MALIGNANT FIBROUS HISTIOCYTOMA OF THE HEART

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A 33-year-old woman presented signs and symptoms which suggested mitral stenosis and insufficiency. Subsequent echocardiographic and angiographic testing demonstrated a left atrial tumor which was suspected clinically to be a left atrial myxoma. At surgery, the tumor was partially resected and histological examination revealed that the mass to be a malignant fibrous histiocytoma. At autopsy, the tumor was found to be localized in the heart, and there was no metastasis.

We encountered a patient with a malignant fibrous histiocytoma of the heart. A left atrial tumor arising from the posterior wall of the left atrium was diagnosed before surgery. Histological examination of the resected material indicated malignant fibrous histiocytoma. At autopsy, the tumor was found to be confined to the heart and there were no metastases. The first case of malignant fibrous histiocytoma of the heart was previously reported by Shah et al in 1978. The characteristic features of echocardiography, angiography, and histopathological findings are reported herein.

CASE REPORT
A 33-year-old woman was referred to the Yamaguchi University Hospital because of persistent congestive heart failure. Dyspnea and palpitation upon exertion and occasional hemoptysis had begun insidiously 10 months before admission. Four months before admission she had a single, transient attack of right-sided hemiparesis and dysarthria. Her symptoms went from bad to worse. She began to have orthopnea, a severe cough with bloody sputum, and edema of the face and extremities. There was no past history of rheumatic fever and she had never had a heart murmur.

The family history was not contributory. Upon admission, she was alert and had orthopnea. The blood pressure was 108/86 mmHg, and her pulse rate was 106/min and regular. The rate of respiration was 20/min and her temperature was 38°C. Edema was evident in her face and extremities. The cervical vein was engorged about 3 cm above the sternal angle at elevation of 90°. Cardiac dullness was slightly enlarged to the left. The apex beat could be palpated at the 5th intercostal space in the midclavicular line and the left parasternal impulse was present. On auscultation, the first heart sound was loud. The second heart sound was physiologically splitting and had an accentuated pulmonic component. A grade IV/VI holosystolic murmur that radiated to the left axilla was heard at the apex. At the

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4th intercostal space, there was a grade III/VI holosystolic murmur that increased with inspiration. A grade II/VI diastolic rumbling murmur was heard at the apex. A low pitched, early diastolic sound (tumor plop sound), best heard at the apex, was phonocardiologically recorded at 0.08 to 0.10 second after the aortic component of the second heart sound. The heart sounds and murmurs were extremely variable and position dependent. Rough breathing sounds were heard at the base of both lung fields, but there were no rales. The edge of the liver was felt 3 cm below the right costal margin.

Laboratory data included: erythrocyte sedimentation rate 16.5 mm in hour, C-reactive protein 3\+, hemoglobin 11.9 g/100ml, red blood cell count 4,460,000/mm\(^3\), white blood cell count 9,100/mm\(^3\), serum albumin 2.5 g/100ml and serum globulin 3.2 g/100ml, total bilirubin 1.9 mg/100 ml, glutamic oxalacetic transaminase (GOT) 35 U, glutamic pyruvic transaminase (GPT) 46 U, and lactic dehydrogenase (LDH) 717 U.

The chest X-ray showed a left atrial enlargement and pulmonary venous hypertension (Fig. 1). The electrocardiogram, which showed a regular sinus rhythm, demonstrated right ventricular hypertrophy and left atrial enlargement (Fig. 2). An apex cardiogram showed a prominent notch in the systolic rise of the tracing.

Single beam echocardiography strongly suggested the presence of a tumor in the enlarged left atrium (Fig. 3A). M-mode scanning showed tumor echoes posterior to the anterior leaflet of the mitral valve in the left ventricle during ventricular diastole, and in the left atrium during ventricular systole. Two-dimensional echocardiography also showed the pendular motion of a tumor between the left atrium and left ventricle during ventricular systole and ventricular diastole (Fig. 3B). However in this record, the tumor did not seem to have a stalk arising in the

atrial septum as is seen in typical myxoma. Furthermore, the tumor seemed to be expanding from the posterior wall of the left atrium with a wide attachment.

Right and retrograde left heart catheterization were performed and cineangiograms of the left heart chambers were obtained by the injection of contrast material into the pulmonary artery and left ventricle. The mean pressure of the right atrium was 12 mmHg, the right ventricle, 100/11 mmHg, and the pulmonary artery, 94/44 mmHg. The pulmonary arterial wedge pressure was 38 mmHg. The left ventricular pressure was 111/4 mmHg. The cardiac output by the thermodilution method was 3.05 l/min, the cardiac index, 2.16 l/min/m², and the stroke volume, 22 ml/beat. In the angiogram, tumor shadow, a large filling defect, was detected in the left atrium, and was found to prolapse through the mitral valve orifice into the left ventricle during ventricular diastole, then return into the left atrium during ventricular systole. According to the angiogram, the contour of the tumor seemed irregular. In the pulmonary angiogram, regurgitation of the contrast material could be seen through the pulmonary valve. Mitral regurgitation was not clear in the left ventriculogram.

At cardiac surgery, a bloody pericardial effusion was evident. The left atrium was opened. A polypoid and lobulated mass of soft, yellow-whitish tumor was found to occupy most of the left atrial cavity, obstructing 4 orifices of the pulmonary vein. The tumor arose from the posterior wall of the left atrium and expanded towards the left hand side of the pericardial cavity. The tumor in the left atrial cavity only was partially resected and was histopathologically proven to be a malignant fibrous histiocytoma.

Postoperatively, radiation and anti-tumor drugs were not given. The patient died of advanced cachexy and heart failure 84 days after the surgery.

PATHOLOGICAL FINDINGS

Autopsy findings
Adhesion of the pericardial sac was evident. The heart was extremely enlarged and weighed 1490 grams. Incision into the left atrium revealed a large, soft, lobulated mass occupying most of the chamber (Fig. 4), and the tumor color was yellow-whitish, and partially reddish. The main portion of this tumor was about 5 cm. The tumor infiltrated through the posterior wall of the left atrium and exclusively expanded towards the left hand side of the pericardial cavity (Fig. 4).

Macroscopically, metastatic lesions were not observed.

Fig. 3A. Echocardiography recorded before surgery, showing tumor echoes posterior to the anterior leaflet of the mitral valve in the left ventricle during ventricular diastole. Arrow indicates the tumor echoes. Abbreviations: AML = anterior leaflet of the mitral valve; RV = right ventricle; IVS = interventricular septum; LAPW = posterior wall of the left atrium; ECG = electrocardiogram.

Fig. 3B. Two-dimensional echocardiography recorded before surgery. The pendular motion of the tumor attached to the left atrial wall between the left atrium and left ventricle during ventricular systole and ventricular diastole can be detected. Abbreviations: RV = right ventricle; Ao = aorta; IVS = interventricular septum; LA = left atrium.
Light microscopic findings

The sections revealed a cellular tumor expect in the massive necrotic areas and there were two distinct histological features. One was a highly ordered storiform pattern and the other a more pleomorphic appearance.

Storiform lesions consisted of a spindle cells, similar to fibroblasts, and larger polygonal cells resembling histiocytes (Fig. 5A). Considerable amounts of mucoid materials were seen in the stroma and small numbers of collagen fibers were also present between the spindle cells. The spindle cells, having oblong nuclei, were arranged in short fascicles that often formed cartwheel appearances. The polygonal cells had rounded, pale-staining nuclei with large eosinophilic nucleoli present in small aggregates around the slit-like blood vessels or were admixed with the spindle cells.

Pleomorphic areas were vaguely lobulated and often merged with typical storiform lesions and necrotic areas. The pleomorphic areas could be differentiated from storiform lesions by pleomorphic giant cells, Plumper fibroblast-like cells with more nuclear atypia and also by greater numbers of polygonal histiocyte-like cells (Fig. 5B). These cells were all randomly dispersed with respect to blood vessels, except for the giant cells which accumulated near the margin of the lobules. The giant cells had multiple hyperchromatic and irregular nuclei that were frequently folded and contained cytoplasmic invaginations. A deeply eosinophilic or a foamy cytoplasm with several vacuoles was also evident.

Both typical and atypical mitotic figures were quite evident in both the spindle and polygonal cells. In places, there were moderate numbers of inflammatory cells, usually lymphocytes.

Lipid stain (Sudan III) showed small droplets of neutral fat within a few of the foamy histiocyte-like cells as in the giant cells. PAS stains, with and without diastase digestion, showed essentially no glycogen in any type of tumor cells. No evidence of muscle type cross-striation and hemosiderin deposits were demonstrated by PTAH and Fe stains, respectively.

Electron microscopic findings

Under electron microscopy the majority of
tumor cells resembled histiocytes (Fig. 6). These cells contained large numbers of short and rough endoplasmic reticula with dilated lumens. Lipid droplets were frequently seen and mitochondria were plentiful while cytoplasmic lysosomes with limiting membranes were rare. These lysosomes had a microvillous border. Phagocytosis was occasionally seen in these cells. In places, more
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Fig. 6. Electron micrograph showing representative cells which resemble histiocytes.

elongated and densely stained cells were seen. These cells somewhat resembled fibroblasts, but only small amounts of collagen were noted in the intercellular spaces.

There was no evidence to suggest an origin from cardiac muscle.

From these findings, this tumor was classified as a malignant fibrous histiocytoma.

DISCUSSION

Atrial myxoma constitutes more than half of the primary neoplasms in the heart\(^3\) while primary sarcomas of the heart are relatively rare\(^3\). It has been reported that cardiac myxoma occurs frequently in the left atrium\(^3\). Cardiac sarcomas more frequently occur in the right heart, especially in the right atrium\(^7\). The case was diagnosed in the clinical examinations before surgery to be a left atrial tumor and the clinical features strongly implied a left atrial myxoma. The patient had a transient episode of right-sided hemiparesis and dysarthria suggested cerebral embolism, despite a regular sinus rhythm. Positional variations of murmurs with a tumor plop sound and systolic notch in the apex cardiogram were detected. These are familiar to us as signs of a left atrial myxoma\(^6\). In addition, echocardiography and angiography also showed features specific to this condition\(^2\).\(^5\).\(^9\). The pendular motion of a tumor attached to the left atrial wall between the left atrium and left ventricle during ventricular systole and ventricular diastole could be detected clearly in the echocardiogram. The motion of the tumor in the heart was also demonstrated by angiography. All of these features strongly suggested a left atrial myxoma. Two-dimensional echocardiography, however, showed that this tumor did not have a stalk rather that it occurred from the posterior wall of the left atrium with a wide attachment. The angiogram showed that the contour of the tumor was irregular. There are some differences between these features and those found in left atrial myxoma. For example, left atrial myxoma forms a round mass that almost always has a stalk attached to the interatrial septum near the margin of the fossa ovalis\(^3\). For this reason we were hard put to diagnose the condition as a left atrial myxoma, but, before surgery, a left atrial myxoma seemed the most likely owing to the frequency of occurrence.

Histopathologically, the mixture of two histological features, storiform and pleomorphic cellular patterns, is typical of a malignant fibrous histiocytoma\(^4\).\(^8\). Some mesenchymal sarcomas, however, are difficult to differentiate from this condition. Pleomorphic liposarcoma is probably the most difficult tumor to distinguish from

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malignant fibrous histiocytoma. The large pleomorphic giant cells in malignant fibrous histiocytoma often have a striking resemblance to lipoblasts. However, no lipoblasts of typical form and structure were observed in present materials except for the so called 'pseudolipoblasts' that are seen in malignant fibrous histiocytoma as result of a nonspecific vacuolar change. Most importantly, a storiform pattern is not found in liposarcoma.

Myxoid liposarcoma is easily separated from malignant fibrous histiocytoma since mitoses are rare in this form of liposarcoma and common on malignant fibrous histiocytoma. The syncytial arrangement and stellate configuration of stromal cells are quite different from the orientation found in malignant fibrous histiocytoma.

Pleomorphic rhabdomyosarcoma is frequently considered in the differential diagnosis of malignant fibrous histiocytoma because the pleomorphic giant cells in malignant fibrous histiocytoma have a granular, eosinophilic cytoplasm suggesting differentiation towards the muscle. Cross-striations, however, were not observed in our materials and it has been postulated that the storiform pattern is not seen in rhabdomyosarcoma.

Electron microscopy of the tissues showed that the basic cell types were histiocyte-like and fibroblast-like. There was no evidence to suggest an origin from cardiac muscle. These findings are consistent with the diagnosis of malignant fibrous histiocytoma.

Histologically, the structure of pericardium was preserved to a considerable extent. The tumor had not apparently infiltrated into the muscles of the left ventricle, right ventricle, or right atrium. The primary site of the tumor was probably the endocardium or epicardium of the left atrium.

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REFERENCES