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PRIMARY PLEOMORPHIC LIPOSARCOMA OF THE HEART AND BRENNER TUMOR IN THE OVARY: A CASE REPORT WITH AN ULTRASTRUCTURAL STUDY

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ABSTRACT

A 79-year-old female with primary liposarcoma of the heart, an extremely rare malignancy, and a right ovarian Brenner tumor was reported. Histological features of the sarcoma on the routine histological slides were so varied that it was necessary to differentiate whether the histology was that of malignant fibrous histiocytoma or pleomorphic rhabdomyosarcoma. Most of the tumor cells including fibroblastic and bizarre giant cells, however, were stained intensely with histochemical methods for lipids and conclusively diagnosed as pleomorphic liposarcoma. Many lipid droplets supporting the histological diagnosis were demonstrated in the cytoplasm of the tumor cell by a transmission and also a scanning electron microscope. Immunohistochemistry of the tumor tissue using antibodies against myoglobin, myosin, neuron specific enolase, alpha-1-antitrypsin, alpha-1-antichymotrypsin, and S-100 protein failed to detect specific immunoreactivities.

INTRODUCTION

Liposarcomas are uncommon neoplasms which principally occur in the retroperitoneum and lower extremities. They have also been found to arise in the abdomen, buttock, vulva, neck[3] and mediastinum.[12] Primary liposarcoma of the heart or epicardium, however, is extremely rare, and so far only 6 cases have been reported until

now.[1,2,4,9,10,14] Recently the current authors had a chance to examine an autopsy case with pleomorphic liposarcoma of the heart. The case also had a right ovarian Brenner tumor. This report deals with the first case having both cardiac liposarcoma and Brenner tumor, and the ultrastructural characteristics of the sarcoma cells.

Case Report

A 79-year-old woman was the case; her familial history was not relevant and her past history was as follows: at 40 years of age, appendectomy; at 70, left oophorectomy (disease unknown); and since 76 years of age arthropathia deformans of bilateral hip joints as a sequela of luxatio coxae.

She came down suddenly with dry cough about two months before admission and was treated with medication for a while, though not effectively. About one month later, dyspnea appeared and gradually worsened, and a "pressed feeling" in the epigastrium also developed. Chest x-ray film on this occasion revealed the enlargement of a cardiac shadow and an accumulation of bilateral pleural effusion. She was treated with digitalis glycosides and diuretics under the diagnosis of chronic congestive heart failure. Cardiac echogram at that time illustrated a paradoxical movement of ventricular septum, enlargement of the left atrium, left ventricle and aorta, and a massive accumulation of pericardial effusion. Afterwards, however, enlargement of the cardiac shadow on chest x-ray film became more prominent and pleural effusion did not subside. So, she was admitted to a hospital with chief complaint of dyspnea and "pressed feeling" in the epigastrium. Physical examination revealed pitting edema on legs but no lymph node swelling or hepatosplenomegaly. Laboratory data including urine and blood analysis, blood chemistry, and hepatic function tests were within normal limits. Blood pressure was 140/90 mmHg and a grade 2/6 systolic murmur was heard. ECG showed a pattern of ischemic changes. After admission, dyspnea became more pronounced and she was forced to be in orthopnea. Cardiac shadow on x-ray film also became more increased in size. Two days after admission, she died of cardiac failure.

Morphological Study

Autopsy was performed 2 hours after death. The heart was hypertrophic and weighed 540 g. The left pericardial cavity bulged with the accumulation of 300 ml of fresh blood. There was a firm tumor between the left atrium and pulmonary artery measuring approximately 4.0× 3.5× 3.0 cm. On being cut, the surface of the tumor tissue was whitish in color and parenchymatous without hemorrhage or degeneration. (Fig. 1) The tumor was relatively ill-defined and had invaded directly to the wall of the pulmonary artery and left atrium, and had also spread to surface of the left epicardium, forming several small hematomas on it. A hard, whitish tumor, 1.8 cm in diameter, was found in the right ovary. Bloody pleural effusion, right 300 ml and left 400 ml, was also noticed. The tissue blocks from the tumors and the other organs or tissues were fixed

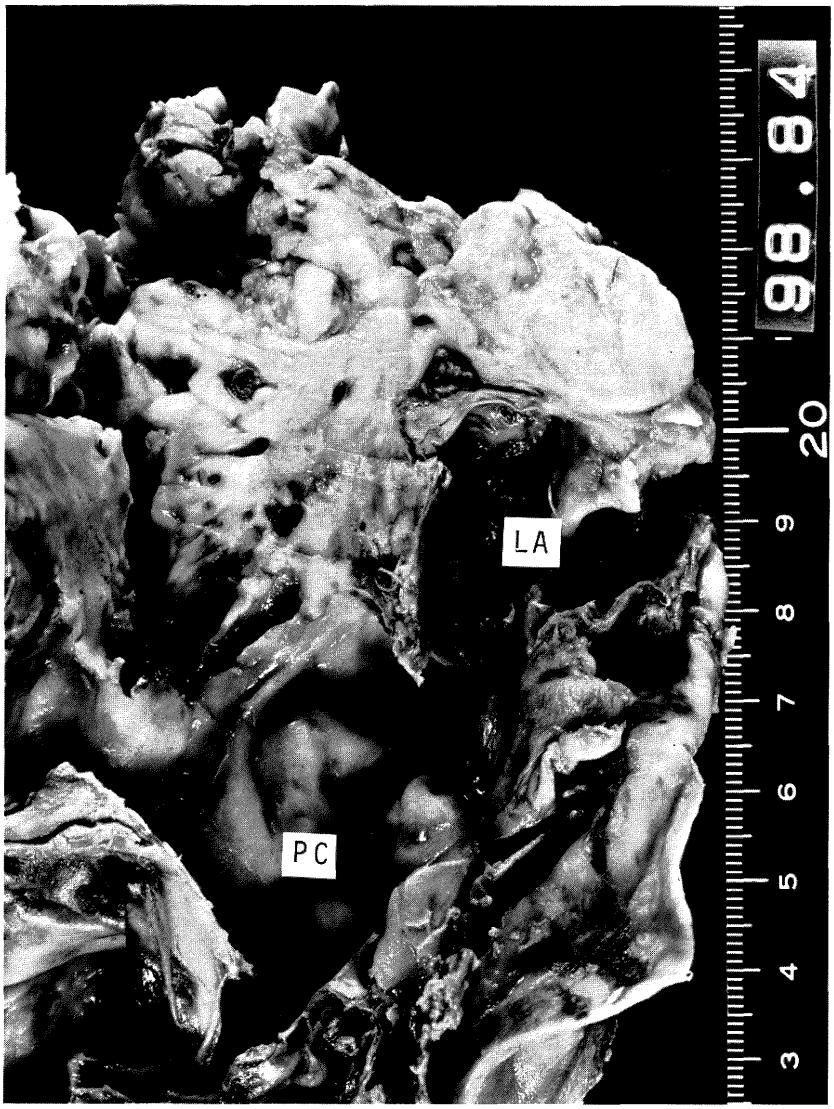

Fig. 1. Close up view of the cut surface of the tumor. Whitish firm tumor with relatively ill-defined margin and without hemorrhage or degeneration (LA: left atrium, PC: pericardial cavity opened).

in 10% formaldehyde solution and processed in the conventional manner for light microscopy. Several special stainings including periodic acid Schiff (PAS), diastase digested PAS, Mallory's phosphotungstic acid hematoxylin (PTAH), Weigert's method for elastic fibers, Mallory's method for collagen and alcian blue pH 2.5 method for mucosubstances were applied to the tumor tissue slides. Cryostat sections of the tumor tissue and, as a control, normal fat tissue were stained with several histochemical methods for lipids such as Sudan III, oil red O, Sudan black B and Nile blue.

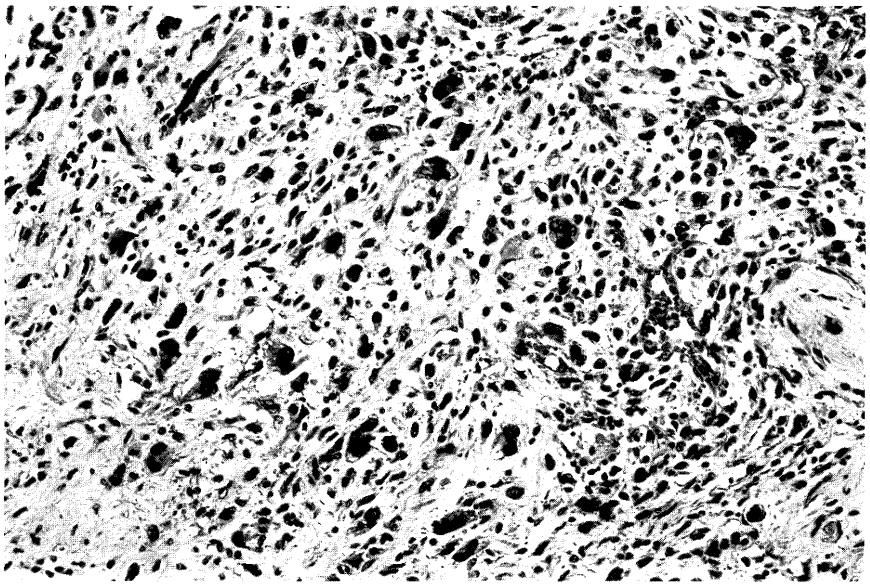

Fig. 2. Representative histological features of the tumor tissue show intermingled proliferation of many kinds of giant cells and fibroblastic cells.

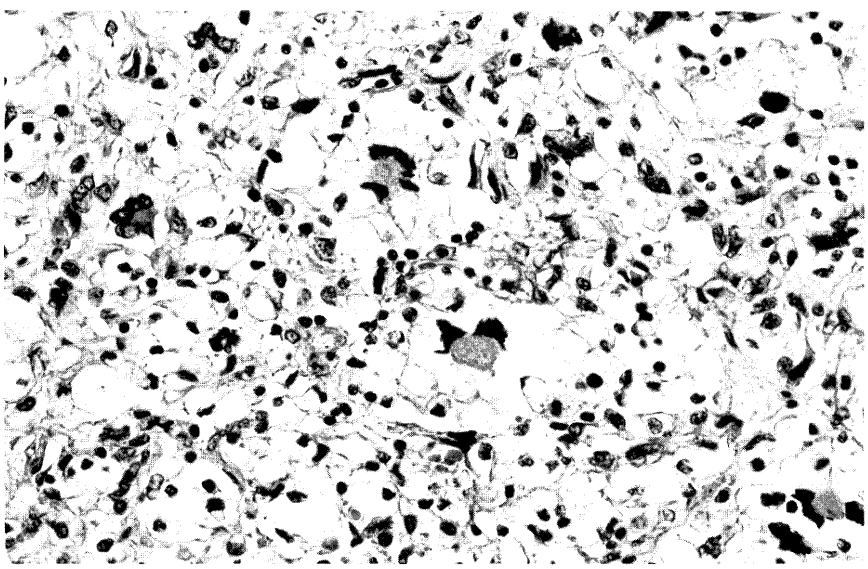

Fig. 3. A part of the tumor highly suggestive of liposarcoma including multivacuolated giant cells.

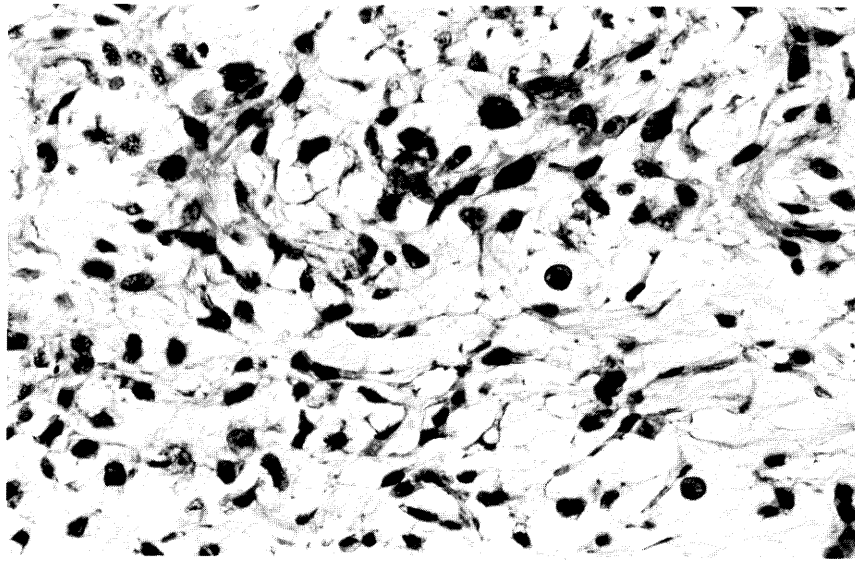

Fig. 4. Myxoid pattern in a limited area of the tumor.

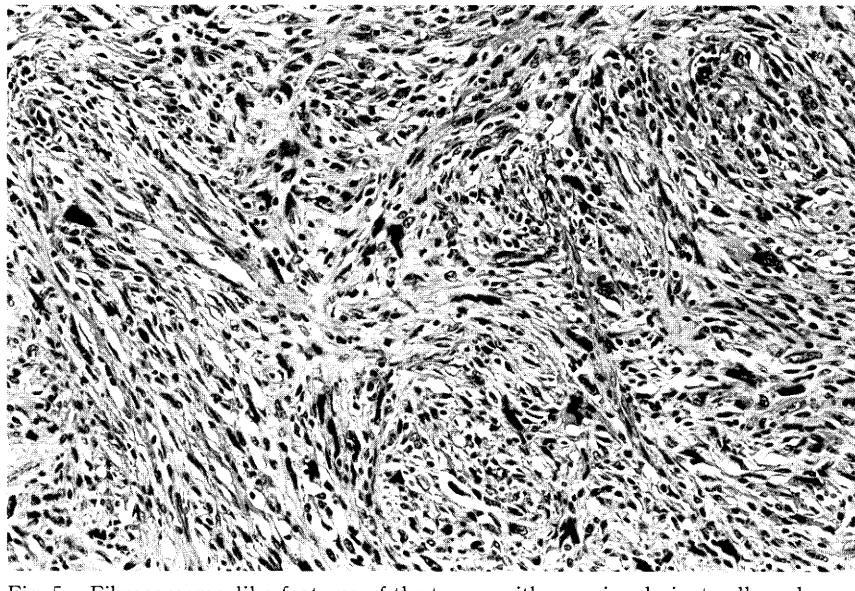

Fig. 5. Fibrosarcoma-like features of the tumor with occasional giant cells and vague storiform pattern.

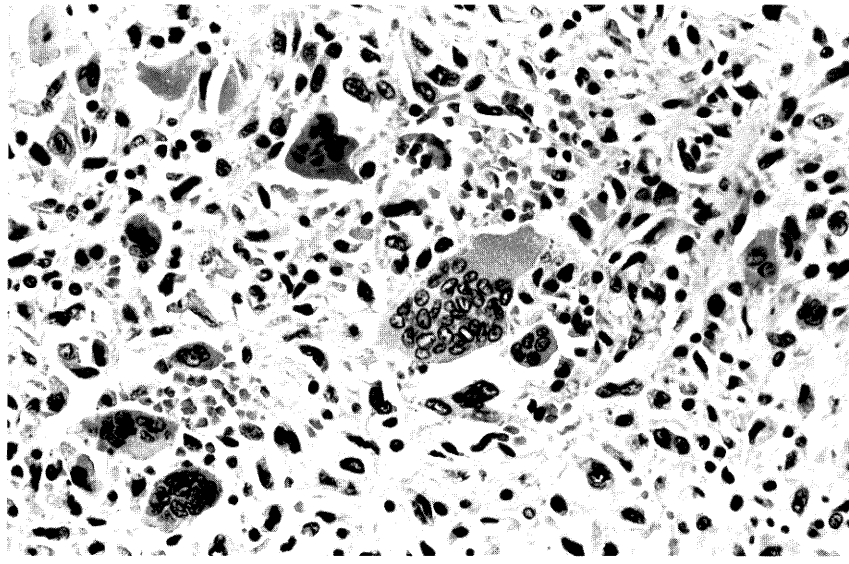

Fig. 6. Giant cells with broad cytoplasm and multiple non-atypical nuclei.

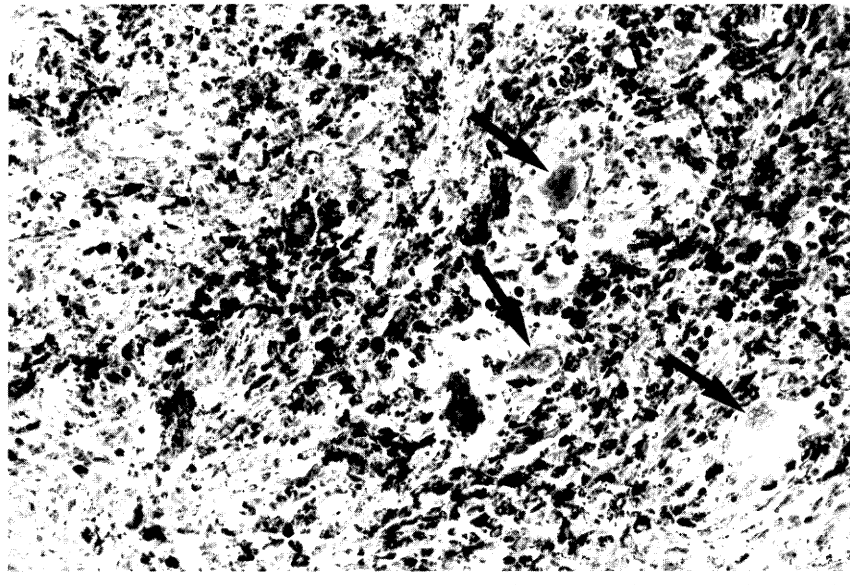

Fig. 7. Lipid staining of the tumor tissue. Many of proliferated cells including atypical giant cells and fibroblastic cells are stained intensely but non-atypical cells (arrows) are unstained (Sudan III, original magnification, ×100).

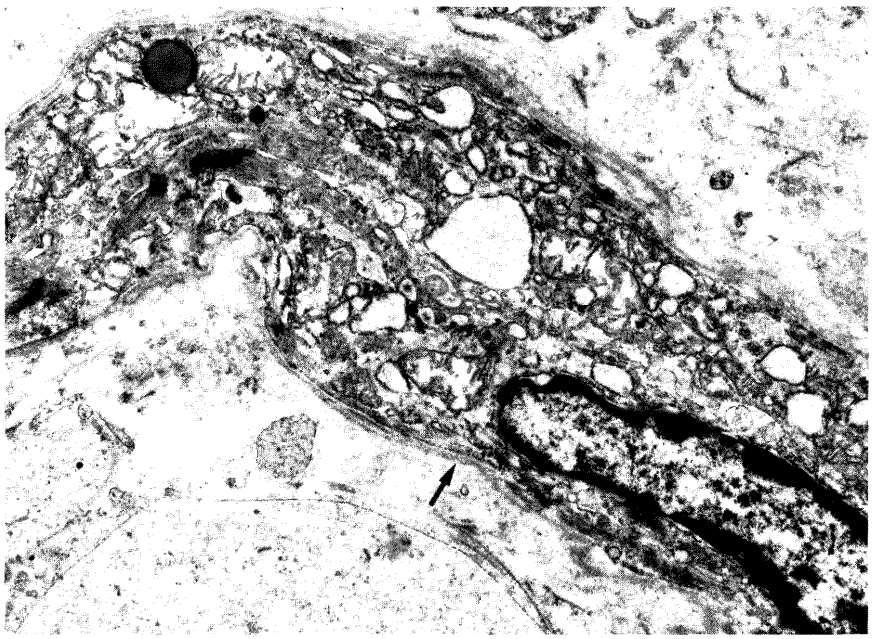

Fig. 8. A myofibroblastic cell characterized by dense patches and a basement membrane-like structure (arrow) in close association with the cell membrane (original magnification, ×7,000).

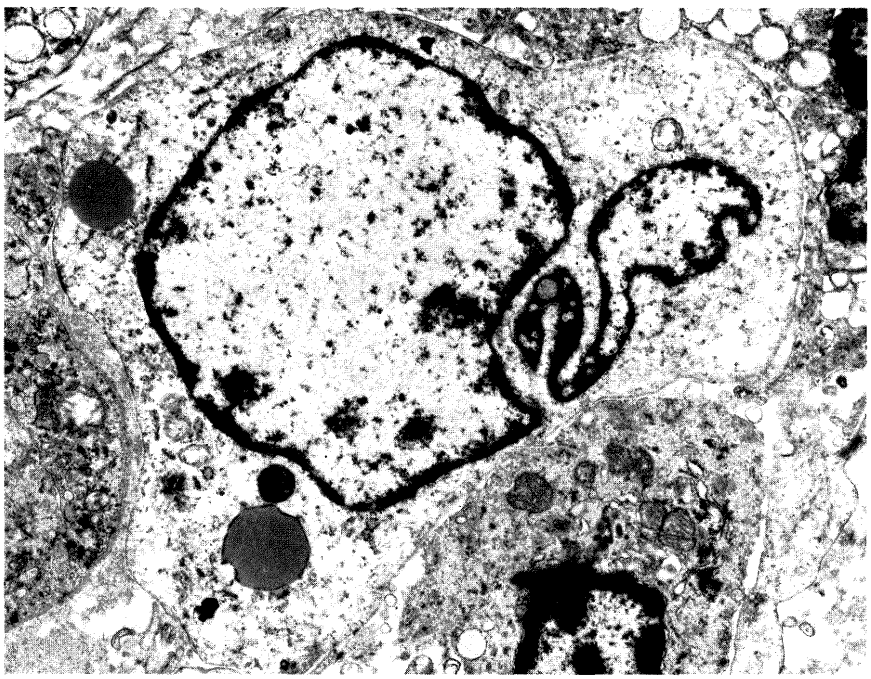

Fig. 9. A round primitive tumor cell with few cell organellae but two apparent lipid droplets (original magnification, ×7,000).

Immunohistochemical staining was done on the tumor tissue slides according to the peroxidase-antiperoxidase complex method. Antibodies used were as follows: anti-myoglobin (DAKO, Denmark), myosin (Transformation Res., Inc. USA), alpha-1-anti-trypsin (Behringwerke A. G. W., Germany), alpha-1-antichymotrypsin (DAKO), neuron specific enolase (IBL, Takasaki, Japan) and S-100 protein (IBL). A portion of the tumor was minced into small pieces and immediately fixed with 2.5% glutaraldehyde in 0.1 M phosphate buffer at pH 7.4, post-fixed with 1% osmium tetroxide in the same buffer, dehydrated and embedded in Epon 812. The ultrathin sections were stained with uranyl acetate and lead citrate, and examined in a Hitachi H-800 electron microscope (Hitachi Ltd., Tokyo). A portion of the tumor was also cut into small "twigs" measuring approximately 2 mm cube × 15 mm in length and fixed with 4% glutaraldehyde in the phosphate buffer, post-fixed with 1% osmium tetroxide, dehydrated through the graded series of ethanols, freeze-fractured, and soaked in isoamylacetate. The specimen, after this, was critical-point-dried, evaporation-coated with gold palladium, and observed in a field emission scanning electron microscope (Hitachi S450LB) under accelerating voltage of 20KV.

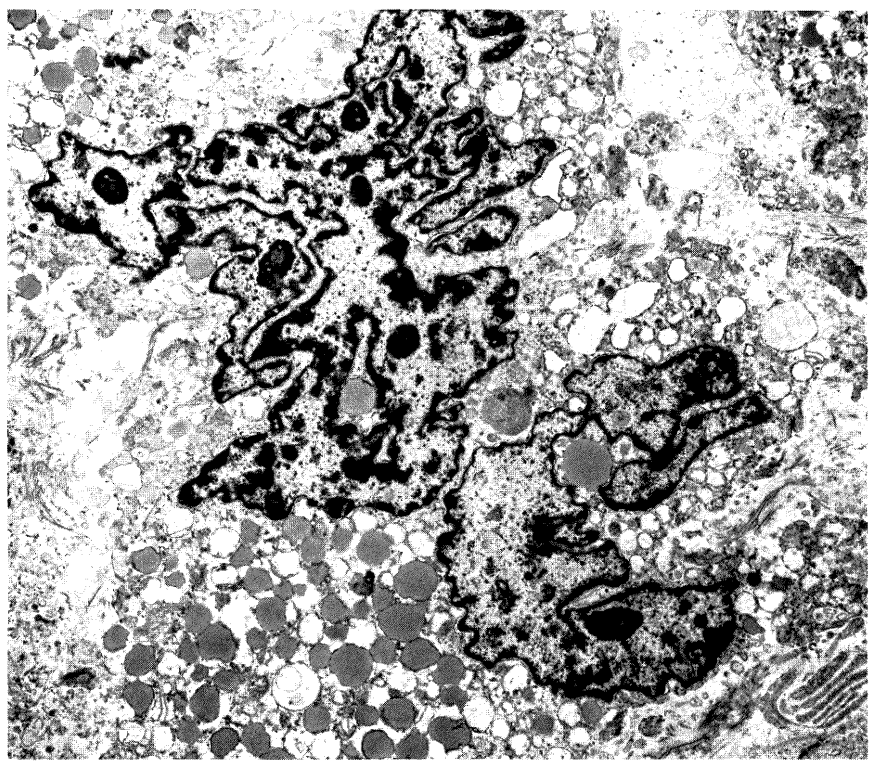

Fig. 10. An atypical giant cell. Nuclei are very irregular in shape and have relatively abundant heterochromatins. Cytoplasm is filled with numerous lipid droplets (original magnification, ×2,000).

RESULTS

The histology of the cardiac tumor exhibited various morphological features. There were mainly pleomorphic tumor cells with bizarre giant cells (Fig. 2), but a limited area of foamy cells with small round nuclei including multivacuolated giant cells (Fig. 3), a part of myxoid region (Fig. 4), and fibrosarcoma-like region (Fig. 5) were also observed. Giant cells were generally multinucleated with nuclear atypia or pyknosis. They showed marked pleomorphism with eosinophilic cytoplasm to greatly varying degrees. Differing from these atypical giant cells, another type of giant cells which had numerous small non-atypical nuclei was observed mainly in the hemorrhagic region or superficial layer of the tumor tissue which had invaded to the epicardium (Fig. 6). The main histological features suggested those of plemorphic rhabdomyosarcoma or malignant fibrous histiocytoma. Glycogen granules or striation, however, was not demonstrated by diastase-PAS or PTAH staining. Immunohistochemistry failed to detect myoglobin, myosin, neuron specific enolase, alpha-1-antitrypsin, alpha-1-antichymotrypsin, and S-100 protein-like immunoreactivities. On the other hand, most of tumor cells, including atypical giant cells, though not non-atypical giant ones, were intensely stained with every histochemical method used for lipids (Fig. 7). Consequently the cardiac tumor was diagnosed as pleomorphic liposarcoma originated from the epicardial fat tissue. No distant or nodal metastasis was observed.

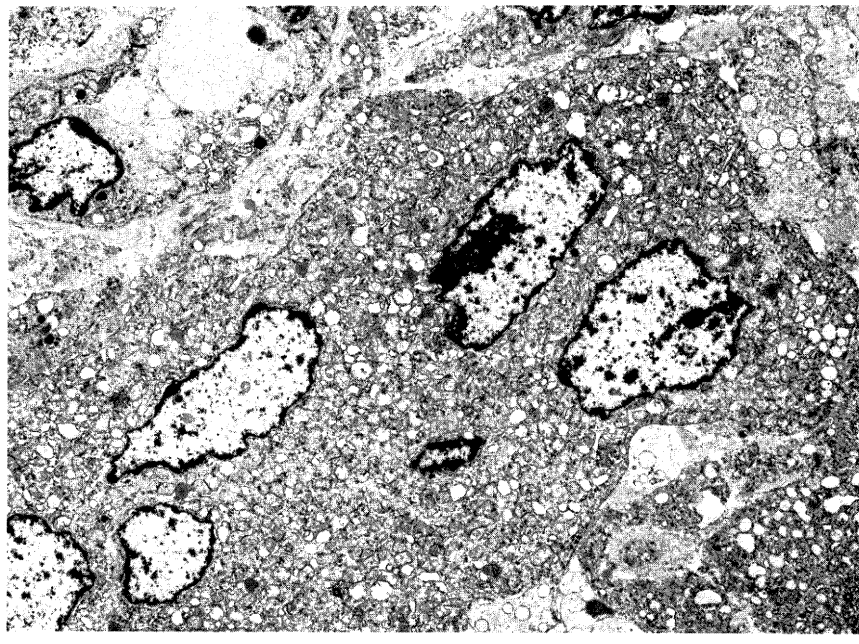

Fig. 11. A non-atypical giant cell. Nuclear irregularity is absent, and low content of heterochromatins. Cytoplaplasm is filled with mitochondria and vesicles but lipid droplets are very few in it (original magnification, ×2,000).

The transmisson electron microscopic examination revealed several types of tumor cells. In an area with abundant collagen fibers, fibroblastic and myofibroblastic tumor cells were observed. The latter had characteristic dense patches in the cytoplasm, especially at the cell margin, and a basement membrane-like structure was associated with these types of tumor cells (Fig. 8). Desmosome-like junctional complex at the membrane was also infrequently noticed between fibro- and myofibroblastic tumor cells. A round tumor cell resembled to a primitive mesenchymal cell was another representative type of tumor cell (Fig. 9). Supporting the histological diagnosis, most of tumor cells contained lipid droplets of various sizes and numbers irrespective of cell types. Giant cells with atypical nuclei had markedly indented nuclei with heterochromatins mainly associated with nuclear membrane. The cytoplasm was rich in cell organellae and filled with lipid droplets (Fig. 10). A giant cell with non-atypical nuclei, however, had smooth contoured nuclei with a few heterochromatins. The cytoplasma was very broad and contained numerous mitochondria and vesicles but few lipid droplets (Fig. 11).

The scanning electron microscopy revealed irregularly oriented bundles of collagen fibers in the fibrosarcoma-like area (Fig. 12). Close up view showed that a tumor cell embedded in collagen bundles had many hemispherical lipid droplets in the cytoplasm

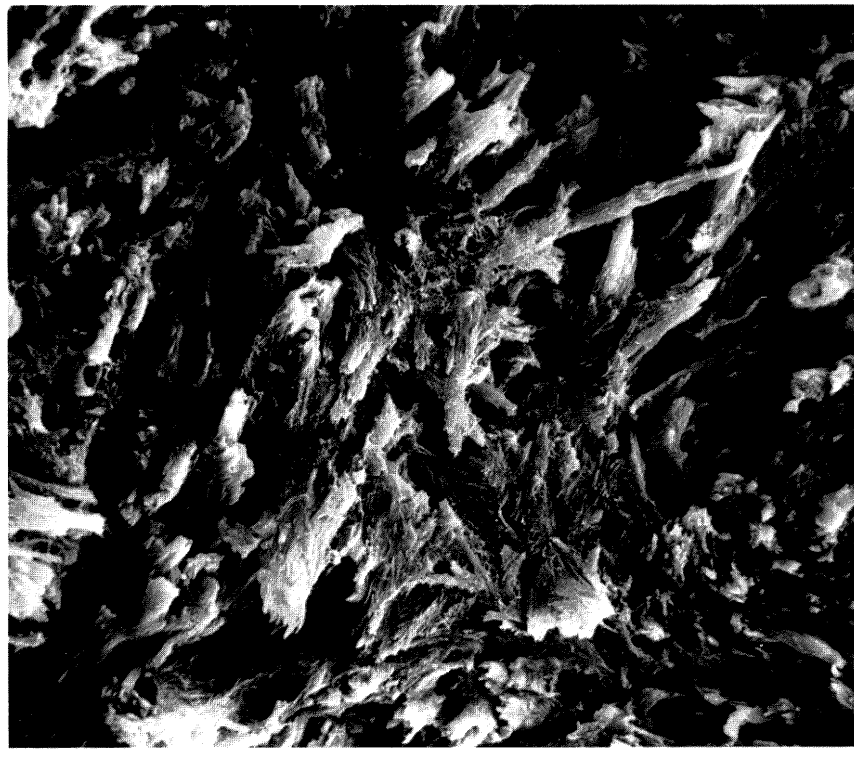

Fig. 12. Scanning electron micrograph of fibrosarcoma-like lesion of the tumor. Bundles of collagen fibers run at random (original magnification, ×700).

Fig. 13. Scanning electron micrograph of fibrosarcoma-like lesion of the tumor on the fractured-surface. There are many spherical and hemispherical structures suggestive of lipid droplets in the cytoplasm of the tumor cell (original magnification, ×5,000).

(Fig. 13). On the fractured surface of a round tumor cell, there were apparent nuclear contour, and several round concaves in the cytoplasm suggestive of lipid droplets (Fig. 14).

Histologically, the right ovarian neoplasm was a Brenner tumor (Fig. 15).

DISCUSSION

Primary neoplasms of the heart and epicardium are extremely rare, with an incidence between 0.0017 and 0.028 per cent in reported or collected autopsy series.[7] Primary malignant ones are even more infrequent, and in the literature only 6 cases with cardiac liposarcoma have been reported so far. This case is the 7th one. Brenner tumor in the right ovary may be an accidental association but no case with such a second tumor has been described.

Histologically liposarcomas are subdivided into five subtypes;[6] myxoid, round cell, well differentiated, pleomorphic, and mixed. The liposarcoma presented here is categorized as a pleomorphic type, since the tumor cells showed a wide range of morphological features including a number of bizarre giant cells, and the myxoid pattern was limited to

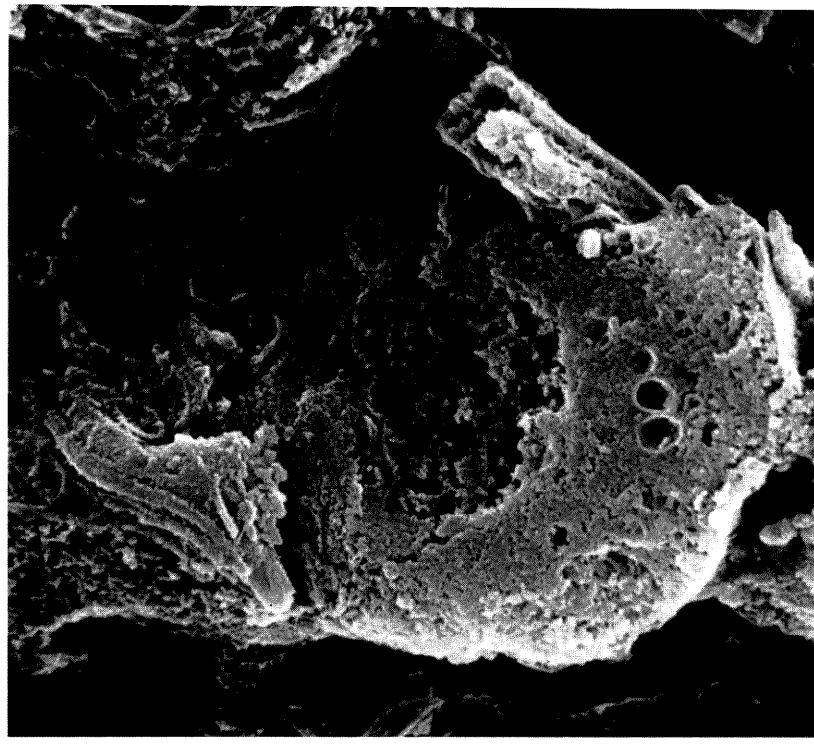

Fig. 14. Fractured surface of a round tumor cell. There are nuclear contour and round concaves suggestive of lipid droplets in the cytoplasm (original maginification, ×5,000).

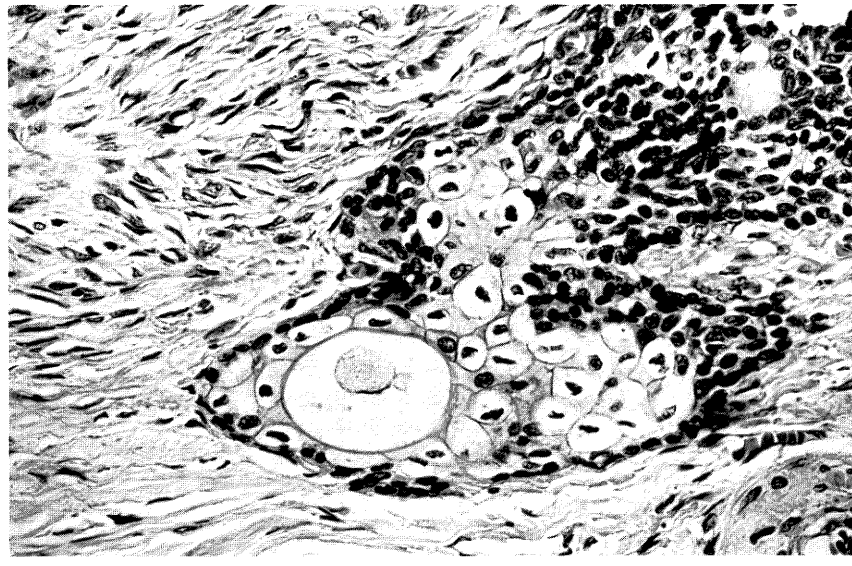

Fig. 15. Histology of the ovarian neoplasm showing a typical Brenner tumor.

a small area. The morphological features of this case were far more polymorphous than those of usual pleomorphic liposarcomas described in the literature. Therefore, it was necessary to differentiate whether it was pleomorphic rhabdomyosarcoma or malignant fibrous histiocytoma. Histochemical methods for lipids, however, dissolved this problem and ultrastructures of the tumor cells provided further evidence that they were fat cells in nature. Immunoreactivities of alpha-1-antitrypsin or alpha-1-antichymotrypsin, good markers of histiocytes,[5] were not demonstrated in any sarcoma cells including multinucleated giant cells. This fact excludes the possibility that the tumor cells were histiocytic in origin. Many fat droplets were clearly demonssrated in the cytoplasm by a transmission electron microscope, while numerous small membrane-bound vesicles in pleomorphic liposarcoma, distended cisternae containing an electron dense substance in myxoid type described by Kalderon and Fetheire,[8] and abundant glycogen granules in well differentiated type[13] were not found in this case.

Scanning electron micrographs illustrated three-dimensional architecture of the tumor tissue and also revealed spherical lipid droplets in the cytoplasm of the tumor cell. A scanning electron microscope, therefore, may provide useful information on tumor pathology when applied to selected cases.

The tumor cells might originate from fibroblastic pre-adipocytes and/or mesenchymal cells, judging from ultrastructural characteristics of the most primitive tumor cell. This hypothesis, however, remains to be substantiated. Circumstantial evidence of *in vitro* differentiation of 3T3-L2 fibroblasts into adipose cell,[11] nevertheless, supports in part our hypothesis.

Giant cells with nonatypical numerous nuclei were also frequently observed in this case. Their nature may not be neoplastic but reactive, since they were not stained with lipid staining and did not show any transition form from the sarcoma cells or atypical giant cells.

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