CASE REPORT

Malignant Plexiform Tumor of the Uterus: An Unusual Variant of Epithelioid Leiomyosarcoma

HIDEKI KURODA, M.D.,* IKUO KONISHI, M.D.,*1 KANako NANBU, M.D.,* MASaKI MANDAI, M.D.,* TAKAYUKI KOMATSU, M.D.,* SHINICHI YAMAMOTO, M.D.,* HIROHIKO YAMABE, M.D.,† AKIHIRO KIDA, M.D.,‡ AND TAKAHIDE MORI, M.D.*

*Department of Gynecology and Obstetrics, Faculty of Medicine, Kyoto University, Sakyo-ku, Kyoto 606, Japan; and ‡Department of Obstetrics and Gynecology, Yamatotakada City Hospital, Yamatotakada 635, Japan

Received May 6, 1996

A 46-year-old woman with the complaint of hypermenorrhea underwent hysterectomy for a presumed uterine myoma. The solid tumor in the myometrium was gray in color, was 4 cm in diameter, and showed hemorrhage and necrosis. Histologically, the tumor consisted of round or polygonal cells arranged in cords and nests, and its histological features closely resembled those of plexiform tumor which had been reported as a benign, epithelioid smooth muscle tumor of the uterus. In the tumor in our patient, however, mild nuclear atypia and two to three mitoses/10 high-power fields were present. Two months after the hysterectomy, the patient was found to have metastatic foci in the lumbar vertebrae and iliac bone, which contained tumor cells with the same histological features. Accordingly, the present tumor might be interpreted as a malignant plexiform tumor of the uterus, an unusual variant of epithelioid leiomyosarcoma.

INTRODUCTION

Plexiform tumor of the uterus is a rare neoplasm, in which round or polygonal cells are arranged in epithelioid pattern with cords and nests within dense hyaline stroma [1–4]. Those tumors are believed to be clinically benign, and none have been reported to recur or metastasize [3–17]. Recently, we encountered a patient with a uterine mesenchymal tumor, the histological appearance of which closely resembled that of plexiform tumor, but which produced distant metastases. In this report, the clinical course of the patient and histopathological findings including immunohistochemical analysis of the tumor are presented.

CASE REPORT

A 46-year-old, nulligravid woman consulted us with the complaint of hypermenorrhea in September 1993. Her past history was negative. Pelvic examination revealed an enlarged uterus of 10-week gestational size. Ultrasonography disclosed the presence of an intramural solid tumor in the uterine fundus (Fig. 1A). Vaginal and endometrial smear tests were negative. The results of peripheral blood analysis and serum biochemistry including serum lactic dehydrogenase (LDH) level were normal. The level of the serum tumor marker CA125 was within the normal range. The uterine tumor was clinically diagnosed as a uterine myoma, and the patient was followed up at 2-month intervals. Six months after her first visit, the patient complained of abdominal pain, although the size of the uterine tumor had not changed (Fig. 1B). Exploratory laparotomy on April 15, 1994, revealed an enlarged uterus having smooth surface. Bilateral ovaries and tubes were intact. There were no abnormalities in the abdominal cavity, and simple total hysterectomy was performed. The initial diagnosis of the hysterectomy specimen was benign plexiform tumor of the uterus, since we found insufficient evidence of malignancy. The patient complained of lumbar pain 2 months after the surgery, and CT scan disclosed tumors of L4 and L5 vertebrae and iliac bone. The open biopsy showed the iliac bone tumor to be a metastatic one from the uterine lesion. The patient underwent radiation therapy for the metastases and is alive with the tumors 24 months after the hysterectomy.

MATERIALS AND METHODS

The surgical specimens were routinely processed for pathological examinations. For histopathology, materials were fixed in 10% formalin and embedded in paraffin. Deparaffinized sections, 4 μm in thickness, were stained with hematoxylin–eosin, periodic acid Schiff (PAS), Alcian-blue, Masson trichrome, and silver impregnation stains. Serial sec-
tions were studied for immunohistochemical expression of vimentin, desmin, $\alpha$-smooth muscle actin, cytokeratin, epithelial membrane antigen (EMA), factor VIII, and p53 protein by avidin–biotin peroxidase complex method using the respective primary antibodies (vimentin, V9; desmin, D33; $\alpha$-smooth muscle actin, 1A4; cytokeratin, LP34; EMA, E29; factor VIII, A082; p53 protein, DO-7) (DAKO, Glostrup, Denmark).

**RESULTS**

**Gross Anatomy and Histopathology**

The cut surface of the hysterectomy specimen showed a gray soft mass 4 cm in diameter with necrosis and hemorrhage located in the uterine fundus (Fig. 2). The tumor was well circumscribed, and had smooth pushing borders. Histologically, the majority of the tumor tissue was necrotic. The

**FIG. 1.** Ultrasonographic appearance of the tumor at the patient’s first visit (A) and after 6 months of conservative observation (B). The size of the tumor did not change during the intervening period.

**FIG. 2.** Macroscopic appearance of the hysterectomy specimen. The cut surface exhibits a tumor with hemorrhage and necrosis (arrow). A typical myoma is also seen (arrowhead).
FIG. 3. Microphotographs of the tumor showing hyalin necrosis (A) and the tumor with smooth pushing borders (B). Original magnification: A, ×80; B, ×40.

FIG. 4. Microphotographs of the tumor cells showing arrangement of the tumor cells in a characteristic plexiform pattern (A) and mild nuclear atypia with a mitotic figure (B) (arrow, mitotic figure). Original magnification: A, ×200; B, ×800.
FIG. 5. Microphotographs of the metastatic foci demonstrating the tumor cells with the same plexiform appearance as the primary lesion (A) and the tumor cells with clear cytoplasm (B). Original magnification ×200.

FIG. 6. Immunohistochemical staining of the uterine tumor demonstrates the positivity for α-smooth muscle actin in the tumor cells. Magnification ×800.
band of paucicellular hyalinized collagen surrounded the necrotic area, and an abrupt transition between viable and non-viable tumor cells was not observed (Fig. 3A). Therefore, the necrotic pattern in this case was not coagulative but hyalin type. In the remaining part, round or polygonal tumor cells were arranged in a characteristic plexiform pattern (Fig. 3B). Gland formation of the tumor cells was not identified. A loose collagenous stroma surrounded the tumor nests (Fig. 4A). Each tumor cell had round or oval nucleus with small nucleoli and scant eosinophilic cytoplasm. Mild nuclear atypia was identified (Fig. 4B). Mitotic figures were rare, but in the areas with the highest number of mitotic counts, two to three mitoses were observed in 10 high-power fields (HPF) (Fig. 4B). No vessel permeation of the tumor cells was identified. In the other part of the myometrium, one leiomyoma with usual histological feature was present. There were no macroscopic or microscopic abnormalities in the endometrium or in the cervix. The biopsy specimen from the metastatic foci in the iliac bone contained the tumor cells with the same histologic features as those seen in the uterine tumor (Fig. 5A), whereas other tumor cells in the metastatic lesion had clear cytoplasm (Fig. 5B).

Special Stains and Immunohistochemistry

The tumor cells in the uterus were positive for Masson trichrome and negative for PAS and Alcian-blue stains. Silver impregnation stain showed filamentous black fibers surrounding the nests of tumor cells, which mimicked the epithelial pattern of cell arrangement.

Immunohistochemically, the tumor cells in the uterus exhibited positive reaction for vimentin and desmin, and they were partly positive for α-smooth muscle actin (Fig. 6). On the other hand, they were negative for cytokeratin, EMA, factor VIII, and p53 protein.

DISCUSSION

Our patient had a mesenchymal tumor of the uterus with unusual histological appearance which closely resembled that of plexiform tumor. The tumor cells were round or polygonal in shape and were arranged in a characteristic epithelioid pattern with cords and nests. The smooth muscle nature of this tumor was suggested by the Masson trichrome staining as well as immunohistochemical positivity for desmin and α-smooth muscle actin. The reticular pattern seen on silver impregnation stain was consistent with the previously reported finding in the plexiform tumor [13]. The presence of tumor cells with clear cytoplasm in the metastatic foci may also support our diagnosis, since mixtures of epithelioid, clear cell, and plexiform patterns occur with sufficient frequency in a single entity, epithelioid smooth muscle tumor [4]. Accordingly, the present tumor is classified as the plexiform variant of epithelioid smooth muscle tumor. At the time of histological assessment of the hysterectomy specimen, however, the diagnosis of malignancy was difficult because the nuclear atypia was mild and mitoses were a few in number.

Plexiform tumor of the uterus was first described in 1958 by Borghard-Erdle and Hirsch [5], and approximately 50 cases have been reported to date [3–17]. The age of the patients ranges between 36 and 67 with a median age of 47 years. The tumor is usually located within the myometrium, varying in size up to 8 cm in diameter. A microscopic nodule of this entity has been referred to as plexiform tumorlet [15]. Histologically, epithelioid-like cells are arranged in cords and nests within a dense hyaline stroma. Ultrastructural studies have disclosed the presence of intracytoplasmic myofilaments [11–13, 15]. Immunohistochemically, the tumor cells are positive for vimentin, desmin, and muscle-specific actin and negative for factor VIII, S-100 protein, and cytokeratin [16–18]. These findings suggest the smooth muscle differentiation of the tumor cells, although the localization of microscopic nodules may also implicate an endometrial stromal origin [15]. In the plexiform tumor or tumorlet, the tumor cells have been reported to exhibit neither nuclear atypia nor mitosis, although infiltrative pattern of tumor cell growth has frequently been observed [15]. Clinically, none of these tumors recurred or metastasized, and therefore the plexiform tumor is classified as a variant of epithelioid leiomyoma [1, 2]. In contrast, our patient showed bone metastases, and the tumor might be interpreted as a malignant plexiform tumor which represents an unusual variation of epithelioid leiomyosarcoma of the uterus.

In the histological assessment of the malignant potential of a uterine smooth muscle tumor, one of the essential points is the number of mitotic figures [1, 2]. According to Hendrickson and Kempson [2], epithelioid smooth muscle tumors have been classified as benign tumors if the mitotic counts per 10 HPF are fewer than two; tumor of uncertain malignant potential if it is between two and five; leiomyosarcoma if it is greater than five. Recently, they reported that coagulative tumor cell necrosis is an important prognostic indicator in uterine smooth muscle neoplasms with usual smooth muscle differentiation [19]. In epithelioid smooth muscle neoplasms, all tumors with coagulative necrosis in their series behaved in a malignant fashion and should be diagnosed as leiomyosarcoma, although the clinical experience is limited [20]. Kempson also reported that all noncoagulative epithelioid tumors with atypia and an mitotic index of more than two/10 HPF should be considered leiomyosarcoma, and that tumors without atypia or necrosis are a problem because 1 of the 12 patients showed treatment failure [21]. Bone metastasis was observed in the present case which did not show coagulative tumor cell necrosis but exhibited mild nuclear atypia with two to three mitoses/10 HPF. Therefore, the prognosis of patients with epithelioid smooth muscle tumors is less predictable than that of tumors with usual smooth muscle differentiation. When a uterine resembling plexiform tumor is encountered, thorough histological
examination for the above prognostic factors as well as careful follow-up of the patient is needed.

The preoperative diagnosis of leiomyosarcoma of the uterus is usually difficult. Interestingly, in our case, the size of the uterine tumor did not change during the period of observation before hysterectomy, nor was the patient’s serum LDH level elevated. Differentiation from benign leiomyoma was impossible by ultrasonography. Although magnetic resonance imaging (MRI) was recently recommended for the preoperative assessment of the malignancy of uterine smooth muscle tumors, we encountered another patient with epithelioid leiomyosarcoma at our department in whom the MRI findings mimicked those of leiomyoma [22].

REFERENCES