Wilson 1976). It is difficult to account for these discrepancies, but part of the reason may lie in differences in the methods of measurement and in the fact that the active A form of alpha-galactosidase may not increase, while the inactive B form does rise after transplantation (Krivit *et al.* 1972). Whatever the results of these measurements, however, striking non-renal clinical improvement is noted in nearly all cases.

Clarke *et al.* (1972) reported a drop in ceramide trihexoside levels with a parallel reduction in the levels of the precursors of ceramide trihexoside. It is known that a large proportion of the circulating ceramide trihexoside and its precursors is derived from the normal destruction of senescent red cells. Clarke *et al.* (1972) proposed that renal transplantation, by reducing the rate of red cell destruction, decreased the delivery of ceramide trihexoside to the circulation. They did not detect any rise in enzyme activities but did note considerable improvement in the non-renal manifestations of the disease.

The hypothesis that the deficient enzyme is produced within the allograft and circulated to the tissues would seem to be an oversimplification. It has been proposed that the striking clinical improvement could be accounted for by the transplanted kidney acting as a localized 'cleaving' machine for total body substrate, aided by the reduction in substrate levels as a result of increased red cell survival (Krivit *et al.* 1972). It has been suggested that enzyme replacement *per se* is unlikely to be the complete answer to the treatment of Anderson-Fabry disease since heterozygous female carriers would, on average, be expected to have 50% of alpha-galactosidase A activity and yet may suffer significant symptoms of the disease (Beutler 1979). It is noteworthy that, as in our patient, there have been no reports of sphingolipid deposition in the grafted kidney on biopsy or autopsy (Bühler *et al.* 1973, Clarke *et al.* 1972, Van den Bergh *et al.* 1976, Wilson 1976) so it would appear that the healthy graft does protect itself, preventing recurrent renal failure.

In conclusion, therefore, successful renal transplantation in patients with Anderson-Fabry disease not only corrects the uraemia but also produces marked improvement in other clinical manifestations of the disease. The mechanisms by which this happens are as yet unclear, but probably involve both reduction in the amount of sphingolipid delivered to the circulation and increased catabolism of ceramide trihexoside, either locally in the transplanted kidney or, possibly, at distant sites.

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Myocardial metastasis from carcinoma of pancreas presenting as acute myocardial infarction[1]

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A case is reported of a patient presenting with the clinical signs of acute myocardial infarction who was found to have carcinoma of the pancreas and a metastasis in the myocardium. Such presentation is unusual.

Case report

A 92-year-old man was admitted to hospital having recently developed a productive cough and

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symptoms of transient vertebrobasilar ischaemia. He had some recent loss of appetite but no other symptoms referable to the gastrointestinal tract and there were no symptoms of cardiovascular disease. He had been prescribed Brinaldix K. On examination he appeared well. His pulse rate was 90 per minute and his blood pressure 140/100. The only significant abnormality noted was the presence of coarse crackles at the right lung base. No mass was palpable in the abdomen or on rectal examination. Investigation results included a haemoglobin of 12.3 g/dl, a slight neutrophil leukocytosis and an erythrocyte sedimentation rate of 9 mm/hour. The urea and electrolytes, liver function tests, serum calcium and serum phosphate were within normal limits. The chest X-ray showed slight cardiomegaly with clear lung fields and the electrocardiogram was normal.

The patient's chest infection responded to antibiotic therapy, but eighteen days after admission his condition suddenly deteriorated when he became drowsy and dyspnoeic. His blood pressure fell to 100/50 and he developed a pulse rate of 140 per minute. The jugular venous pressure was elevated and crackles were heard at both lung bases. An electrocardiogram obtained soon after he collapsed showed sinus rhythm with 1 mm ST elevation in leads V_1 to V_3, and T wave flattening with 1 mm ST depression in leads V_5 and V_6 (Figure 1). A minor degree of right bundle branch block had also developed. The serum creatinine phosphokinase concentration in a blood sample obtained at the same time was 81 u/l (normal range <90 u/l). The patient's condition continued to deteriorate and he died five hours later from what was presumed to be cardiogenic shock following an acute anteroseptal myocardial infarct.

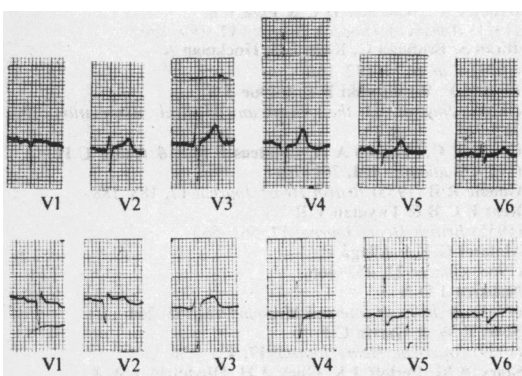

Figure 1. Precordial leads of electrocardiograms from the patient on admission to hospital (top line) and after he collapsed (bottom line), showing changes compatible with acute anteroseptal myocardial infarction. (The two ECG machines used gave an identical rectangular trace with the ImV test signal)

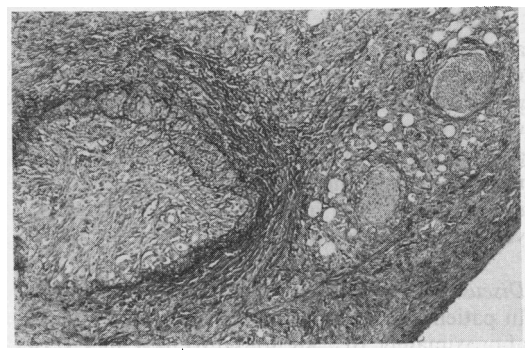

Figure 2. Myocardial metastasis from carcinoma of the pancreas showing nerve bundles surrounded by tumour and a vein occluded by malignant cells. (Orcein for elastic $\times 100$)

Post-mortem examination revealed a carcinoma in the body of the pancreas with small metastases in the lungs, liver, right kidney and left adrenal gland. A metastasis of approximately two centimetres in diameter was also found in the anteroseptal region of the myocardium. It did not occupy the full thickness of the cardiac muscle, and a residual one centimetre thickness of uninvolved myocardium remained. Macroscopically the metastasis did not involve any of the major coronary arteries. On histological examination a medium sized artery was seen to be surrounded by metastatic tumour with no encroachment on its lumen; adjacent nerve bundles were also surrounded by tumour, and an adjacent vein was invaded and completely occluded by malignant cells (Figure 2). Extensive inflammatory cell infiltrate, which included many polymorphonuclear leukocytes, surrounded the metastatic tumour and extended into the myocardium (Figure 3). No evidence of haemorrhage was seen either on macroscopic or microscopic examination of the tumour.

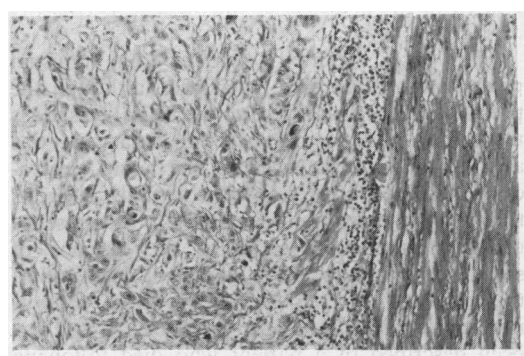

Figure 3. Myocardial metastasis from carcinoma of the pancreas showing an extensive inflammatory cell infiltrate at the tumour edge which extended into the myocardium. (H&E $\times 250$)

In the coronary arteries only mild patchy atheromatous change with no significant lumen reduction was found. No pericardial fluid or mediastinal lymphadenopathy were present. There was no evidence of pulmonary embolism or gastrointestinal haemorrhage, and in the central nervous system the only abnormality noted was moderately severe atheromatous disease of the vertebrobasilar system.

Discussion

In patients dying as a result of malignant disease approximately 10% are found to have metastases in the heart and pericardium (Scott & Garvin 1939, Goudie 1955). This percentage does not include patients suffering from leukaemia, in whom infiltration of the heart frequently occurs (Bisel *et al.* 1953, Young & Goldman 1954). The incidence of cardiac metastases is highest in patients suffering from carcinoma of the lung, carcinoma of the breast, malignant melanoma and malignant lymphomas (Young & Goldman 1954, Cham *et al.* 1975).

Clinical attention is directed towards the heart in only 16% of cases with cardiac metastases (Goudie 1955), the usual presenting features being dysrhythmias or evidence of pericardial involvement. Dysrhythmias which have been recorded include sinus tachycardia, atrial fibrillation or flutter and heart block (Young & Goldman 1954). Pericardial involvement usually presents with signs of effusion, inflammation, tamponade or constriction (Wallace & Logue 1946, Young & Goldman 1954, Goudie 1955). Less common presentations include cardiac failure (Nabarro 1953), isolated electrocardiographic abnormalities such as T wave inversion (Young & Goldman 1954), cardiac rupture (Keat & Twyman 1955), or features of intracavity proliferation (Stark *et al.* 1977). Ischaemic cardiac damage is usually incidental, only rarely being directly related to the presence of the metastasis (Bisel *et al.* 1953).

The case reported here is an unusual presentation of cardiac metastases, although the precise pathogenesis of the acute clinical episode is uncertain. The position of the metastasis was anatomically consistent with the acute electrocardiographic changes, which strongly suggests that these changes were secondary to the presence of the tumour, especially in the absence of significant coronary artery disease or occlusion of the coronary arteries by either direct tumour involvement or tumour embolization. A case has been described of a patient who died following clinical and electrocardiographic evidence of myocardial infarction and at post-mortem examination there was also no definite evidence of coronary artery occlusion, although severe coronary artery disease and multiple tumour emboli in small vessels of the heart were found (Malaret & Aliaga 1968). Neither of these features was present in the patient presented in this report.

Although metastatic disease of the heart and pericardium is infrequently diagnosed during life, the condition is of more than academic interest since successful treatment has been reported with use of radiotherapy (Cham *et al.* 1975), systemic and intrapericardial chemotherapy (Biran *et al.* 1977) and surgery (Bailey *et al.* 1971, Stark *et al.* 1977). Ante-mortem diagnosis relies on maintaining a high index of suspicion when confronted with unanticipated cardiac abnormalities in patients with a history of malignant disease. In such patients sudden dysrhythmias, symptoms and signs of pericardial disease or congestive cardiac failure, especially when refractory to treatment, should alert the clinician to the possible aetiology. The diagnosis can be supported by electrocardiography, common features being ST elevation or low voltage as well as dysrhythmias (Young & Goldman 1954), and an enlarged cardiac shadow on the chest X-ray (Cham *et al.* 1975). Confirmatory investigations include pericardiocentesis (Cham *et al.* 1975), echocardiography (Stark *et al.* 1977) and radionuclide imaging of the heart (Steiner *et al.* 1970).

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