ANGIOSARCOMA OF THE HEART

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The clinical features and pathological details of a primary cardiac angiosarcoma are described. The significance of the various clinical manifestations of primary cardiac tumours is discussed. The incidence, the histological diagnosis, and the histogenesis of primary cardiac angiosarcoma are considered.

The heart is rarely the site of neoplastic diseases. Lymburner (1934) found 56 cardiac tumours in 8,550 necropsies, Scott and Garvin (1939) 79 cases in 11,100 necropsies, Reisinger, Pekin, and Blumenthal (1942) an incidence of 1.7% in 355 necropsies, Lange and Christiansen (1947) 40 cardiac neoplasms in 4,915 necropsies, and Amsterdam, Grayzel, and Louria (1949) 19 cases in 5,000 necropsies. In this hospital seven cardiac tumours were found in a series of 1,643 necropsies.

Primary cardiac neoplasms are rarer than secondary tumours. Different proportions of primary to secondary growths have been reported by various workers. Lymburner (1934) recorded one in 13, Lange and Christiansen (1947) one in 39, Amsterdam *et al.* (1949) one in 18, and Cheng and Sutton (1955) one in 16. In the cases collected from this hospital the proportion was one in seven.

Mahaim (1945) reviewed 329 primary cardiac tumours. Eighty-seven of these growths were sarcomata, of which three were angiosarcomata. A search of the literature has revealed 13 more examples of angiosarcomata, thus giving an apparent total of 16 cases, details of which are set out in Table I. It is evident that primary cardiac angiosarcomata are very rare tumours. It is considered, therefore, that it will be of interest to record another case.

Case Report

Clinical History.—J.C., a woman aged 52 years, had had good health until December 3, 1957, when she developed a pain in the chest which she thought was due to a cold, but she continued with her work as a part-time cleaner until December 7. The next day, apart from the chest pain she felt well. In the afternoon she complained of a pain in the abdomen, but she continued with her housework. On December 9 she felt unwell and stayed in bed, but did not

feel ill enough to send for her doctor. Two days later, as she was no better, she treated herself by taking a proprietary fever medicine. On the afternoon of December 13 her condition worsened and her doctor was summoned. He found her seriously ill. She died in the ambulance on her way to hospital.

Necropsy.—The necropsy was done 20 hours after death.

Both pleural cavities contained a small quantity of straw-coloured fluid. Mucopus was present in the trachea and bronchi. The lungs were oedematous. The liver had a vivid nutmeg pattern. The left ovary contained small simple cysts and the uterus was atrophic. The spleen, pancreas, adrenals, alimentary and urinary tracts, brain, and skeletal systems showed no abnormalities. Metastases were not seen in any of the above organs. The pericardial sac was distended with blood.

Heart.—The heart weighed 665 g.

Most of the wall of the right atrium was replaced by a purple tumour. It measured 7 cm. by 4.5 cm. by 5 cm. and extended upwards to involve the auricular appendage and backwards almost to the site of pericardial reflexion. Its external surface was irregular and the cut surface showed an outer rim of tissue, 0.5 cm. to 1 cm. thick, which enclosed a central core of blood clot. The neoplastic material had a spongy appearance, but in the inner portion it was more compact and formed a thin capsule around the blood clot (Fig. 1). The endocardium of the atrium was smooth and pale apart from a few areas on its lateral wall where the purple tumour lay beneath it. Numerous flat or hemispherical nodules were scattered over the epicardial surface of the ventricles and the inner surface of the pericardium (Fig. 1). The largest one was situated on the left ventricle just in front of the auricular appendage and measured 2 cm. by 2.5 cm. by 2.5 cm. The cut surface of these nodules had a similar appearance to that of the main growth. The cardiac valves were normal. Neither the cardiac valves nor coronary arteries showed any connexion with the neoplastic process.

TABLE I
SUMMARY OF REPORTED CASES OF ANGIOSARCOMA OF HEART

Author	Age (Yr.)	Sex	Clinical Features	Site of Origin	Metastases
Menning (1888) quoted by Mahaim (1945)	18	F	Haemopericardium	Right auricle	Pericardium
Gödel (1922)	44	M	Pericardial effusion	„ „	Pericardium, lungs, brain
Hewer and Kemp (1936)	62	F	Cough, haemoptysis, paraplegia	„ „	Pericardium, bronchial lymph nodes, omentum, bones
Gross and Englenart (1937)	45	F	Old rheumatic endocarditis with mitral stenosis, left hemiplegia, congestive heart failure	Left „	None
Choisser and Ramsey (1939)	26	M	Congestive heart failure	Right „	Pericardium, pleura, liver, omentum, pericardium
	30	M	Pericardial effusion	„ „	
Weller (1940)	30	M	Cough, swelling of face and neck, pericardial effusion, hepatomegaly	„ „	None
	26	M	Influenza attack, hepatomegaly, lymphadenopathy	„ „	Pericardium, pleura, lungs, peritoneum, spleen, liver, kidneys
Lange and Christiansen (1947)	47	M	Pericardial effusion	„ ventricle	Pericardium, pleura, lungs, mediastinal lymph nodes
Amsterdam <i>et al.</i> (1949)	54	M	Congestion of face and veins of neck, bilateral pleural effusions, congestive heart failure	Infundibular cusps of the tricuspid valve	None
Glassy and Massey (1950)	26	M	Congestive heart failure, precordial pain, dyspnoea	Right auricle, or right ventricle	Pericardium, pleura, lungs
Tacket <i>et al.</i> (1950)	45	F	Congested veins of neck, swollen face, tachycardia, pericardial effusion, hepatomegaly	Interauricular septum of right auricle	Pericardium, lungs
Blanchard and Hethrington (1952)	25	M	Cough, precordial pain, cyanosis of head, neck, and chest, pleural and pericardial effusion, hepatomegaly	Right auricle	Pericardium, lungs, liver, adrenals
	33	M	Precordial pain, dyspnoea, bilateral pleural effusions, pericardial effusion	„ „	Pericardium, lungs, liver, bones
Schwartz and Loder (1952)	37	M	Precordial pain, dyspnoea, pericardial effusion	„ „	Pericardium, pleura, lungs, spleen
Cheng and Sutton (1955)	45	M	Cough, haemoptysis, precordial pain, dyspnoea, swelling of face and feet, pericardial effusion	„ „	Pericardium, lungs, liver

Histology.—Several blocks of tissue were taken from the tumour on the wall of the right atrium and the nodules on the epicardial surface of the ventricles and pericardium. Sections prepared from these blocks were stained with haematoxylin and eosin, Mallory's phosphotungstic acid haematoxylin, Heidenhain's haematoxylin and eosin, Heidenhain's haematoxylin combined with Masson's trichrome stain, and Gordon-Sweet reticulin stain counterstained with haematoxylin and eosin.

The neoplastic tissue was composed of spindle, round, cubical, or oval cells and their nuclei were round or oval and vesicular in type (Fig. 6). Some nuclei were hyperchromatic and an occasional mitotic figure was seen. The arrangement of the cells varied in different portions of the growth. In the outer areas of the tumour they formed a loose network in which small vascular channels were apparent (Fig. 2). These channels became larger towards the centre of the growth and were separated from one another either by a considerable amount of cellular tissue or by less cellular strands (Figs. 3 and 4). The vascular spaces contained red blood cells and were lined by flattened or cubical cells (Figs. 3, 4, 5, and 6) and in scattered foci these cells were heaped up on each

other (Figs. 5 and 6). Reticulin-stained sections showed that there was a free anastomosis between the vascular channels (Fig. 7). Areas of haemorrhage and necrosis were present in the inner zones of the growth, which obliterated the blood spaces or filled them with polymorphonuclear leucocytes. Infiltration and destruction of the myocardium by the neoplastic tissue was seen in the outer portions of the growth (Figs. 2, 5, and 7).

The nodules on the epicardial surface of the ventricles and pericardium had a similar histological structure to that of the tumour of the right atrium (Fig. 8).

Discussion

Mahaim (1945) considered that persons who had benign pedunculated cardiac neoplasms might be cured by operative procedures. It is important, therefore, to attempt to diagnose these tumours in life. Yater (1931), Mahaim (1945), and Whorton (1949) studied the clinical features of these growths. They showed that unremitting heart failure of obscure origin, precordial pain, cardiac arrhythmias, signs of obstruction of the superior

FIG. 1.—The heart with the right atrium opened and small portion of the pericardium to show the primary tumour in the right atrium and secondary nodules on the epicardial surface of the ventricles and pericardium.

FIG. 3.—Same tissue as Fig. 2 showing medium-sized vascular spaces containing red blood cells, lined by flattened or cubical cells and separated by a considerable amount of cellular tissue. Haematoxylin and eosin. $\times 180$.

FIG. 2.—A section from the primary growth showing extension into the myocardium and the loosely interlaced neoplastic cells forming small vascular spaces. Haematoxylin and eosin. $\times 180$.

FIG. 4.—Same tissue as Fig. 2 showing large vascular channels containing red blood cells, lined by flattened or cubical cells and separated by smaller strands of cellular tissue. Haematoxylin and eosin. $\times 180$.

FIG. 5.—Same tissue as Fig. 2 showing vascular spaces lined by flattened or cubical cells, some of which are heaped up on each other and muscle fibres infiltrated by the neoplastic cells. Haematoxylin and eosin. $\times 325$.

FIG. 7.—Same tissue as Fig. 2 showing anastomosing vascular channels, which infiltrate muscle fibres. Gordon-Sweet reticulin stain. $\times 325$.

FIG. 6.—Same tissue as Fig. 2 showing spindle, round, cubical, or oval cells with round, oval, and vesicular nuclei and vascular channels lined by flattened or cubical cells. Haematoxylin and eosin. $\times 410$.

FIG. 8.—Section from nodule on pericardium showing anastomosing vascular spaces containing red blood cells and separated by a variable amount of neoplastic tissue. Haematoxylin and eosin. $\times 29$.

mediastinum, haemopericardium, non-pulsating enlargement of the right auricle, and sudden death could be caused by cardiac tumours. The clinical features presented by previously reported cases of angiosarcoma of the heart (Table I) show that these tumours may evince any of the above clinical manifestations except sudden death. Thus it is apparent that there is no special clinical feature which will distinguish between benign and malignant cardiac tumours. Contrariwise, a haemopericardium indicates that the neoplasm is either a primary cardiac tumour which has spread to the pericardium, or one which is arising from the pericardium, and is not a benign pedunculated cardiac growth. It is interesting that in the case reported above the large cardiac tumour gave rise to no clinical manifestations until 10 days before death, and probably these were caused by the cardiac tamponade.

Evans (1956) has pointed out that angiosarcomata should be differentiated from mesenchymomas which show vasoformative and other lines of mesenchymal differentiation. In this case special staining procedures failed to demonstrate any line of mesenchymal differentiation other than vasoformative; thus this tumour cannot be considered to be a mesenchymoma with vasoformative tendencies.

In this case the diagnosis of an angiosarcoma was made on the criteria laid down by Stout (1943). He considered that these tumours were composed of atypical endothelial cells, which were formed in greater number than required to line vascular spaces by a single layer of endothelium. These channels formed an anastomosis with each other and were surrounded by a delicate framework of reticulin. The neoplastic cell varied from a polygonal to a spindle-shaped cell and could form a single layer, heaps of cells within the vascular lumen, or sheets of cells outside the vascular channel. All these features were evinced by the tumour described above.

Since the site of origin of primary cardiac angiosarcoma is the wall of the heart, the angiosarcoma arising from a coronary artery described by Schwarzkopf and Gais (1953) and the angiosarcomata originating from the pericardium reported by Greenberg and Angrist (1948), Florange

(1954), and Grosse-Brockhoff and Schreiber (1955) have not been included in the list of published cases of primary angiosarcoma of the heart noted in Table I.

McClure (1921) has shown that primitive mesenchymal tissue in any part of the body can form angioblasts. Primary cardiac angiosarcoma thus probably arise from these cells which normally lie dormant in the myocardium. This is in agreement with the opinions expressed by Straus and Merliiss (1945) and by Tacket, Jones, and Kyle (1950), who considered that primary cardiac tumours arose from mesenchyme. The latter authors observed that most of these tumours grew from the septal area of the heart, which is the last zone for complete structural formation. They considered, therefore, that this site of origin was corroborative evidence of the mesenchymal origin of primary cardiac tumours.

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