PRIMARY ANGIOSARCOMA OF THE HEART: AN AUTOPSY CASE REPORT WITH IMMUNOHISTOCHEMICAL OBSERVATIONS

HIROSHI MARUYAMA[1], YOSHIHIKO YOKOSE[1], EISAKU KOBAYASHI[1], TAKEHIRO ENDO[1], TOSHIFUMI TSUJIUCHI[1], MASAHIRO TSUTSUMI[1], DAI NAKAE[1], KIYOSHI NISHIMINE[2], SOICHIRO KITAMURA[3] and YOICHI KONISHI[1]

[1] *Department of Oncological Pathology, Cancer Center, Nara Medical University*
[2] *Department of Oncoradiology, Nara Medical University*
[3] *Third Department of Surgery, Nara Medical University*

Received January 31, 1995

Abstract: An autopsy case of primary angiosarcoma of the heart is reported. The patient was a 24 year old male and developed a tumor mass in the right atrium with a first symptom of pericardial effusion. As a result of intensive therapies including surgical operation and radiation therapy, the patient survived just 2 years after his first visit, and died of the rupture of the multiple metastatic tumors in the liver. The tumor cells of the present case were mainly composed of three types: (1) endothelial cells, (2) spindle cells and (3) epithelioid cells. Endothelial cells in the cavernous area showed positive reactivity to antibodies for Ulex europaeus agglutinin 1 (UEA-1), factor VIII-related antigen (F VIII), CD 31, BNH 9 (a new blood group-related antigen) and vimentin (Vim). Spindle tumor cells reacted to antibodies for CD 31, BNH 9 and Vim. However, epithelioid cells reacted only to Vim. The positive rate of proliferating cell nuclear antigen (PCNA) in spindle tumor cells showed a higher tendency than that in endothelial tumor cells.

Index Terms

angiosarcoma, heart, immunohistochemistry

INTRODUCTION

Primary angiosarcoma of the heart is rare, but the most frequently occurring primary cardiac sarcoma (7.3 %), followed by rhabdomyosarcoma and mesothelioma according to 533 cases in the AFIP Series. Cardiac angiosarcoma has a very low incidence of 0.0017 % to 0.28 % in autopsy series[1]. In general, primary angiosarcoma occurs in males more frequently than in females (a ratio of 2 to 3 : 1). Average age of the patients is between 30 and 40 years. The tumors are most commonly located in the right atrium, followed by the left atrium and ventricles[2]. In most cases, the tumors have already extended widely at the time of discovery into pericardial, vena calal, and valvular invasion, suggesting advanced cases and short survival. Although these tumors are often histologically subclassified into malignant hemangioendothelioma or hemangiopericytoma, their clinical course and prognosis are described as identical[1]. The purpose of this report is to describe histological and immunohistochemical features of primary angiosarcoma of the heart occurring in a 24-year-old male.

MATERIALS AND METHODS

Deparffinized sections from paraffin-embedded tumor tissues were stained with hematoxylin and eosin (HE), silver imprenation, Masson trichrome and PAS reaction. Immunohistochemical examinations of the tumor were also performed on the paraffinembedded, formalin-fixed tissue sections using the ABC method. The primary antibodies were biotinylated Ulex europaeus agglutinin I (UEA-I, 1 : 400), anti-factor VIII-related antigen antibody (anti-FVIII RAg, 1 : 50), monoclonal mouse anti-swine vimentin antibody (anti-Vim, 1 : 25), monoclonal mouse anti-human JC 70 antibody (anti CD 31, 1 : 70)[3], monoclonal mouse antihuman BNH 9 (anti-blood group-related Ag, M 7017, undiluted)[4], anti-smooth muscle actin antibody (anti SMAC, 1 : 100) and anti-proliferating cell nuclear antigen antibody (anti PCNA, ×100), which were obtained from Dakopatts, Kyoto. The antibodies of CD 31 and BNH 9 are reported to be possibly useful markers for malignant vascular tumors[3,4].

The positive rate of PCNA was counted each 200 to 300 cells in five visual fields (objective magnification ×200).

CLINCAL FINDINGS

A 24-year-old Japanese, who had smoked 20 cigarettes per day, complained of left chest pain for 3 months before his admission to our hospital in June, 1986. On admission, he had bloody effusions in the left pleural (about 1000 ml) and pericadial (250 ml) cavities. The cytologic examinations of the pericardial and pleural effusions were negative (Papanicolaou class I). Laboratory data showed no abnormality in blood and serum biochemical tests including liver and kidney function tests. Serum Creactive protein was negative and blood sedimentation rate was 5/10. The electrocardiogram showed a two-peak pattern of P-wave in leads II, aVr and V 2-V 6, and the chest X-ray film revealed right atrial enlargement. The echocardiogram and dynamic CT scan (Fig. 1) also revealed a widespread mass from the anterior wall to the right lateral wall in the right atrium, indicating thrombosis or a tumor.

In his past history, he suffered from acute hepatitis (A-type) at the age of 18. In his family history, his father suffered from hyperthyroidism, but his immediate relatives did not have cadiac diseases.

A surgical operation was performed in our hospital under the suspicion of a right atrial tumor. The pericardium was found to be tightly adhesive to the heart because of post-pericarditis, and the right atrium appeared to be protruded outside. Since the right atrial mass had extensively invaded the pericardial wall, it was removed together with the atrial wall, suggesting a malignant tumor. Although the pathological diagnosis was angiosarcoma, postoperative chemotherapy or radiotherapy were not performed. Seven months after the surgical operation, however, recurrence of the original tumor in the right atrium and metastatic tumors in the liver were found by a whole body CT scan. Therefore, the patient has readmitted to our hospital and treated with radiation therapy. Simultaneously, multiple hepatic tumors were treated by a double application of the transcathetral arterial embolization technique (TAE) in combination with various antioncologic agents (15 mg Lipiodol, 30 mg Adriamycin, 50 mg Cisplatin and 10 mg Mitomycin C), followed by a single therapy of percutaneous ethanol infusion technique (PEIT), resulting in decreases of the multiple metastatic liver tumors. The

recurrent tumors of the right atrium were also treated with radiation therapy (Liniac, 30 Gy). In spite of the combination of three therapeutic approaches including surgical resection, chemotherapy and radiation therapy for a total of 8 months, he had progressive metastatic liver tumors and died from rupture of liver tumors approximately two years after his first symptoms.

PATHOLOGICAL FINDINGS

The surgically-resected tumor was grossly ill-margined, soft and dark-reddish with expensive hemorrhage and necrosis. Microscopically, the tumor was composed of small vascular spaces lined by spindle-shaped cells with some mitoses (0-2/HPF) and diagnosed as well differentiated angiosarcoma (Fig. 2).

At autopsy, three cardiac tumors were grossly confirmed at the right atrium (30×25×20 mm), right ventricle and left atrium, without that of the left ventricle (Fig. 3). The heart weighed 200 g. Histologically, the right atrial tumor showed a nodular arrangement from myocardium to pericardium (Fig. 4), and the spindle tumor cells formed slitlike vascular spaces (Fig. 4 b). With reticulin staining, the tumor showed clear anastomosing vascular channels. The histology of the left atrial tumor revealed capillary vessel neoworks (Fig. 5). Bloody ascites (1100 ml) was coagulated because of rupture from metastatic liver tumors. The liver weighed 2100 g and was diffusely occupied by multiple black-colored metastatic nodules (Fig. 6), histologically observed as large dilated vascular channels with spindle tumor cells (Fig. 7).

IMMUNOHISTOCHEMISTRY

Antibodies for UEA-1, FVIIIRAg, CD 31, BNH 9, SMAC, Vim and PCNA were immunohistochemically examined (Table 1). Antibodies for UEA-1 and FVIIIRAg were demonstrated within the endothelial cells forming the cavernous spaces but were not observed in the spindle tumor cells. Antibodies for CD 31 and BNH 9 were positively observed in both cavernous areas (Fig. 8 a) and spindle cell nests (Fig. 8 b). Epithelioid tumor cells were negative to antibodies for CD 31 and BNH 9. All tumor cells were positive to antibodies for Vim. Positive rates of PCNA were about 15 % in spindle cell areas and about 7 % in cavernous areas.

Table 1. Immunohistochemical results observed in angiosarcoma case

	Endothelial cells in cavernous area	Spindle cells in Solid area	Epithelioid cells
UEA-1	+	−	−
FVIII	+	−	−
CD31	+	+	−
BNH9	+	+	−
SMAC	−	−	−
Vim	+	+	+
PCNA count	7.0±3.2	14.6±2.5	——

DISCUSSION

The pathological features of the present case were consistent with primary angiosarcoma (subclassified as malignant hemangioendothelioma) of the heart supported by immunohistochemical examination. As described in the literature[2,5-7], immunostaining reactivity of FVIIIRAg and UEA-1 for endothelial cell surface substances is known to be often very weak or negative on paraffin sections of formaldehyde-fixed tissues in angiosarcoma, because of the dedifferentiation of the malignant tumor. In the present case, tumor cells that made cavernous areas were positive for antibodies for UEA-1 and FVIIIRAg, but spindle tumor cell areas were negative for those. However, spindle tumor cells of this cardiac sarcoma were positive to new monoclonal antibodies, for CD 31 and BNH 9. This result suggests that spindle tumor cells might be more differentiated to endothelial cells from primitive mesenchmal cells. Although the present case was first found to have pericardial effusion and the space occupying lesion of the right atrium, relatively prolonged survival (2 years) was achieved by using a combination of three intensive therapeutics. At last, the patient died from rupture of the metastatic liver tumors.

Since Redtenbacher reporoed the first case of primary cardiac angintarcoma in 1889[8], at last 150 cases of primary cardiac angiosarcoma in one century have been reported in the foreign literature[6] and about 40 cases in Japan[9]. According to their reports[6,7], the patients ranged from 12 to 70 years old with a mean age of [42,10] ; the cited clinical diagnosis was frequently heart failure, pericarditis, or pulmonary diseases[11], but only 8 cases were diagnosed as cardiac tumor before death. The primary tumor site was the right atrium followed by the pericardium, left atrium and right vetricle[12]. Although the survival time was below 9 months in 88 % of the reported cases, 34 to 36 months-duration of long survival has been described[13,14].

It has already been indicated that three valuable histologic features of angiosarcoma are anastomosing vascular channeles, foci of endothelial tufting and areas of spindle cell formation[12]. In the present case, the spindle cell nests, cavernous type proliferation and papillary proliferation (tufting-like) were confirmed (Figs. 4 a, 4 b, 5, 7).

It has been reported that the common sites of metastases from cardiac angiosarcomas in autopsy cases were lungs, liver, brain, bone, and lymph nodes[6,9]. Previously, an autopsy case of a 30-year-old housewife with malignant hemangioendothelioma of the heart was reported with leukemoid reaction and anemia[15]. That patient was first found by pericardial effusion, and surgical operation was undertaken but she sied of pulmonary complication about 1 mouth after the surgery. In our case, the hematologic disorders associated with angiorarcoma were not found, but a end stage anemia was observed. The diagnosis against cardiac angiosarcoma is important in differentiating bening lesions of hemangioma and myxoma[16], and malignant lesions of Kaposi's sarcoma and metastatic cancer etc. In our case, the resected tumor of the right atrium was histologically diagnosed as angiosarcoma because of the atypical spindle tumor cells with slit-like blood vessels and the surgically unresectable tumor. Better prognosis can be expected recently through earlier diagnosis and surgery. We would stress that immunohistochemical examinitions, in addition to histological observation, are very helpful for confirning various histologic features of cardiac angiosarcoma.

ACKNOWLEDGMENTS

The authors are grateful to Dr. Yoichi Tani, Dako Japan Co. Ltd., Kyoto for his excellent advice, and also to Mrs. Hiroko Megumi for her help in preparing manuscript.

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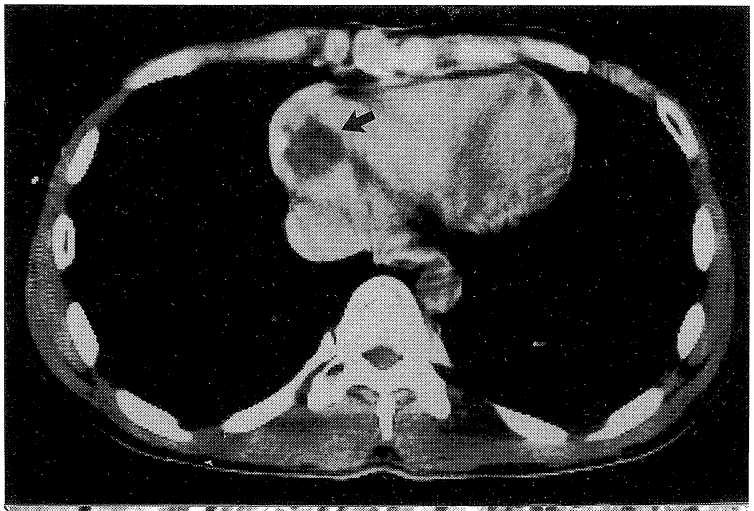
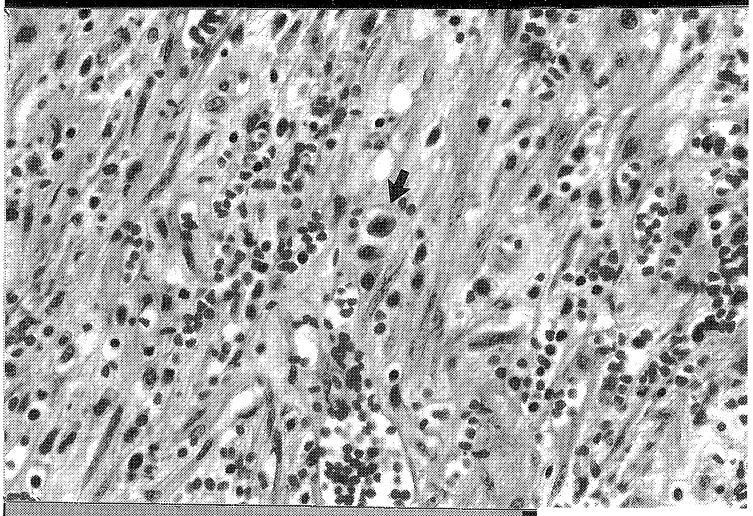


Fig. 1



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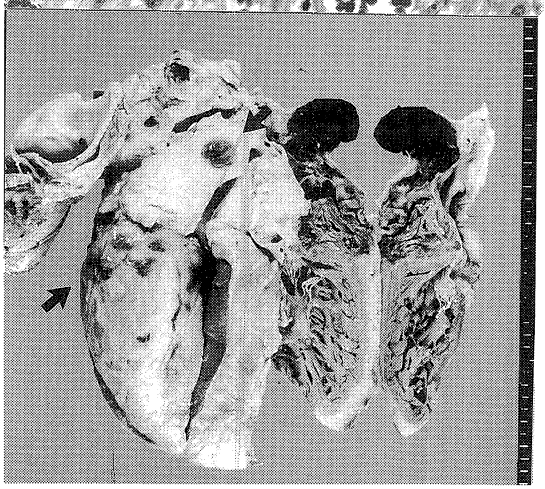

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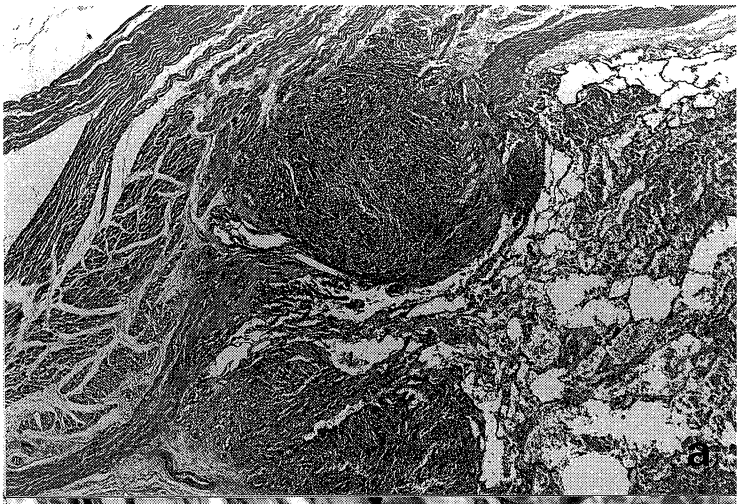
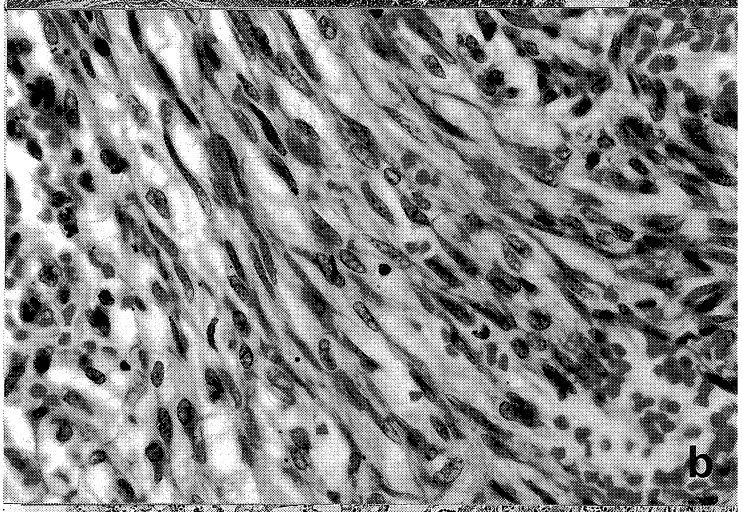


Fig. 4a



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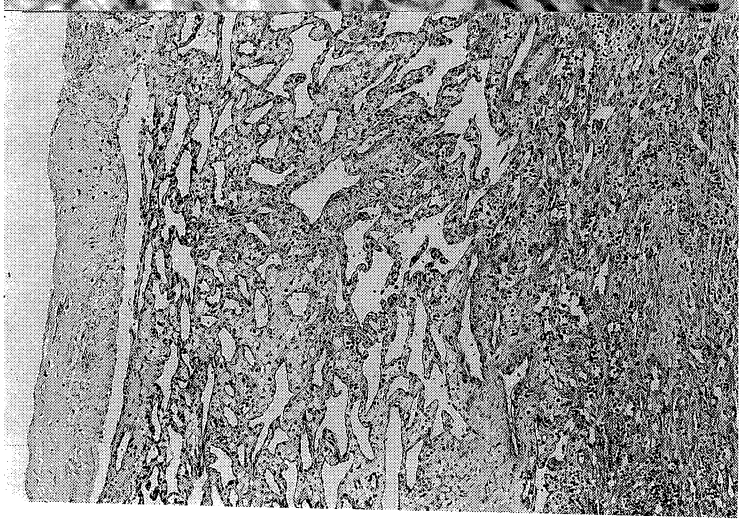
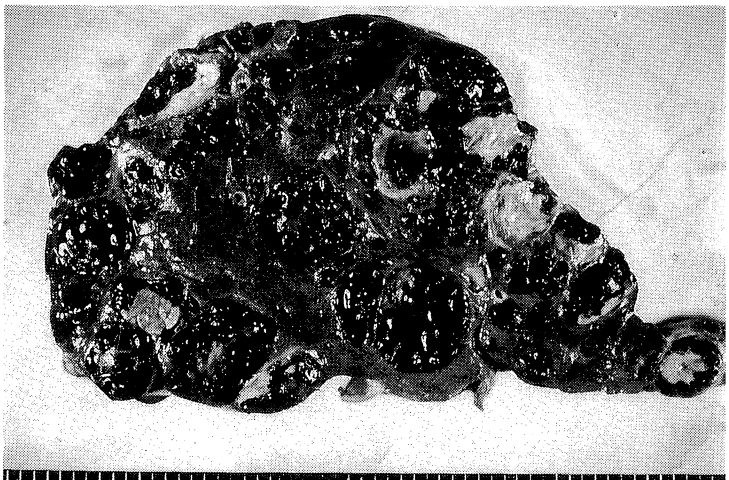


Fig. 5



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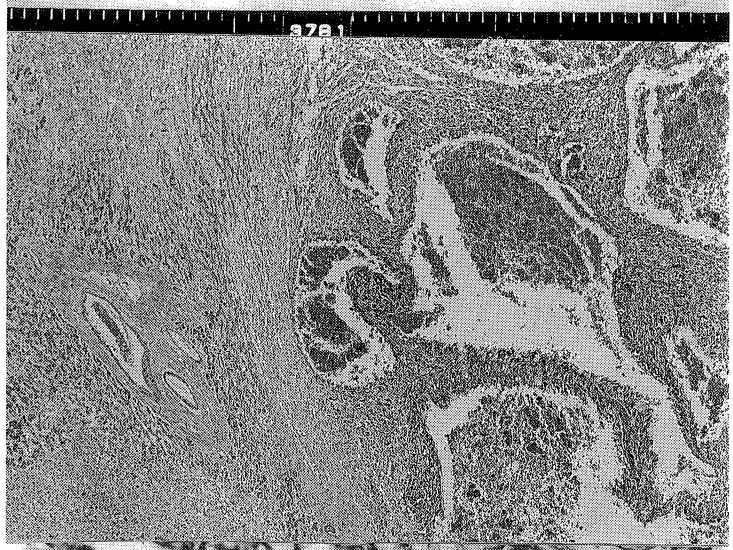

Fig. 7

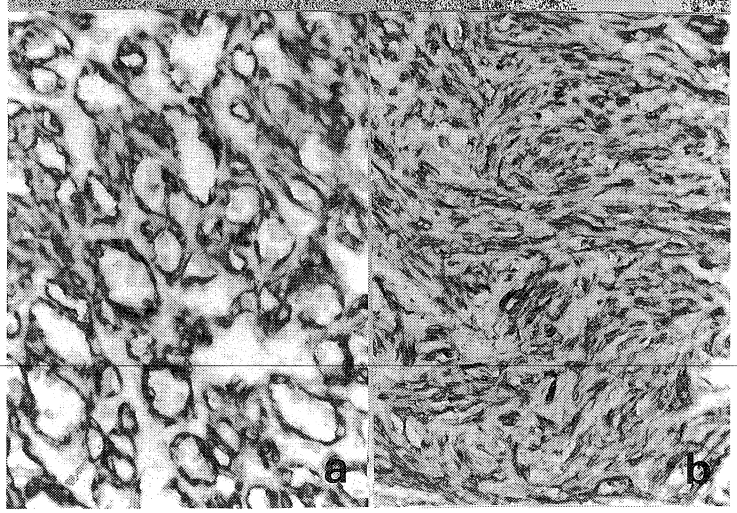

Fig. 8a　　Fig. 8b

Fig. 1. CT scan of the heart showed irregular low density area (arrow) at right atrium, suggesting a tumor mass.

Fig. 2. Histologically, the surgically resected tumor was composed of spindle-shaped cells with small vessels. A few mitoses (arrow) were observed. (HE, x100)

Fig. 3. Gross appearance of the heart at autopsy showed black-colored mass at right atrium, and several black spots (arrows) were observed in left atrium and right ventricle.

Fig. 4a. Histologically, the right atrial tumor was composed of spindle cell bundles in myocardium to pericardium. (HE, x20)

Fig. 4b. At higher magnification, the spindle tumor cells of the right atrial tumor formed slit-like vessels. (HE, x200)

Fig. 5. The tumor of left atrial tumr showed multiple neotworks of small vessels. (HE, x100)

Fig. 6. Grossly, multiple metastatic liver tumors were observed in black-reddish color.

Fig. 7. Histologically, the liver tumor showed large blood lakes lined by spindle-shaped tumor cells. (HE, x40)

Fig. 8a. Immunohistochemically, endothelial tumor cells in cavernous area were positive for CD31. (ABC, x100)

Fig. 8b. Immunohistchemically, spindle-shaped tumor cells were positive for BNH 9. (ABC, x100)