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Angiosarcoma of the heart

MARGARET SHACKELL, ANNA MITKO, P. L. WILLIAMS, AND G. C. SUTTON

From the Cardiac Departments of Hillingdon and Harefield Hospitals and the Pathology Department of Hillingdon Hospital, Middlesex

SUMMARY Two cases of angiosarcoma of the heart are described. In one the tumour, which arose from the right atrium, was demonstrated during life by angiography. In the other, diagnosed only at necropsy, the tumour arose from the right ventricle. Both cases illustrate many of the typical features of this rare tumour and the difficulties of antemortem diagnosis.

Primary tumours of the heart are rare. Straus and Merliss (1945), in a review of 480 331 necropsies, found the incidence of primary cardiac tumour to be 0·0017 per cent. Angiosarcoma is among the least common. It usually arises from the right atrium and only rarely from the pericardium, right ventricle, or left atrium.

Case reports

CASE 1

A 42-year-old man was admitted in July 1976 complaining of severe lumbar and epigastric pain. He had first developed lumbar pain after a fall 2 years previously, but it had become more severe in the 6 months before admission. In March 1976 he had been admitted to the orthopaedic department of another hospital complaining of lumbar and epigastric pain, malaise, and weight loss. During that admission he was found to be anaemic, but no definite diagnosis was made and he was discharged on oral iron and indomethacin. There was no history of contact with vinyl chloride.

On examination he had a low grade pyrexia, intermittent mental confusion, and mild tachypnoea. The jugular venous pressure was raised 3 cm and he was in sinus rhythm at 70 to 110/min. The blood pressure was 90/50 mmHg without paradox. A pericardial friction rub was audible throughout the praecordium. The electrocardiogram was normal and the chest *x*-ray film showed globular cardiac enlargement with normal lung fields. The haemoglobin was 12·1 g/dl with normal indices, the white cell count 13·3 × 10^9/l with 70 per cent neutrophils, and the erythrocyte sedimentation rate was 77 mm/hour. A Mantoux test and investigations for collagen disease were negative. *X*-ray film of the lumbar spine showed mild degenerative changes only. M-mode echocardiography confirmed the clinical impression of a pericardial effusion.

Six days after admission cardiac tamponade developed. Twenty-five ml blood-stained pericardial fluid were aspirated, with relief of the tamponade. Malignant cells were not seen on cytological examination of the aspirate. One month after admission open pericardial biopsy was carried out through a left thoracotomy. No tumour was seen. The biopsy showed a grossly thickened pericardium with extensive fibroblastic proliferation and focal aggregates of lymphocytes, but no evidence of malignancy.

The jugular venous pressure returned to normal after pericardial biopsy, and remained so during the rest of his illness. However, the patient continued to deteriorate. In October 1976 a bone scan showed patchy loss of uptake in the lumbar region and malignant cells were found on bone marrow aspiration. The patient developed a sinus tachycardia with a gallop at this time, and the electrocardiogram showed nonspecific ST and T wave abnormalities, though the chest *x*-ray film showed a normal cardiac silhouette. His condition deteriorated further and he died in December 1976.

At necropsy the main tumour was in the anterior part of the right ventricle, measuring 5 × 4 × 4 cm and infiltrating the full thickness of the myocardium and endocardium. The pericardium was firmly adherent to the heart and contained numerous haemorrhagic metastases on the outer surface. There was confluent subpericardial tumour, approximately 0·5 cm thick, surrounding the whole heart. There was also a large number of haemorrhagic metastases in the lungs, liver, spleen, and lumbar

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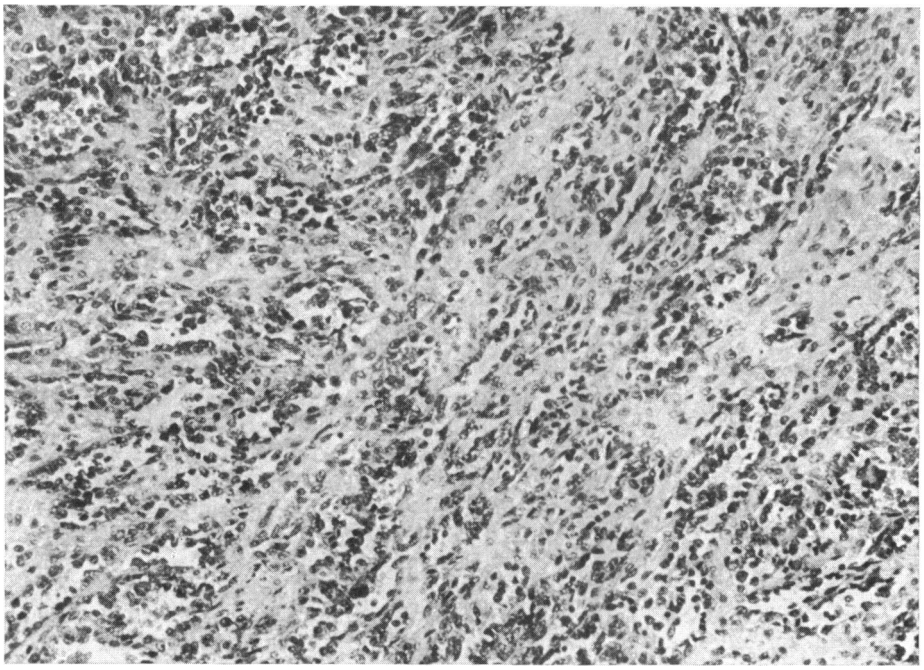

Fig. 1 *Photomicrograph of a solid part of the tumour from the right ventricle showing a pleomorphic, spindle-cell pattern, with numerous capillary sized vascular spaces. (H and E. × 150.)*

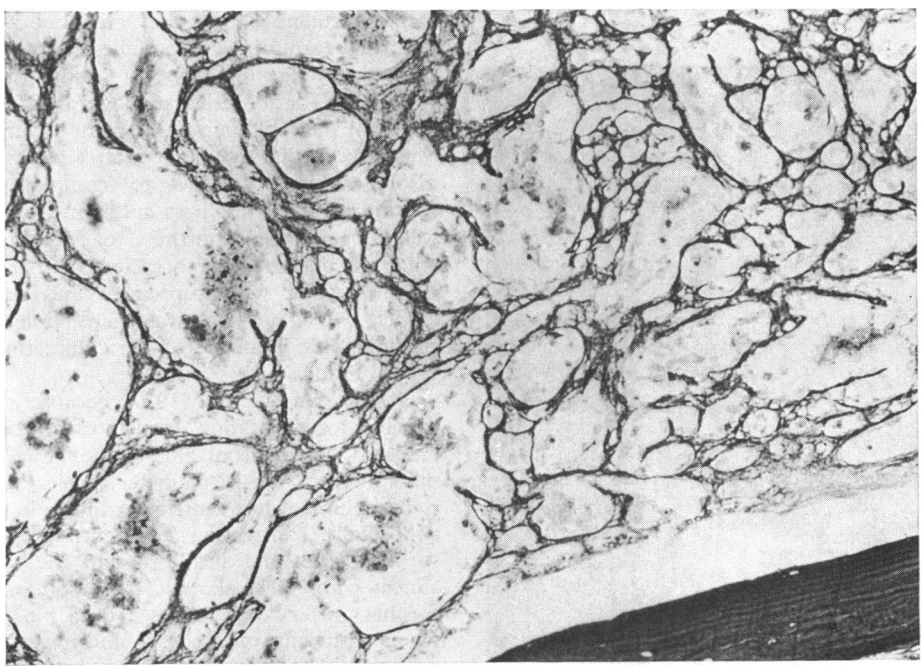

Fig. 2 *Vertebral metastasis showing the vasoproliferative nature of the tumour and outlining the vascular spaces. (Reticulin. × 150.)*

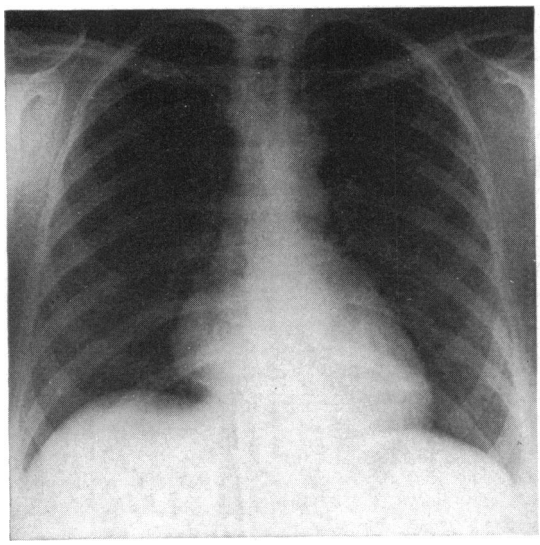

Fig. 3 *Chest x-ray film (case 2) showing a bulge on the right border of the heart.*

vertebrae. The histological appearance of the tumour in the pericardial space was that of a solid spindle-cell sarcoma, but in other sites, such as the liver and right ventricular wall, there were large vascular spaces in the tumour itself. In the vertebrae the tumour had definite vasoformative properties.

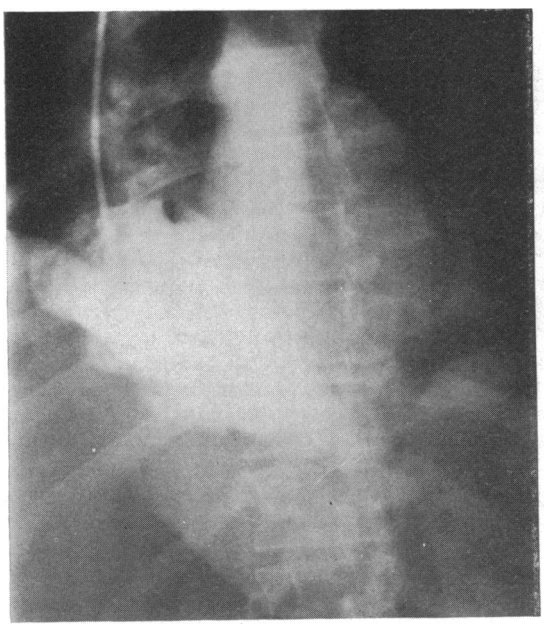

Fig. 4 *Angiogram (case 2) after right atrial injection, showing an apparent outpouching of the right atrium.*

The overall appearances were those of angiosarcoma (Fig. 1 and 2).

CASE 2

A 48-year-old woman underwent subtotal thyroidectomy for a multinodular goitre with substernal extension in January 1977. The histology was of a benign nodular colloid goitre. Her only symptom after operation was nonspecific chest pain. But whereas before operation the chest *x*-ray film had been normal, afterwards it showed gross cardiac enlargement. There were no abnormal physical signs but the electrocardiogram showed generalised flattening of the T waves and frequent ventricular ectopic beats. M-mode echocardiography showed a large pericardial effusion. The haemoglobin was 10·3 g/dl with a normal blood film and the erythrocyte sedimentation rate was 50 mm/hour. Antinuclear factor, autoantibodies, and Mantoux test were negative, and a diagnosis of viral or idiopathic pericarditis was made.

One week later a pericardial friction rub was heard. The effusion cleared spontaneously, confirmed by echocardiography, with conservative management only and the patient was discharged 3 weeks after admission for subtotal thyroidectomy.

Chest pain and malaise continued after discharge and treatment with tetracosactrin zinc 0·5 mg twice weekly was started 2 months later. This was changed to prednisolone 40 mg daily after one week, when she was readmitted. The chest *x*-ray film now showed a bulge on the right border of the heart (Fig. 3). Right atrial angiography showed an apparent outpouching of the right atrium (Fig. 4). She was discharged again after 3 weeks, on prednisolone, but continued to complain of nonspecific pain in the chest and arms, together with weight gain and shortness of breath. She was admitted on 2 further occasions with an increase in the jugular venous pressure and sinus tachycardia, but at no stage was there clinical or echocardiographic evidence of reaccumulation of pericardial fluid.

At the end of June 1977, because of her unexplained deterioration, cardiac catheterisation was repeated. Right atrial angiography now showed a mass about 2 cm in diameter, projecting into the right atrium. A left ventricular injection showed an abnormally contracting left ventricle, its anterior surface, from the aortic root to the apex, being almost completely akinetic. Injection into the left coronary artery was followed by a blush over the whole of the base of the heart, and injection into the right coronary artery showed the proximal part of the vessel to be displaced around a non-opacified area. After arterial clearing there was again a blush in the

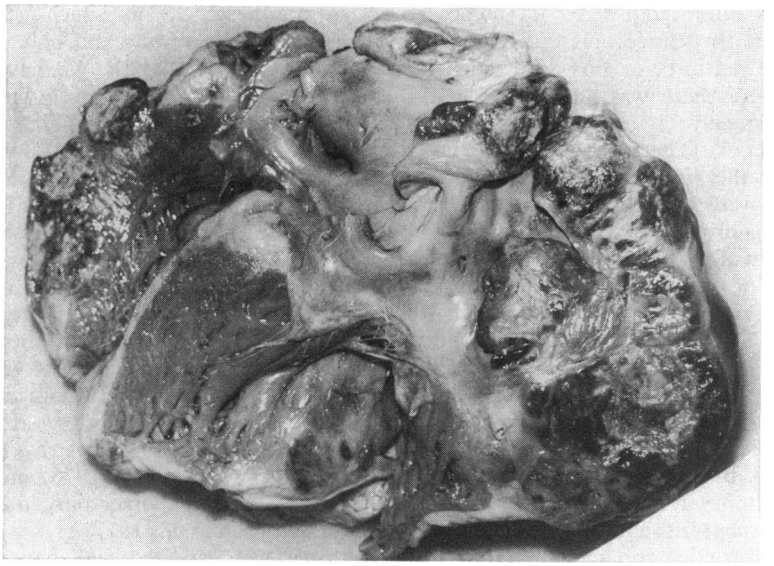

Fig. 5 *Opened heart (case 2) showing the main mass of tumour infiltrating the right atrial wall, with intracavitary extension. Multiple smaller nodules of tumour are visible on the cut surface of the interatrial septum and left ventricle, and an epicardial tumour nodule is on the upper part of the interventricular septum.*

region between the right coronary artery and the right border of the heart. The appearances were those of a tumour of the right atrium with involvement of the base of the heart.

Subsequent chest *x*-ray films suggested secondary deposits in the lungs. Needle biopsy of the lung was attempted in order to make a histological diagnosis, but no tumour was obtained. The patient died the next day.

At necropsy the heart weighed 1300 g. There were

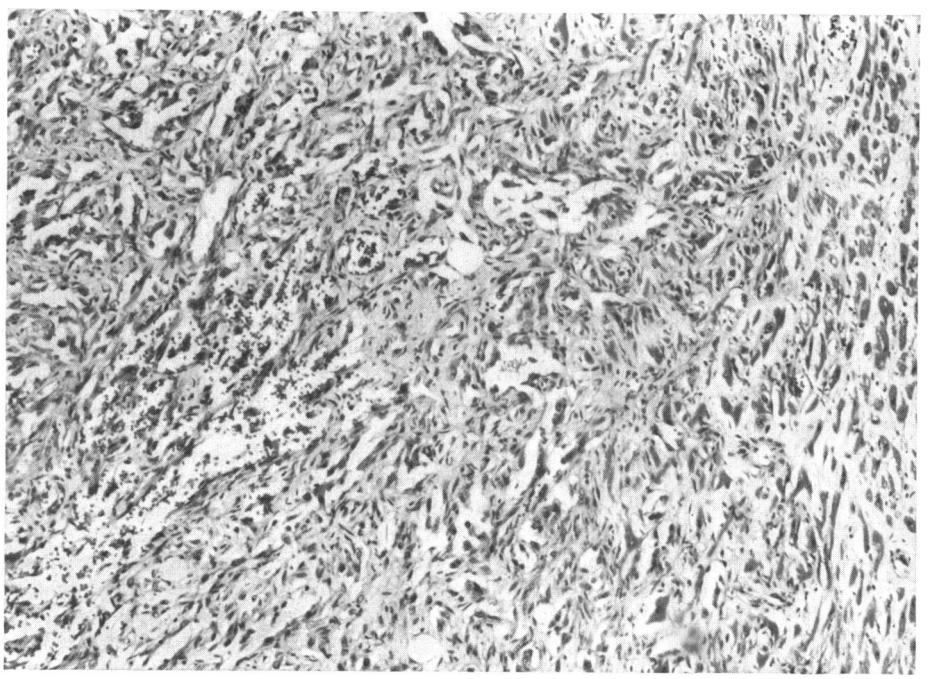

Fig. 6 *Section (case 2) showing a vascular and vasoformative malignant tumour infiltrating myocardium on the right. (H. and E. × 90.)*

multiple haemorrhagic tumour nodules, from 1 to 5 cm in diameter, scattered over the entire epicardial surface. The tumour appeared to be originating from the right atrium where there was an intracavitary extension, approximately 4 cm in diameter, reducing the cavity (Fig. 5). There were multiple pericardial adhesions to the surface over epicardial nodules. Metastases were present in brain, lungs, liver, and ovaries, mainly 0·5 to 2 cm in diameter. The histology was that of angiosarcoma (Fig. 6).

Discussion

The constancy of symptoms and physical signs in patients with angiosarcoma of the heart has been stressed by many authors (McNalley *et al.*, 1963; Glancy *et al.*, 1968; Hollingsworth and Sturgill, 1969). The most frequent symptoms are general malaise, chest pain, fever, and haemoptysis, and the physical signs include a pericardial friction rub and raised jugular venous pressure. The chest *x*-ray film may show cardiomegaly, sometimes with a bulge on the right border of the heart. The electrocardiogram may be normal at the time of presentation or show nonspecific ST and T wave abnormalities. Echocardiography may confirm a pericardial effusion, which typically is blood-stained on aspiration. Ports *et al.* in 1977 described 4 cases of right ventricular tumour, 3 myxomas, and 1 metastatic melanoma, in which the tumour was seen on M-mode echocardiography. In 2 cases the site of attachment of the tumour was shown by two-dimensional echocardiography.

The prognosis is poor, with few patients surviving more than a few months from presentation.

At necropsy there is obliteration of the pericardial sac by tumour and often pulmonary and rib metastases. Though it is often difficult in the presence of extensive infiltration of surrounding structures by the tumour to determine the precise site or origin, it usually appears to arise from the right atrium. Other sites are much less common.

We have found 15 cases reported in which the probable or possible site of origin was the pericardium (Glancy *et al.*, 1968; Hollingsworth and Sturgill, 1969; Hansson *et al.*, 1970; Poole-Wilson *et al.*, 1976), 6 in which it was the right ventricle (Lange and Christiansen, 1947; Amsterdam *et al.*, 1949; Tatsumi *et al.*, 1949; Glassy and Massey, 1950; Groom, 1956; Thompson *et al.*, 1977), and 2 in which it was the left atrium (Gross and Englehart, 1937; Hager *et al.*, 1970).

Few cases of angiosarcoma of the heart have been diagnosed in life. In a review of the published reports in 1968, Glancy *et al.* found, out of 41 cases of angiosarcoma of the heart, 12 in which the diagnosis had been suspected clinically and only 7 in which it was confirmed before death. We have found a further 8 cases in which the diagnosis was made before death (Allaire *et al.*, 1964; Hollingsworth and Sturgill, 1969; Hager *et al.*, 1970; Laws *et al.*, 1973; Poole-Wilson *et al.*, 1976; Rossi *et al.*, 1976; Thompson *et al.*, 1977).

In the 7 cases cited by Glancy *et al.* the diagnosis was made by biopsy of the tumour or its secondary deposits in 4, by demonstrating tumour cells in the pericardial fluid in 2, and the diagnosis was suspected at right heart angiography in 1, though not confirmed histologically during life. In the 8 other cases we have found, the diagnosis was made at thoracotomy in 6 cases (Allaire *et al.*, 1964; Hollingsworth and Sturgill, 1969; Hager *et al.*, 1970; Laws *et al.*, 1973: cases 1 and 4; Poole-Wilson *et al.*, 1976) and by angiocardiography followed by thoracotomy in 2 (Rossi *et al.*, 1976; Thompson *et al.*, 1977).

Despite the fact that we suspected malignancy from an early stage in our first case, we were unable to confirm this until a bone-marrow aspiration 10 weeks after initial admission, and in spite of cytological examination of the pericardial fluid and open pericardial biopsy. It was particularly unusual to fail to make the diagnosis at open exploration of the pericardium, especially as this was carried out at a time when the disease must have been far advanced. The histological diagnosis of angiosarcoma of the heart was only made at necropsy. There are a number of other published cases in which cytological examination of the pericardial fluid or pericardial biopsy was unhelpful (Hollingsworth and Sturgill, 1969; Hager *et al.*, 1970; Hansson *et al.*, 1970; Patt *et al.*, 1974; Poole-Wilson *et al.*, 1976). Nevertheless, open pericardial biopsy or thoracotomy remain the most fruitful methods of diagnosis.

In our second case a cardiac tumour was diagnosed shortly before death by angiocardiography. In this case the unusual features were the spontaneous resolution of the pericardial effusion and the appearance of an outpouching of the right atrium at the first angiocardiogram. In retrospect the latter feature was probably produced by the tumour, though it was not suggestive of this at the time. Spontaneous resolution of pericardial effusion in this condition has not been described previously, though Patt *et al.* in 1974 described a case of resolution occurring after a single pericardiocentesis.

In neither of our cases did M-mode echocardiography show any evidence of a tumour. Echocardiography is an invaluable aid in the diagosis of pericardial effusion, but the M-mode technique may not be useful in detecting pericardial or myocardial tumours. Two-dimensional echocardiography is

more likely to provide diagnostic information, as described by Ports *et al.* (1977).

We conclude nevertheless that the best methods of making the diagnosis of primary angiosarcoma of the heart are by open exploration of the heart and pericardium, and by angiocardiography. The former should enable a histological diagnosis to be made, though, as our first case illustrates, this is not invariably so. Angiocardiography should disclose a characteristic appearance of a tumour, though correct interpretation may be difficult, as our second case illustrates.

The second case was under the care of Dr Malcolm Towers and Dr A. J. Moon, and we are grateful to them for permision to publish this case, to Dr B. E. Heard and Dr A. J. Salsbury of Brompton Hospital for the report of the histological findings in the pericardial biopsy in the first case, and to Dr A. Pomerance of Harefield Hospital for the necropsy and figures of the second case.

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Requests for reprints to Dr G. C. Sutton, Cardiac Department, Hillingdon Hospital, Uxbridge, Middlesex UB8 3NN.