Angiosarcoma of pericardium

Problems in diagnosis and management

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The clinical histories of two patients with angiosarcoma of the pericardium are described. Both were previously well young men who presented with cardiac tamponade caused by haemorrhagic pericardial effusions. If a pericardiectomy is undertaken for diagnosis, wide excision of the pericardium is recommended. This will provide a large specimen for histological examination and may prevent subsequent development of constriction.

Primary malignant tumours of the pericardium are rare. Over half are mesotheliomas (Dawe, Wood, and Mitchell, 1953) and the remainder are other sarcomas, including angiosarcoma. Secondary involvement of the pericardium by direct invasion from cardiac and lung neoplasms or by metastatic spread is more frequent (Harris, 1960). Thirteen cases of angiosarcoma involving the pericardium have been previously reported (Glancy, Morales, and Roberts, 1968; Hollingsworth and Sturgill, 1969; Hansson *et al.*, 1970), and two further cases are presented in this paper. They illustrate the need for an extensive pericardial excision to provide sufficient tissue for histological examination and to prevent the development of constriction.

Case reports

Case 1

Two weeks before admission a previously fit 45-year-old clerk noticed increasing exertional dyspnoea, dull central chest pain, and night sweats. He had no orthopnoea or haemoptysis. He smoked 40 cigarettes a day and had had no contact with the manufacture of plastics.

On examination he was pale and febrile (38.7°C). The jugular venous pressure was raised 12 cm from the sternal angle, the blood pressure was 90/60 mmHg (12.0/8.0 kPa) and there was 25 mmHg (3.3 kPa) pulsus paradoxus. The cardiac impulse was not palpable, but a third heart sound was heard at the apex. There was no sacral oedema and there were no added sounds in the lungs. The liver edge extended 4 cm below the costal margin. Other clinical findings were normal. The

haemoglobin was 9.9 g/dl, white blood count 9300/mm³, and platelets 150 000/mm³; the serum sodium was 137 mmol/l, potassium 4.0 mmol/l, bicarbonate 24 mmol/l, and urea 3.0 mmol/l. On the chest film the cardiac silhouette was globular, and the electrocardiogram showed sinus rhythm with a mean frontal QRS axis of +30° and abnormal repolarization in most leads compatible with pericarditis or pericardial effusion. Tests for antinuclear factor and rheumatoid factor were negative. Blood culture was sterile. Liver function tests, prothrombin ratio, and partial thromboplastin test were all normal. Echocardiography confirmed the presence of pericardial fluid. A diagnosis of cardiac tamponade was made and 1500 ml heavily blood-stained fluid were aspirated. The fluid was sterile on bacteriological and viral culture, and no malignant cells were found.

Although he was symptomatically improved after pericardiocentesis, the signs of cardiac constriction recurred after two weeks. At operation, the pericardial sac was obliterated with fibrous adhesions, and posteriorly there were loculi of blood. The pericardium was excised to the atrioventricular groove to relieve constriction. Bacteriological and viral cultures of the pericardium were sterile. The postoperative course was uncomplicated. He received a course of external irradiation to the mediastinum and has remained well for six months.

The specimen consisted of 11 fragments of pericardium, the two largest measuring 9×5 cm, with thickness varying between 0.5 and 1 cm. Histological sections showed great thickening of the pericardium caused by organizing blood clot and fibrous tissue. There were multiple foci of malignant tumour, consisting mainly of spindle cells which formed many capillary-sized, and some larger, blood vascular spaces (Fig. 1). There were many mitoses. The appearances of this tumour were those of angiosarcoma.

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FIG. 1 Case 1. Pericardial biopsy showing pleomorphic spindle-shaped tumour cells with capillary-sized blood spaces. ($\times 390$.)

Case 2

The patient was a 20-year-old man who had been healthy until he presented with epistaxis and haemoptysis. Part of his nasal mucosa was cauterized. Four months later he was admitted to hospital complaining of malaise and pain in the right hip, epigastrium, and right hypochondrium. He had a pyrexia of 30°C . He had no industrial contact with plastics. The initial diagnosis was a viral infection.

Within one week he developed bilateral pleural effusions and peripheral oedema. The venous pressure was raised 10 cm above the sternal angle and there was 25 mmHg (3.3 kPa) of pulsus paradoxus. The blood pressure was 95/70 mmHg (12.6/9.3 kPa). Pleural and pericardial rubs were heard, but there were no cardiac murmurs. The liver was enlarged 5 cm below the costal margin. A diagnosis of cardiac tamponade was made. Thoracocentesis yielded straw-coloured fluid and pericardiocentesis heavily blood-stained fluid. He did not respond to treatment with antibiotics and in the following two weeks two further aspirations of the pericardium were performed. At this time the haemoglobin was 7.8 g/dl, white blood count $25\,000/\text{mm}^3$, and platelets $260\,000/\text{mm}^3$; the serum sodium was 130 mmol/l, potassium 3.9 mmol/l, bicarbonate 26 mmol/l, and urea 3.8 mmol/l; bilirubin $46\,\mu\text{mol/l}$; alkaline phosphatase 14 King Armstrong units/dl and AST 350 IU/l. The prothrombin ratio and the partial thromboplastin test were normal. Chest x-ray examination showed increase in size of the heart shadow, with bilateral pleural effusions. The electrocardiogram was normal. Blood cultures were sterile. No bacteria, acid-fast bacilli, or

malignant cells were found in the pleural or pericardial aspirates. Viral studies were negative.

Neither x-rays after introduction of 100 ml air into the pericardium nor a right atrial angiogram showed a discrete tumour. Antituberculous therapy was begun. At thoracotomy, the pericardium was thickened, granular, oedematous, and vascular. The inner surface was red and haemorrhagic. Histological examination showed great thickening of the pericardium caused by organizing blood clot and many proliferating capillary blood vessels. Many of these vessels were lined by atypical endothelial cells showing frequent mitoses (Fig. 2). Though the possibility of angiosarcoma was considered, the evidence was thought insufficient and the histological appearances were interpreted as those of organizing blood clot and atypical granulation tissue.

Two days after operation he developed weakness of his left arm and then gradually a complete left hemiplegia. The cerebrospinal fluid contained protein 5g/l, red blood cells $160/\text{mm}^3$, white blood cells $610/\text{mm}^3$, and glucose 1.9 mmol/l. Right carotid angiography showed a large mass in the right posterior parietal region and a 1.5 cm leftward shift of the cerebral vessels. He became more confused and was treated with large doses of intravenous antibiotics for a possible cerebral abscess. While being prepared for operation he had a large haemoptysis. He rapidly deteriorated and died five months after the onset of his illness.

At necropsy the pericardium was thickened, with fibrous, haemorrhagic, and gelatinous material adherent to the heart, which was normal. Both main bronchi were partially obstructed by recent blood clot. The right

FIG. 2 Case 2. Pericardial biopsy originally interpreted as atypical granulation tissue. ($\times 390$.)

FIG. 3 Liver metastases showing tumour cells with bizarre nuclear pattern and large blood-filled spaces. ($\times 390$.)

lung contained firm, spherical masses of pinkish grey tissue varying from 0.2 to 1.5 cm in diameter. The liver (2470 g) was enlarged and contained several haemorrhagic masses from 0.2 to 2 cm in diameter. A blood clot 5 × 5 × 3 cm occupied much of the parietal white matter of the right cerebral hemisphere. Microscopical examination showed haemorrhagic malignant tumour in the pericardium, lungs, and liver. The tumour was composed of solid clusters of cells with oval and spindle-shaped vesicular nuclei tending to form capillary-sized blood channels or, more rarely, cavernous blood-filled sinuses (Fig. 3). Many mitoses were present. Several sections of the brain did not show tumour, but it is possible that a small deposit was responsible for the cerebral haemorrhage.

Discussion

Angiosarcoma is a rare malignant neoplasm characterized by the presence of atypical vascular spaces lined by bizarre, malignant endothelial cells. The tumour has recently provoked much fresh interest because of the association between exposure to vinyl chloride and angiosarcoma of the liver (*British Medical Journal*, 1974). There was no history of exposure to vinyl chloride in either of our cases. Angiosarcoma has been reported in the spleen, bone, breast, uterus, heart, skin, and subcutaneous tissues. Primary angiosarcoma of the pericardium is extremely rare, but the clinical picture is surprisingly uniform (Hansson *et al.*, 1970).

The age incidence of this tumour is maximal between the third and fifth decades of life. The patients have usually been well, are mostly male, and present with chest pain, fever, and pericardial and pleural effusions, suggesting an infective process (Glancy *et al.*, 1968). Culture of the pericardial fluid for bacteria, acid-fast bacilli, and viruses, and examination for malignant cells should precede biopsy.

A formal open biopsy is required for a definitive diagnosis. Wide excision of the pericardium is necessary to avoid sampling errors. Removal of the pericardium to the atrioventricular groove provides sufficient tissue for histological examination and also frees the ventricle, thus preventing subsequent constriction. There is sometimes a conspicuous papillary proliferation of endothelial cells, with large hyperchromatic nuclei in the vessels of organizing haematomas, and this histological ap-

pearance may be very difficult to distinguish from that of angiosarcoma (Masson, 1923). This point is well illustrated by our second patient, in whom the original biopsy was interpreted as showing organizing blood clot and atypical granulation tissue, but on review of the sections in the light of the post-mortem findings, the appearance was in fact that of angiosarcoma. Constriction may be caused by organization of haemorrhagic pericardial fluid, as in the first case report, or by encasement of the heart by tumour (Glancy *et al.*, 1968).

The prognosis of patients with this tumour is extremely poor, with few surviving more than 12 months. Some success with a combination of radical excision, radiotherapy, and chemotherapy has been reported by Hollingsworth and Sturgill (1969). As the tumour was apparently limited to the pericardium in the first patient reported here, early radical excision, besides establishing the diagnosis and preventing constriction, may in conjunction with radiotherapy, alter the usual malign course of this tumour.

The second patient was under the care of Sir John Richardson, and we are grateful for his permission to publish this case. The necropsy was performed by Dr. Pauline Kahn at the National Hospital for Nervous Diseases, Maida Vale, W9, and we are grateful to Dr. R. O. Barnard for details of the microscopical findings.

References

- Dawe, C. J., Wood, D. A., and Mitchell, S. (1953). Diffuse fibrous mesothelioma of the pericardium. *Cancer (Philadelphia)*, **6**, 749.
- Glancy, D. L., Morales, J. B., and Roberts, W. C. (1968). Angiosarcoma of the heart. *American Journal of Cardiology*, **21**, 413.
- Hansson, H.-E., Möller, B., Sjögren, I., and Westermark, P. (1970). Malignant haemangioendothelioma of the pericardium. *Scandinavian Journal of Respiratory Diseases*, **51**, 223.
- Harris, H. R. (1960). Angiosarcoma of the heart. *Journal of Clinical Pathology*, **13**, 205.
- Hollingsworth, J. H., and Sturgill, B. C. (1969). Treatment of primary angiosarcoma of the heart. *American Heart Journal*, **78**, 254.
- Masson, P. (1923). Hémangioendothéliome végétant. *Bulletin et Memoires de la Société Anatomique de Paris*, **93**, 517.

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