Case reports

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Lymphatic metastasis in the mitral valve

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The case is reported of a 45-year-old woman with a metastatic tumour within the mitral valve.

Involvement of the heart by metastatic neoplasm is not uncommon. Postmortem studies of patients with malignant disease show that cardiac involvement occurs in up to 21 per cent of cases (Bisel, Wróblewski, and LaDue, 1953). The pericardium, epicardium, and myocardium are the areas of the heart most commonly involved by secondary tumour; spread to the endocardium and heart valves is rare (Coller, Inkley, and Moragues, 1950). We report a case of secondary tumour spread into the substance of the mitral valve; this was a chance finding on histological examination of a surgically removed rheumatic valve.

Case report

A 45-year-old woman presented with the features of mitral valve stenosis. She had had rheumatic fever in childhood and developed progressive dyspnoea in her mid-30s. A closed mitral valvotomy at the age of 39 resulted in conspicuous symptomatic improvement. She remained well for 5 years when increasing dyspnoea, tiredness, and weight loss made her seek medical advice.

On examination she was thin and had a malar flush. The pulse was 70 per minute and regular. Her blood pressure was 130/70 mmHg. There were clinical signs of right ventricular hypertrophy and mitral stenosis. Chest, abdomen, and central nervous system were normal to clinical examination.

Laboratory investigations showed a normal blood picture and liver function. A chest x-ray film showed an enlarged left atrium with upper lobe venous diversion. The electrocardiogram showed evidence of right ventricular hypertrophy. An echogram revealed a stenosed, thickened mitral valve. The diagnosis was mitral stenosis with a dilated left atrium and hypertrophied right ventricle and a further operation was advised.

At operation the heart showed only the changes associated with mitral stenosis. Open exploration of the mitral valve showed thickening and calcification of both cusps, with fibrosis and shortening of the subvalvular mechanism. The valve was replaced by a Björk-Shiley prosthesis.

Histological studies were done of the excised valve: routine paraffin sections were prepared from the formalin fixed specimen and stained with haematoxylin and eosin and Machiavello's and the phloxine tartrazine method for inclusion bodies as part of a separate study being conducted into the association of psittacosis and valvular disease.

The valve showed fibrotic thickening with a moderate degree of calcification and several areas of myxoid connective tissue in which were dilated small blood vessels and endothelium lined spaces resembling lymphatics. There were no vegetations and no bacterial involvement. There were two small clumps of neoplastic cells lying within the 'lymphatics', which were present only in two successive sections at one level, which had been stained by the phloxine tartrazine and Machiavello's methods. Numerous further sections were cut but no more tumour was found.

The tumour cells showed considerable nuclear pleomorphism and a high nuclear/cytoplasmic ratio. There was no apparent mucin or pigment production and a diagnosis was made simply of 'poorly differentiated carcinoma'. No attempt was made to restrain either of the positive sections.

The possibility that these deposits were 'floaters' was excluded by a careful check on the other specimens cut up and processed at the same time, in none of which was a similar carcinoma processed. Moreover, the appearance of the deposits in two successive sections is not characteristic of an artefact (Fig. 1 and 2).

FIG. 1 *One of the two fragments of tumour, lying within a ? lymphatic. (Machiavello's stain. $\times 260$.)*

FIG. 2 *Higher power view of the other fragment. (Machiavello's stain. $\times 640$.)*

Further clinical examination and investigations failed to reveal a primary tumour or any other secondary deposits. Of the tumours known to metastasize from occult primary sites, oat cell carcinoma, melanoma, breast, and thyroid tumours were considered most likely. We did not think the histological appearance of the deposits gave any definite indication of the primary source.

The patient made a good postoperative recovery and was allowed home two weeks after operation. She is being followed up in the out-patient clinic and appears to be making good progress.

Discussion

The antemortem histological diagnosis of metastatic spread to a cardiac valve has not been previously described. The antemortem diagnoses of cardiac metastases have been mainly presumptive diagnoses in patients with known malignant disease who develop disorders of cardiac performance and non-specific electrocardiographic abnormalities (Goudie, 1955). Positive histology has been reported in patients with malignant pericardial effusions. Improvement in cardiac performance has resulted from irradiation of hearts involved by malignant disease (Hanfling, 1960); and it may be that radiotherapy will be of use in our patient should she develop a cardiac dysfunction which does not respond to conventional treatment.

The previous reports of secondary spread to cardiac valves were of postmortem cases and showed either direct implantation of tumour on to valve endothelium or infiltration into the valve from neighbouring myocardial deposits (Hanfling, 1960). Clancy and Roberts (1968) reported 2 examples of tricuspid valves involved by malignant melanoma and Roberts, Clancy, and DeVita (1968) reported one tricuspid valve involved by lymphoma, but the exact mode of involvement was not specified.

The case described here was one of secondary spread into an endothelium-lined space within a mitral valve and we think that this vessel was a valve lymphatic. However, while the existence of lymphatics in animal atrioventricular valves has been clearly shown, evidence for their existence in human valves is not yet so convincing.

Miller, Pick, and Katz (1961) injected India ink suspension into the atrioventricular valves of beating canine hearts and then subjected the valves to routine light microscopy. They described carbon particles within thin-walled endothelium-lined channels with little surrounding connective tissue. Other workers using India ink, dye, or hydrogen peroxide have reported similar findings (Johnson and Blake, 1966; Ullal *et al.*, 1972b).

Leak and Burke (1966) described the electron microscopical features of amphibian and mammalian lymphatics, which have neither basement membrane nor condensed connective tissue support but were recognizable by the presence of 'half desmosomes'—fibrillary structures appearing to anchor the endothelium directly to the surrounding connective tissue. Bradham, Parker, and Greene (1973) using these criteria demonstrated lymphatics in canine atrioventricular valves with electron microscopy.

Studies in human valves have met with less success. Eberth and Belajeff reported lymphatics in human cardiac valves in 1866. Johnson and Blake (1966) also reported lymphatics in two human mitral valves.

Reading the papers cited leads us to believe that lymphatics are present in animal and human atrioventricular valves mainly on the atrial surface and that their number and appearance may vary with disease and age.

In our case we found tumour in thin-walled endothelial tubes without connective tissue support or a clear basement membrane. This, coupled with the less reliable criterion of a complete lack of blood cells in numerous sections at different levels, led us to believe that these channels were lymphatics.

We have noticed numerous and varied vascular channels in many diseased valves removed surgically but have not yet had the opportunity of subjecting them to electron microscopy.

Kline (1972) thought that lymphatics were an important pathway for secondary tumour spread to the heart. He found the mediastinal lymph nodes were almost always involved by tumour and subsequent retrograde lymphatic spread of tumour to the heart resulted in lymphatic obstruction. The appearance of secondary tumour in dilated lymphatics which he described resembles the picture in our case. He did not, however, describe valve involvement.

The effect of obstruction to the cardiac lymphatics has been studied in animals (Ullal, Kluge, and Gerbode, 1972a; Miller, Pick, and Katz, 1963). Impairment of myocardial function has been noted. Increased fibrosis in the endocardium has been reported. Fibrosis and myxomatous changes in the atrioventricular valves of dogs has followed ligation of the cardiac lymphatics.

The place of lymphatic obstruction in human cardiac disease is conjectural. It has been suggested as a cause of myocardial damage in rheumatic carditis. Myxomatous degeneration of the mitral valve and endocardial fibrosis have also been linked with lymphatic obstruction.

It is possible that lymphatic obstruction contributed (to a minor degree) to the fibrosis seen in this patient's mitral valve.

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