Primary Myosarcoma of the Heart

Report of a Case Associated with Malignant Carcinoids and Pancreatic Heterotopia

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Precordial pain and pericarditis were the early manifestations of this cardiac tumor. Discovery of bony metastases preceded detection of a rapidly growing intrathoracic mass, erroneously considered a bronchiogenic carcinoma invading the heart. Changing murmurs, chest pain, transient arrhythmia, intermittent fever, and progressive weight loss were the outstanding clinical features. Necropsy revealed a primary cardiac tumor with metastases to pelvic bones, vertebrae, and lung, as well as malignant carcinoids and heterotopic pancreatic tissue.

PRIMARY malignant muscle tumors of the heart are uncommon enough to warrant reporting a single case. The tumor in our case we have classified as a myosarcoma, as it is closely related to the malignant striated muscle tumors of the heart but less differentiated. Only eight striated muscle sarcomas primary in the heart have been described. Leach, reporting such a case, found in the literature 422 primary tumors of the heart and pericardium, of which 89 were sarcomas of different types. Whether the tumor in our case arose from the heart or pericardium could not be determined with certainty, but its origin was most likely in the posterior left ventricular or auricular wall.

Although we were fortunate in being able to observe the patient for nine and one-half months before his death, the correct clinical diagnosis was not made. Since the clinical and pathologic findings are similar in many respects to those of the eight striated muscle sarcomas of the heart which have been described, we have included a brief summary of each of those cases for comparison.

Case Report

H. P. B., a 50 year old white, clothing salesman entered the Veterans Administration Hospital, San Francisco, on December 27, 1946, because of severe midanterior chest pain. This attack of pain had begun two weeks before, and was accompanied by nausea, anorexia, and weakness. Three days before entry the pain increased in severity, became constant, and was aggravated by exertion, cough, or deep breathing. Profuse sweats had occurred for several nights, without chills or known fever.

In 1942 the patient began having substernal chest pain, radiating to both arms and associated with dyspnea. The pain was brought on by exertion and relieved by rest or nitroglycerin. Examination at that time revealed loud systolic murmurs at the cardiac apex and base. He stopped working and had very little pain until the onset of the present illness.

On admission the patient was acutely ill, anxious, and restless. He was pale and perspired freely. The temperature was 100 F., pulse rate 80, respiration rate 20, and blood pressure 120/60. Lung fields were normal, except for a few moist rales at both bases. The heart was not enlarged and the sounds were of good quality. A loud friction rub was heard to the left of the sternum. There were no murmurs. The liver was palpable 4 cm. below the right costal margin, but the spleen was not palpable.

The pain was temporarily relieved by morphine. Although the first diagnosis was myocardial infarction, it soon became evident that the patient’s course was not that of simple infarction. There were many fluctuations in the clinical course, but the overall picture was a gradual progressive decline, with increasing anorexia, weakness, and loss of weight until his death October 14, 1947, nine and one-half months after admission.

During the patient’s entire hospital stay there was intermittent low-grade fever and frequent night sweats. In mid-January, 1947, a nonproductive cough developed which gradually became more severe. The precordial friction rub noted on entry became very loud and persisted for two weeks. A friction rub reappeared eight months later, associated with pain, but lasting only a few days. There was rather severe precordial pain off and on for the first three weeks, and after that occasional bouts of pain, sometimes accompanied by mild shock. Murmurs developed which changed from time to time. Two
days after entry a presystolic murmur was heard, ending in a loud first mitral sound. One month later a loud systolic murmur had developed. This murmur later became less intense and then disappeared. Six months after entry, a systolic and diastolic murmur which persisted with variations in intensity was heard along the left sternal border. The spleen increased in size and became readily palpable. The liver edge remained 3 to 5 cm. below the right costal margin.

During the fourth month of illness, left hemiplegia and aphasia suddenly appeared, most likely the result of an embolus. These signs disappeared in two weeks.

Six weeks after entry a density in the base of the left lung was first noted in the roentgenograms. Two months later there was evidence of partial collapse of the left lower lobe. By the eighth month of hospitalization a large mass filled the lower left side of the chest and displaced the left lung upward (figs. 1 and 2). During the fourth month several metastases were found in the right coxal bone. Subsequent studies showed similar lesions in the left coxal bone and an osteoblastic process in the bodies of the twelfth dorsal and first lumbar vertebrae.

Electrocardiographic tracings were consistently abnormal. The initial tracing showed low voltage and low or flat T waves in Leads I, II, III, aV₃, and V₅ and V₆. During the next two weeks the electrocardiographic changes were those of subacute pericarditis, with inverted T waves in Leads I and aV₆ and in all the V leads (fig. 3). A transient episode of auricular fibrillation with a rapid ventricular rate occurred during the second month, lasting three days. After this there were minor variations in the electrocardiogram. The last tracing made in September, one month before death, was very similar to the tracing made on admission.

Examinations of the urine revealed no significant abnormalities. The stools showed traces of occult blood on several occasions, but were otherwise normal. Blood cultures were repeatedly negative. Sputum examination for malignant cells was negative. The leukocyte count ranged from 9,000 to 13,000 per cu. mm., with normal differential counts. On entry the hemoglobin concentration was 10 grams per 100 cc., with 3.7 million erythrocytes per cu. mm.; a transfusion was given at that time. The sedimentation rate remained elevated at 30 to 35 mm. per hour. One month after entry the serum acid phosphatase level was 2.25 units and the alkaline phosphatase was 28.5 units (King-Armstrong). The alkaline phosphatase rose to 41.2 units in one month and later dropped to 20.7 units. The acid phosphatase remained below 3 units.

With the discovery of the bony lesions in the pelvis, the mass in the lower left side of the chest was thought to be a carcinoma of the bronchus. Toward the end the varying and unusual murmurs suggested that a primary lung tumor was invading the heart.
Abstract of Necropsy Findings

The final anatomic diagnoses were: primary myosarcoma of the heart, with extension within pericardial sac and adhesive pericarditis; partial sarcomatous replacement of posterior surfaces of both two carcinoid tumors of the ileum, with carcinoid metastases to mesenteric lymph nodes; heterotopic pancreatic tissue in the jejunum.

Thorax. A large, partially encapsulated mass, extending from the posterior and posterolateral surface of the heart, filled the lower two-thirds of the thoracic cavity on the left side, forcing the lung into the upper one-third (fig. 4). The tumor, which weighed about 2,100 grams, was composed of grayish-white spongy tissue with large areas of congestion, hemorrhage, and necrosis.
Heart. The estimated weight of the heart exclusive of the tumor was 350 grams. The pericardium was stretched over the surface of the mass. The right coronary and left circumflex arteries were normal in their proximal portions, but posteriorly were obliterated by the tumor. Just above the line of closure of the anterior mitral valve cusp was a rectangular mass of neoplastic tissue, measuring 3.0 by 2.5 by 3.0 cm., projecting from the left auricular wall over the valve opening. The mitral valve and its chordae tendineae were moderately thickened. Replacing a small portion of the anterior left ventricular myocardium was a metastatic nodule, measuring 3.0 by 2.5 by 1.5 cm., composed of tissue resembling that of the large mass. The posterior portion of the myocardium of the left ventricle, a small part of the posterior surface of the right ventricle, and the posterior aspect of both auricles were partially replaced by the tumor (fig. 5).

Other Organs. In the parenchyma of the right lung were three small, grayish-white nodules, metastatic from the tumor of the heart. The left lung, which was small and atelectatic, contained no neoplastic tissue. The hilar nodes were free of metastases. The spleen was enlarged, weighing 400 grams. It contained two old infarcts which showed no evidence of tumor.

In the wall of the ileum were two small, firm, grayish-yellow nodules of neoplastic tissue, the larger measuring 1.0 cm. in diameter. In the jejunal wall was a pink nodule, measuring 1 cm. in diameter, which grossly resembled pancreatic tissue. Two small, firm, grayish-yellow lymph nodes near the origin of the superior mesenteric artery consisted mainly of metastatic tumor tissue like that of the nodules in the ileum.

The left kidney contained an old infarct, measuring 2 cm. in diameter, which contained no tumor.

In the right iliac fossa was a mass, measuring 10.0 by 5.0 by 4.0 cm., composed of homogeneous soft tissue resembling that of the heart tumor. The tumor had displaced the iliacus muscle forward and was invading the innominate bone. The bodies of the twelfth thoracic and first and second lumbar vertebrae were expanded, had a gray color, and were sclerotic.

The brain, liver, pancreas, adrenal glands, prostate gland, testes, thyroid gland, trachea, esophagus, and pituitary gland showed no significant changes.

Histopathology

The neoplastic tissue in the myocardium and intrapericardial mass, lung, metastases, and pelvic mass had the same general structure, with certain
variations. In the portion invading the myocardium, the cells varied considerably in size and shape (fig. 6, D). Most were large, oval cells with large nuclei, but there were many small round cells with pyknotic nuclei. Some were stellate and resembled primitive mesenchymal cells. Also present were many large tumor giant cells, as well as small numbers of strap-like, elongated cells, with oval nuclei, which resembled muscle fibers but lacked transverse striations. These in some areas formed syncytial strands.

Gastro-enteric Tract. The small mass in the jejunum occupied almost the entire thickness of the bowel wall, being covered on one surface by mucosa and muscularis mucosae. It was composed of normal pancreatic tissue, traversed by strands of muscle, with a suggestion of branching. All of the cells had abundant, deeply eosinophilic cytoplasm with many small vacuoles. The mass above the mitral valve was composed mainly of fibrin, with widely dispersed, spindle-shaped, neoplastic cells.

The cells of the metastases were much better differentiated toward mature muscle fibers. In the lung, for example, the metastases were composed mainly of long, ribbon-like cells with elongated, oval nuclei, with delicate chromatin, many containing prominent eosinophilic nucleoli (fig. 6, A, B, C). There were smaller numbers of round cells, but many large tumor giant cells were present like those in the intrapericardial mass. The tumor cells in the lung were arranged in bundles with slight whorling. The cells of the metastases in the pelvis and vertebrae resembled those of the lung metastases. Connective tissue stains revealed occasional longitudinal fibrils but no distinct transverse striations.

The two nodules in the ileum were composed of neoplastic tissue, typical of carcinoid tumors, which replaced the submucosa and much of the muscle, extending centrally to the mucosal epithelium. The tumor cells were small and uniform, with round vesicular nuclei and a small amount of granular cytoplasm with indistinct borders. The cells were closely grouped to form small masses around central capillaries, separated by narrow fibrous strands. In one of the nodules in the ileum the tumor was infiltrating the serosa. One mesenteric node showed complete replacement of its normal structure by carcinoid tumor.
Discussion

Study of the few muscle tumors of the heart which have been described leaves their origin obscure. The association of such a tumor in this case with pancreatic heterotopia suggests that it may have arisen from a congenital rest of muscle, possibly in the wall of the left auricle. Larson and Sheppard,13 in a case more fully described below, found a rhabdomyoma of the left auricle, with sarcomatous extensions, and considered that the rhabdomyoma had undergone malignant change. Júnior9 described a rhabdomyosarcoma of the heart in which all stages of development of cardiac muscle were represented, from primitive myoblasts to cells with distinct transverse striations. A horseshoe kidney was found in his case, and the author felt that the presence of this congenital renal anomaly was evidence that the heart tumor had arisen from a congenital rest.

Classification of striated muscle tumors has been confused by disagreement on the importance of demonstrating striations. Cappell and Montgomery4 divided these tumors into (1) those showing well-defined cross striation and (2) those in which cross striation is lacking. They subdivide the first group into: (a) simple rhabdomyomas and (b) malignant rhabdomyomas, showing well-defined cross striations in at least a small proportion of cells. The second group consists of cells morphologically resembling myoblasts, either showing very delicate striations or completely devoid of striations. The tumor encountered in our case falls into the last group.

Reported Cases of Striated Muscle Sarcoma of the Heart

The first case, reported by Bradley and Maxwell9 in 1928, occurred in a 62 year old man, ill for only seven or eight weeks. The chief symptoms and signs were pain in the upper left side of the chest, swelling of the face and neck, fever, marked dyspnea, and anemia, with 40 per cent hemoglobin. The heart was greatly enlarged roentgenologically. At autopsy, a tumor was found which filled the pericardial sac and invaded the heart muscle. There were metastatic nodules in the myocardium of the septum and left ventricle, lungs, liver, and kidneys. The tumor was composed of striated cells, giant cells, and long spindle cells with eosinophilic cytoplasm. The cells of the metastatic nodules were better differentiated than those in the primary lesion.

Müller,14 in 1932, reported a case of rhabdomyosarcoma of the left auricular wall. No clinical information was included in the report. The tumor consisted of large, striated spindle cells of various sizes, with long nuclei. In the left auricle was a "pseudo-myxoma" which was thrombotic. There were metastases in the left lung, pancreas, and small bowel, as well as in aorta of the spleen, kidney, and brain.

A primary rhabdomyosarcoma of the heart, appearing in a 62 year old woman, was reported by Barnes, Beaver, and Snell1 in 1934. The chief symptoms were pain in the thorax and dyspnea on exertion. There was a pericardial friction rub, and the patient developed complete heart block. A metastasis to the left deltoid muscle was present. At autopsy, diffuse involvement of the right auricle and ventricle with tumor nodules was encountered, with small metastatic nodules in the lungs, mesenteric lymph nodes, and adrenal glands.

A case of rhabdomyosarcoma, occurring in a 16 year old girl, was described by Reeves and Michael13 in 1936. The patient had been ill for only six days with dyspnea, abdominal pain, and marked fatigue. For the previous year she had complained of easy fatigability. Physical examination revealed moist râles throughout both lung fields, pulse rate 140 per minute, and distant heart sounds. At autopsy, both auricles were almost completely replaced by a friable, hemorrhagic, soft, nodular tumor mass, which ruptured into the pericardial cavity posteriorly. It was composed of small and large spindle cells, with fairly numerous giant cells. There were no metastases.

Larson and Sheppard,13 in 1938, described a primary tumor of the heart in a 37 year old woman. A papillary tumor mass hung down from the left auricular lateral wall into the left ventricle. There was a small isolated rhabdomyoma in the adjacent portion of the left auricular wall. The tumor, which extended into the base of the lung near the hilus, appeared sarcomatous in its extensions.

A case similar to ours in certain respects was reported by Júnior9 in 1942. When first seen
the patient, a 39 year old white man, had numerous tumor nodules in the subcutaneous tissues. He soon died in coma, after a febrile course with anorexia, emaciation, general weakness, and pain in the back and limbs. Autopsy revealed a polypoid, soft, red tumor mass in the left ventricular cavity, attached by a pedicle to the anterior wall. The adjoining myocardium was invaded. Metastases were found in the subcutaneous tissues, brain, lungs, bronchial lymph nodes, liver, kidneys, and intestine. The tumor, which looked the same everywhere, was composed of cells in bundles and syncytial strands, with eosinophlic cytoplasm. There were many vacuolated giant cells. Many of the elongated cells had longitudinal striations, with occasional transverse striations. Coincidental findings were a supernumerary spleen and a horseshoe kidney with dilated pelvis.

Wells, Rowe, and Jaffe in 1947 reported a myosarcoma occurring in the heart of a 15 year old boy who had been apparently well until five days before death. His symptoms were pain in the chest, abdominal distress, fatigue, and difficulty in breathing. When examined, the patient was dyspneic and in shock, with weak, distant heart sounds. A diastolic apical murmur was heard on one examination. A pericardial friction rub was heard on the first day of illness, disappearing later. The electrocardiographic findings were: rapid rate; regular rhythm; depressed RS-T segments in Lead II; upright T waves in Leads I, II, and IV; and inverted T wave in Lead III. Autopsy revealed a large, hemorrhagic, friable, pedunculated tumor mass attached to the area of the foramen ovale in the right auricle, filling the tricuspid orifice and right ventricle. The hemorrhagic, necrotic tumor was composed mainly of spindle-shaped cells, with some multinucleated cells.

Leach, in 1947, described a case of primary rhabdomyosarcoma of the heart in a 14 year old boy. He had been seen first in May, 1936, because of coughing, more severe on lying down, and increasing fatigue of three weeks' duration. Roentgenograms revealed a bulging mass in the superior mediastinum. Roentgen-ray therapy was given for three weeks. When seen again in July, 1938, the patient was moribund and soon expired. At autopsy a large mass was found in the mediastinum, replacing the thymus and extending down to a short distance above the diaphragm. The right ventricle was filled with a polypoid tumor mass, composed of ribbon-like cells with eosinophilic cytoplasm, some with longitudinal striations. The heart tumor was not as well differentiated as the mediastinal mass.

Comment

Although cardiac tumors produce no characteristic signs or symptoms, such tumors have occasionally been correctly diagnosed. It is sometimes difficult to correlate the clinical and pathologic features. Very large intracardiac tumors may produce surprisingly few symptoms for a long period of time. The clinical course is often that of cardiac decompensation, resulting from extensive myocardial replacement, obstruction of valve orifices, or pericardial effusion. Changing heart murmurs similar to those in our case have been noted often. Pedunculated tumors sometimes drop through the valve and simulate valvular disease, producing signs which may vary with changes of posture. The mass over the mitral valve in our case did not produce this effect. Emboli from vegetative valve lesions may produce symptoms, such as the transient hemiplegia in our patient. Anginal attacks result from obstruction of the coronary arteries. Roentgenologic changes in the silhouette of the heart sometimes appear early.

Arrhythmias are common, complete heart block or bundle branch block often resulting from invasion of the interventricular septum. However, even with such invasion there may be no alteration of rhythm from the normal. Transient fibrillation such as our patient manifested has been noted before. Fishberg, discussing auricular fibrillation and flutter in metastatic growths of the right auricle, reported two cases of cardiac tumors in which arrhythmia persisted, after onset, until death. In his third case, however, the patient developed flutter fifteen days before death, reverting to normal rhythm in three days. Hamilton-Paterson and Castelden have described a case of round-and-spindle-cell sarcoma of the right auricle in a 45 year old woman in whom auricular fibrillation was noted about four months before death. Four weeks later the rhythm returned to
normal, auricular fibrillation recommencing about a month before death.

Pericardial effusions, recurrent and frequently hemorrhagic, often occur in association with primary and secondary tumors of the heart or pericardium. Mahaim 9 has stated that hemopericardium is the most important sign of malignant tumors of the heart and of benign and malignant tumors of the pericardium.

The strialike shape of the cells of the heart tumor, their strongly acidophilic cytoplasm, the formation of syncytial strands, and the occurrence of large vacuolated giant cells indicate that the neoplastic cells were differentiating towards striated muscle. Longitudinal fibrils were seen in some cells. As in certain of the cases summarized above, the tissue of the primary neoplasm was not as well differentiated as the tissue of its metastases.

In describing a fibrosarcoma of the heart, Woll and Vickery 22 commented that theirs was the first primary tumor of the heart metastasizing to the vertebrae. In our case, metastases in the bones directed attention to the chest, and repeated roentgenograms revealed a tumor mass in the lower left thorax. The tumor was thought to be primary in the lung, involving the heart, but instead, was primary in the heart, displacing the left lung.

Summary
A case is reported in which a primary myosarcoma of the heart, metastasizing to the right lung, ilium, and vertebrae, occurred in conjunction with heterotopic jejunal pancreatic tissue and carcinoid tumors of the ileum, the latter metastasizing to mesenteric nodes. The previously reported cases of striated muscle sarcomas of the heart are briefly reviewed.

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Primary Myosarcoma of the Heart: Report of a Case Associated with Malignant Carcinoids and Pancreatic Heterotopia
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