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An Autopsy Case of Pleomorphic Leiomyosarcoma arising from the Uterus

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A 49-year-old female patient was referred to this hospital due to uterine tumor. Needle biopsy of the uterine body was done after admission which suggested MFH (malignant fibrous histiocytoma) or poorly differentiated adenocarcinoma. The patient died after 11 days of admission before doing any surgical treatment for the tumor. Autopsy disclosed an adult head-sized pelvic tumor mass with multiple metastasis in lung, peritoneum and intestine. We confirmed the diagnosis of the present case as pleomorphic leiomyosarcoma by immunohistochemical study and electron microscopy in addition to routine light microscopy. The DNA distribution pattern of the tumor was determined by cytofluorometry and it was aneuploidy. The case report is presented with histological, immunohistochemical, electron microscopical, and cytofluorometrical study herein.

INTRODUCTION

Leiomyosarcoma (LMS) is a rare malignant tumor of the uterus[1,2]. It accounts for about 30 % of the uterine sarcoma and stand next to malignant müllerian mixed tumor[3]. LMS is usually accompanied with leiomyoma but only 0.49 % of all uterine leiomyoma is accompanied with LMS[4]. Malignant transformation of leiomyoma has not been proved yet[5]. Due to lack of universally accepted standard pathological criteria, the diagnosis is mainly based on hypercellularity, degree of nuclear atypia, and number of mitotic figures. Histologically, most of the uterine LMS are spindle cell tumor with numerous mitotic figures and high cellularity, some have an epitheloid or pleomorphic appearance[6]. Histologically, in our case, the tumor was composed of pleomorphic cells. We performed electron microscopical and immunohistochemical study in addition to routine histopathology for diagnosing the present case. We also carried out cytofluorometrical study of nuclear content and ploidy pattern of the tumor cells to characterize its biological behavior.

CASE HISTORY

A 49-year-old nullipara female patient was admitted to this hospital due to uterine tumor. She was a housewife and had history of leiomyoma of the uterus from the age of 29. No medical or surgical treatment was done for that leiomyoma, and gradually she became anemic due to hypermenorrhea and dysmenorrhea. She had no other significant health problems and her family history was also nothing contributory.

History of present illness : The patient felt abdominal distention in May 1991. It gradually increased around October 1991 and she felt dyspnea at work. In December of the same year, dyspnea became more worsen and it started to occur even at rest. Lately she became bed ridden and then in February 1992 she visited a doctor for the first time. She was found to have a large pelvic tumor with multiple lung metastasis and she was then referred to the University Hospital. After admission general management was done to relieve dyspnea and improve her general condition. But her condition did not improve and she died after 11 days of admission.

PATHOLOGICAL OBSERVATION

Laboratory investigations : Complete laboratory data is given in Table 1. Her WBC count was 45,500/mm^3 with eosinophillia (28 %). Hypoproteinemia, hypoglycemia and increased level of lactic acid dehydogenase (LDH) were observed.

Cytology : Cytology was done with the touch smear of the biopsy specimen. Atypical cells with high N/C ratio containing large pleomorphic and hyperchromatic nuclei were observed in cytological specimen. Bizarre multinucleated giant cells were also seen. Cytological diagnosis of the tumor was done as class V (Fig. 1).

Biopsy : Atypical cells were noted in the needle biopsy specimen of the uterine body. The pleomorphic round or

TABLE : 1

Laboratory investigations:

RBC : 450x104/mm^3
Hb%: 11.5 g/dl
PLT : 39.1x104/mm^3

Biochemistry :

Total protein	:	5.7g/dl	Electrolites	
Glucose	:	64 mg/dl	Na	140 mEg/l
BUN	:	26 mg/dl	K	4.2 mEg/l
Creatinin	:	1.05 mg/dl	Cl	102 mEg/l
GOT	:	10 IU/l		
GPT	:	8 IU/l	Total bilirubin :	
LDH	:	1025 IU/l		0.5 mg/dl
Alkaline phosphatase :		270 IU/l		

Pulmonery function test :

Ph	:	7.456	Base excessory :	1.0 mmol/l
PCo_2	:	35.1 mm of Hg	Oxygen saturation :	87.5 %
PO_2	:	50.6 mm of Hg		
HCO_3	:	24.6 mmol/l		

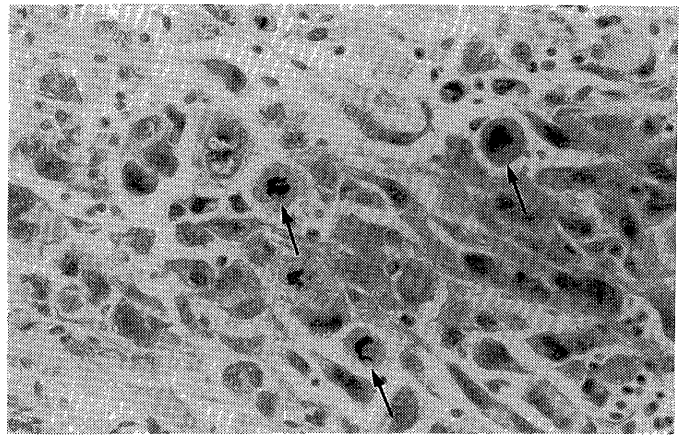

Fig. 3 Histologic feature of pleomorphic leiomyosarcoma of the uterus. Tumor cells with frequent mitotic figures (arrow) (H. E. x 300).

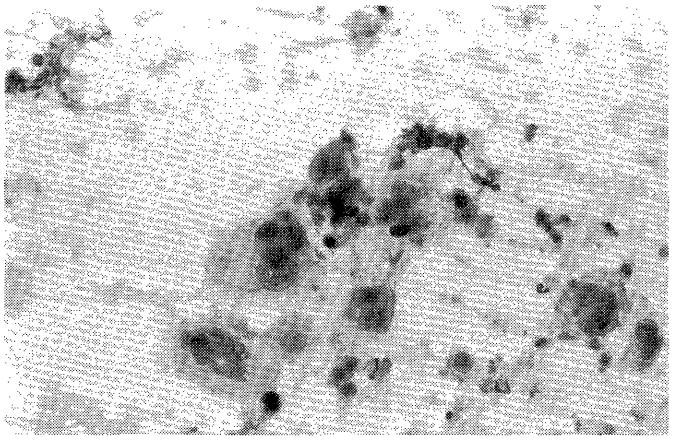

Fig. 1 Cytology showing the atypical bizarre cells (Papanicolaou x 300).

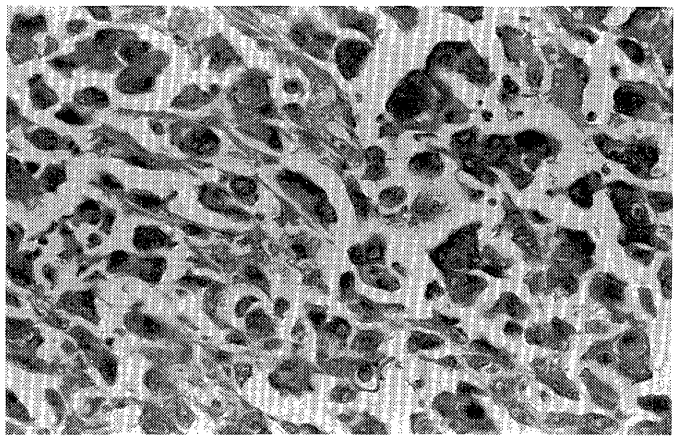

Fig. 4 Tumor cells are positive for SMA (ABC x 300).

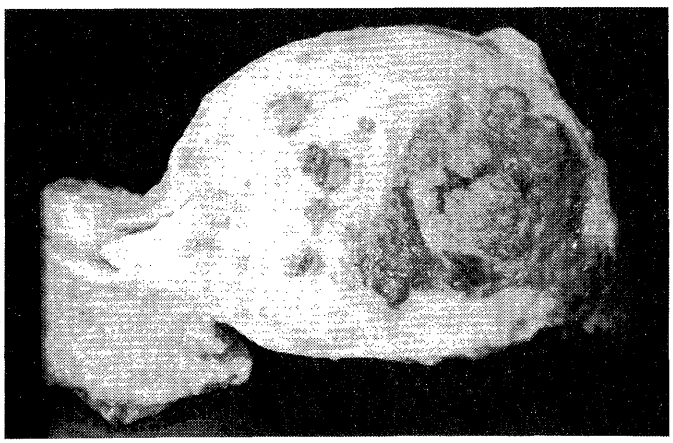

Fig. 2 Macroscopic picture of the uterine tumor.

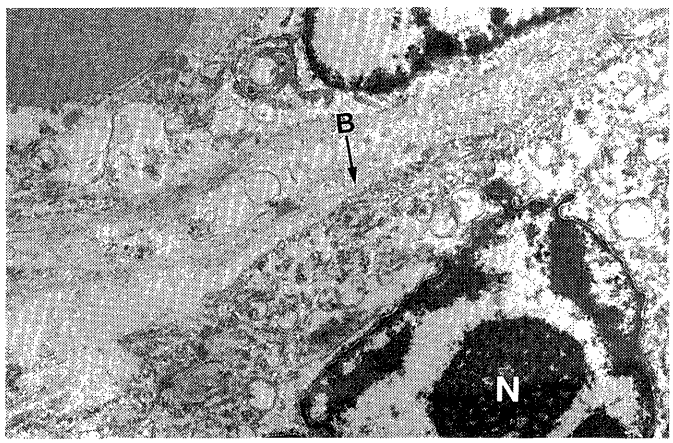

Fig. 5 Note dense basement membrane (B arrow) in tumor cells with prominent nucleoli (N) (x 9000).

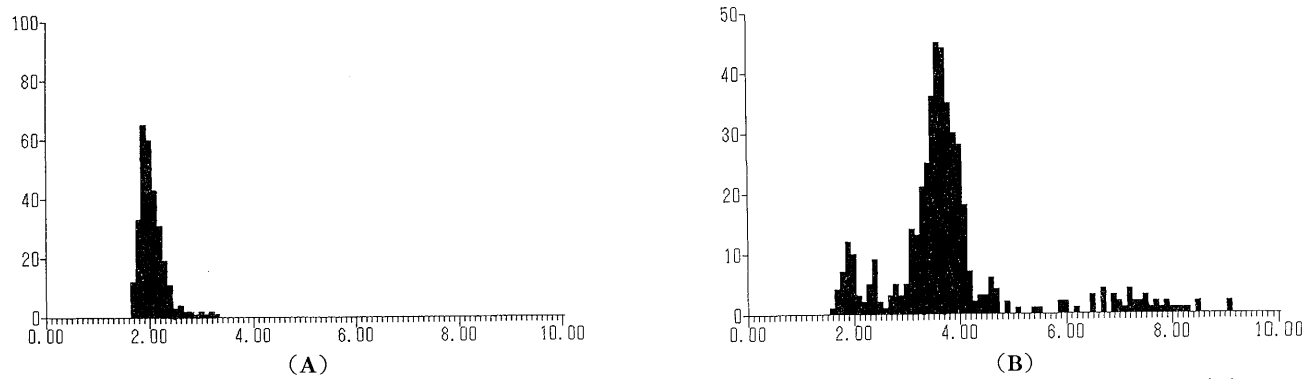

Fig. 6 DNA histograms showing diploid pattern in leiomyoma (A) and aneuploid pattern in leiomyosarcoma (B).

spindle shaped atypical cells had large hyperchromatic and bizarre nuclei. Histological features of the biopsy specimen suggested MFH or poorly diffrerntiated adenocarcinoma.

Autopsy findings : An adult head sized tumor mass occupying the pelvic cavity was found on autopsy (Fig. 2). Disseminated metastatic foci were seen in the peritoneum and intestines. The tumor revealed large necrotic areas. Cut surface of the tumor showed clear distinction between leiomyoma and sarcomatous area. Both of the lungs showed multiple metastatic foci. Largest one among the metaetatic foci was 10 cm in diameter.

Histopathology : By light microscopy proliferation of atypical pleomorphic cells was noted in main pelvic tumor. The tumor cells contained large pleomorphic and bizarre nuclei. Mitotic figures were frequently observed and it was about 25/HPF (Fig. 3). Typical histological feature of leiomyoma was seen in the surrounding area of the main tumor. Metastatic foci of the lung, peritoneum and intestine showed similar histologic feature with that of pelvic tumor.

Immunohistochemistry : An immunohistochimical study was done by ABC method[7] using the antibodies of keratin, EMA, alfa-1 anti chymotrypsin, desmin, vimentin, myoglobin and smooth muscle actin (SMA). The tumor cells showed positive reaction only for SMA (Fig. 4). Keratin, EMA, alfa-1 anti chymotrypsin, vimentin, desmin and myoglobin showed no reaction with the tumor cells.

Electron microscopy : The tumor cells showed degenerative change. But the tumor cells had actin-like filaments with dense patches in the peripheral portion of the cytoplasm, and they were covered by basement membrane (Fig. 5).

Fluorocytometry : Fluorocytometric study was carried out as described prevciously[8]. The DI (DNA index) and PI (Proliferative index) in the area of leiomyoma were 1.00 and 10 % respectively. So the DNA pattern of leiomyoma was diploidy (Fig. 6-A), while LMS showed aneuploidy pattern (Fig. 6-B), and the DI and PI were 1.26 and 29 %, respectively.

DISCUSSION

The incidence of LMS is about 1.3 % in all uterine cancer[9]. Silverberg et al. classified LMS from grade 1-4 according to the tumor cell differentiation, cellular atypism and abnormal arrangement, and frequency of mitotic figures[10]. On the basis of cell type, Fukunaga et al. classified LMS into spindle cell type, epitheloid type, giant cell type and undifferetiated type[11]. Kempson and Bari reported that the prognosis of the cases having mitotic figures more than 5-9/10 HPF is poor[12]. Count of mitotic figures varied in reported cases, but this is one of the important criteria for diagnosis.

We obserbed high count of mitotic figures and it was 25/HPF. The tumor cells had pleomorphic hyperchromatic nuclei. Bizarre multinucleated giant cells were also frequently seen. We diagnosed the case as pleomorphic leiomyosarcoma and it was classified as Silverberg's grade Ⅲ and Fukunaga's giant cell type.

The histologic features of the needle biopsy of the uterine body initially suggested MFH or poorly differentiated adenocarcinoma. LMS can be distinguished histologically from MFH by the presence of less stromal collagen, less inflammatory infiltrate and PAS positivity of tumor cells[5]. Immunohistochemically, we could not detect epithelial tumor markers such as keratin and EMA in these tumor cells. The tumor cells showed positive reaction only for anti-smooth muscle actin. Electron microscopically, the tumor cells had basement membrane and actin-like filaments with dense patches in their cytoplasm. Our immunohistostochemical and ultrastructural studies showed clear proof that the tumor cells had the characteristics of smooth muscle cell.

DNA distribution patterns of various tumors has been determined by cytophotometric, cytofluorometric and flow cytometric method to evaluate the degree of malignancy and prognosis[13]. Hiddemann et al. classified the DNA ploidy as : diploidy, aneuploidy and polyploidy[14]. In our case DNA ploidy of leiomyoma and LMS was diploidy

and aneuploidy, respectively. It was reported that the prognosis of a tumor was good when it showed diploidy pattern but the prognosis was bad in tetraploidy, aneuploidy or polyploidy patterns[15].

High PI is also considered as bad prognostic[16]. PI measured in our case was remarkably high in sarcomatous area than in the surrounding non-tumorous area. Thus, both DNA ploidy and PI were considered to be good indices for assessing and prognosis of a tumor.

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