normal. The coronary arteries showed no significant atherosclerosis, and the myocardium showed no evidence of infarction or fibrosis.

Histologically, the small bowel, lymph nodes, liver, spleen, bone marrow, and pituitary gland showed typical alterations of Whipple's disease. The mitral valve (figs 2–4) had organising platelet-fibrin thrombus on the contact area of the cusps. A few polymorphs, lymphocytes, and histiocytes were present near the surface of the thrombus. Deeper within the vegetation and in the cusp substance were large plump macrophages, which stained faintly with haematoxylin and eosin. These histiocytes contained fine granules that stained strongly by the PAS method to show negative images of rod-shaped bodies in the cytoplasm (fig 4). No Aschoff bodies were seen in the myo-

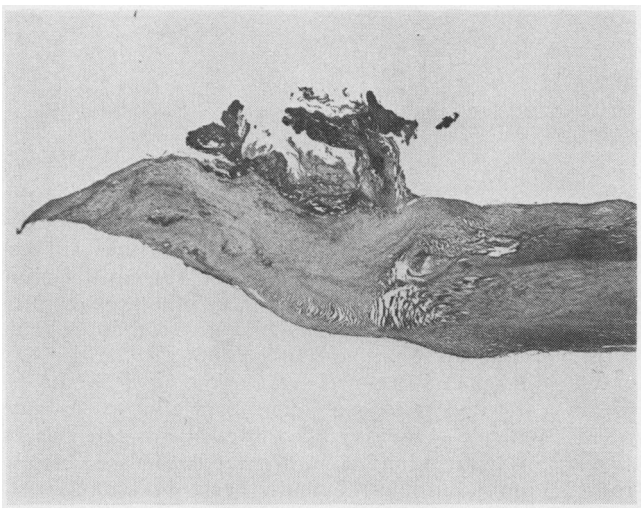

Fig 2 *Section of thickened mitral valve cusp showing platelet-fibrin thrombus on contact area (Haematoxylin and eosin stain, ×8).*

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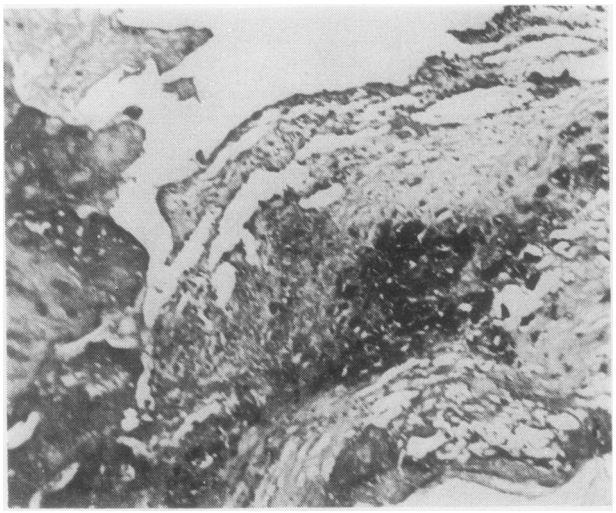

Fig 3 *Dark-staining PAS-positive macrophages within mitral valve cusp and in deeper portion (lower left) of surface thrombus (Periodic acid-Schiff stain, ×60).*

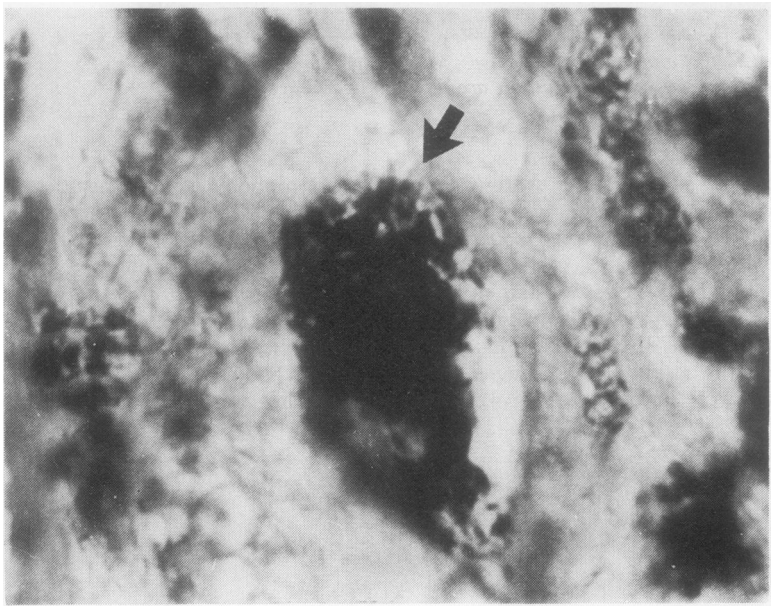

Fig 4 *Ghost outlines (arrow) of numerous rod-shaped bodies are seen within cytoplasm of a darkly stained PAS-positive macrophage lying within substance of mitral valve (Periodic acid-Schiff stain, ×1500).*

cardium. The myocardium and small coronary arteries showed no evidence of being affected by Whipple's disease, and there was no pericarditis.

Discussion

Although cardiac involvement has been reported in Whipple's disease, the cardiac symptoms are usually overshadowed by the prominent intestinal symptoms. Often, as in our patient, the cardiac disease has only been recognised at necropsy. Control of the disease by antibiotics has removed most cases of Whipple's disease from the realm of the morbid anatomist. A case may be missed clinically from time to time, however, and the onus will rest on the pathologist to make the correct diagnosis at necropsy. While changes in other organs provide important clues, the diagnosis is more difficult in less severe or abortive forms of the disease. Any thickened valve with vegetation on it should be carefully examined microscopically to exclude Whipple's disease. The mitral valve sclerosis in this patient and in other reported cases closely mimics chronic rheumatic heart disease. Coexist-

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ent rheumatic disease has been previously postulated as a cause of the cardiac abnormality. Nevertheless, as McAllister and Fenoglio (1975) and Lie and Davis (1976) have shown (and our case confirms) the altered heart valves in Whipple's disease contain the same macrophages with bacilliform bodies in their cytoplasm as characterise the disease in other body organs. In Whipple's disease superimposed valvar vegetations are common; they are large in size and have a yellowish hue. Classic infective endocarditis complicating mitral stenosis comes into the differential diagnosis but is rare.

The cardiac morphological alterations in Whipple's disease are important as they provide the first demonstration that a persistent intrinsic infectious agent may cause valvar deformity. Burch *et al,* suggested in 1967 that valvar deformity and cardiomyopathy may result from viral infection of the heart. The light microscopy in our patient confirms the findings of McAllister and Fenoglio (1975) and Lie and Davis (1976) that the affected valve cusps in Whipple's disease contain macrophages with rod-shaped bodies in their cytoplasm. The above authors were able to confirm the bacterial nature of the bodies by electron microscopy. Our material was too poorly preserved for this purpose. Bacterial-like bodies have been repeatedly shown in the bowel mucosa in Whipple's disease, and electron microscopy has been recommended as a monitor of therapeutic efficacy (Morningstar, 1975).

While endocarditis, valvulitis, and myocarditis occur in Whipple's disease, there has been only one report of coexistent coronary and systemic arterial involvement in this disease (James and Haubrich, 1975). Involvement of other cardiac valves such as the aortic valve has been reported (Farnan, 1958; Chears *et al,* 1961). It is apparent that there are important lessons to be learnt from the cardiac alterations in Whipple's disease. As the disease is being all but eliminated by antibiotic treatment, retrospective studies of stored histological samples and hearts from patients with Whipple's disease may still produce valuable information.

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