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In postmenopausal women, some uterine leiomyosarcomas mimic a cystic degeneration of uterine myoma: two case reports and a literature review

U kobiet w okresie pomenopauzalnym mięsak gładkokomórkowy macicy może imitować zwyrodnienie torbielowate mięśniaka macicy – opis dwóch przypadków i przegląd literatury

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Abstract

Uterine leiomyosarcoma is an uncommon malignancy accounting for approximately 1% of gynecologic oncology cases. Most uterine leiomyosarcomas occur in menopausal women and they are notorious for their aggressive character, early dissemination, and poor prognosis. It is difficult to accurately differentiate uterine leiomyosarcoma from leiomyomas, especially when leiomyomas undergo degenerative changes. We treated two menopausal women with a uterine mass showing cystic change. Clinical work-up included needle aspiration, sonography, computed tomography, and serum tumor markers to differentiate uterine leiomyosarcoma from leiomyoma. All results were negative for malignancy, but uterine leiomyosarcoma was ultimately diagnosed by pathological examination. Until an accurate preoperative diagnostic method is available, menopausal women diagnosed with a degenerating cystic uterine fibroid should be considered to have a malignancy intraoperatively in order to prevent tumor cells from intraperitoneal spreading.

Keywords: degenerating cystic uterine leiomyoma, uterine leiomyosarcoma, uterine malignancies

Streszczenie

Mięsak gładkokomórkowy macicy to rzadki nowotwór złośliwy odpowiadający za około 1% przypadków nowotworów narządów rodnych. Nowotwór ten występuje głównie u kobiet w okresie pomenopauzalnym i jest znany z agresywnego przebiegu, wczesnego rozsiewu oraz złego rokowania. Przeprowadzenie dokładnej diagnostyki różnicującej mięsaka gładkokomórkowego i mięśniaków jest trudne, zwłaszcza w przypadku zmian degeneracyjnych tych drugich. W pracy przedstawiono przypadki dwóch kobiet w okresie pomenopauzalnym, u których w macicy stwierdzono obecność masy wykazującej zmianę torbielowatą. W ramach diagnostyki klinicznej wykonano biopsję aspiracyjną, badanie ultrasonograficzne, tomografię komputerową oraz oznaczono stężenia markerów nowotworowych w surowicy krwi w celu zróżnicowania mięsaka gładkokomórkowego i mięśniaka. Chociaż wszystkie badania dały wynik ujemny dla nowotworu złośliwego, badanie histopatologiczne potwierdziło rozpoznanie mięsaka gładkokomórkowego macicy. Dopóki nie będzie dostępna dokładna metoda diagnozowania przedoperacyjnego, w przypadku kobiet w okresie pomenopauzalnym z rozpoznaniem zwyrodnienia torbielowatego mięśniaka macicy należy śródoperacyjne założyć obecność nowotworu złośliwego w celu uniknięcia dootrzewnowego rozsiewu komórek nowotworowych.

Słowa kluczowe: zwyrodnienie torbielowate mięśniaka macicy, mięsak gładkokomórkowy macicy, nowotwory złośliwe macicy

INTRODUCTION

Uterine leiomyosarcoma (LMS) is a rare tumor, accounting for approximately 1% of uterine malignancies[1,2]. Despite its rarity, LMS has the worst prognosis of all uterine malignancies and a high recurrence rate of 53%[1]. Some study reported that the impact of primarily surgical manipulation in LMS on prognosis is important[3]. However, LMS is usually diagnosed postoperatively because its symptoms and signs resemble those of leiomyoma, and there are no accurate tools available for preoperative diagnosis[1]. We report two cases of LMS in which the diagnosis of leiomyoma was made before surgery. Both cases were initially presumed to be cystic degenerating leiomyomas, and the patients underwent total hysterectomy; the final diagnosis of LMS was made by histopathological examination.

CASE REPORT

Case 1

A 52-year-old Korean woman (gravida 2, para 2) was admitted to our hospital with the chief complaint of vaginal spotting, which had persisted for 1 month. She had taken conjugated estrogens and bazedoxifene for 2 years since menopausal symptoms and had a history of myomectomy 20 years before. Two years ago, the patient was diagnosed with 3 cm, 4 cm, and 5 cm uterine myomas. Gynecological examination revealed a uterus that was similar in size to that of a 10 weeks pregnant woman and a palpable mass. Transvaginal sonography showed three masses in the uterus. One mass measured 6 cm, and was irregular in shape with cystic and solid components as well as calcifications. The other two masses measured 5 cm and 3 cm, were encapsulated by a continuous membrane and filled with fluid contents. Also the thickness of the uterine endometrium was as thin as 0.4 cm. The results of laboratory test were within normal limits: CA-125 7.3 U/mL (normal range 0–35), CA 19-9 ≤3.0 U/mL (normal range 0–37). Abdominal and pelvic computed tomography (CT) showed that the central portion of the mass was cystic with calcifications, and the mass did not invade adjacent tissues; multiple uterine leiomyomas with secondary degeneration, intramural type (Fig. 1A), were diagnosed. Considering the masses to be benign, we performed total abdominal hysterectomy and bilateral salphingo-oophorectomy.

On gross examination, a 6 cm intramural mass was present, consisting of gray white soft tissue with a central irregular cystic lesion filled with clear serous fluid, and with a focally ill-defined margin (Fig. 1B). On microscopic examination, the largest solid region showed coagulative tumor cell necrosis, low mitotic count [<10/high-power field (HPF)], and diffuse moderate cellular atypia (Fig. 1C, 1D). This was consistent with uterine LMS and staged as IB according to the International Federation of Gynecology and Obstetrics (FIGO) classification. Two other histologic diagnoses revealed intramural and subserosal leiomyomas.

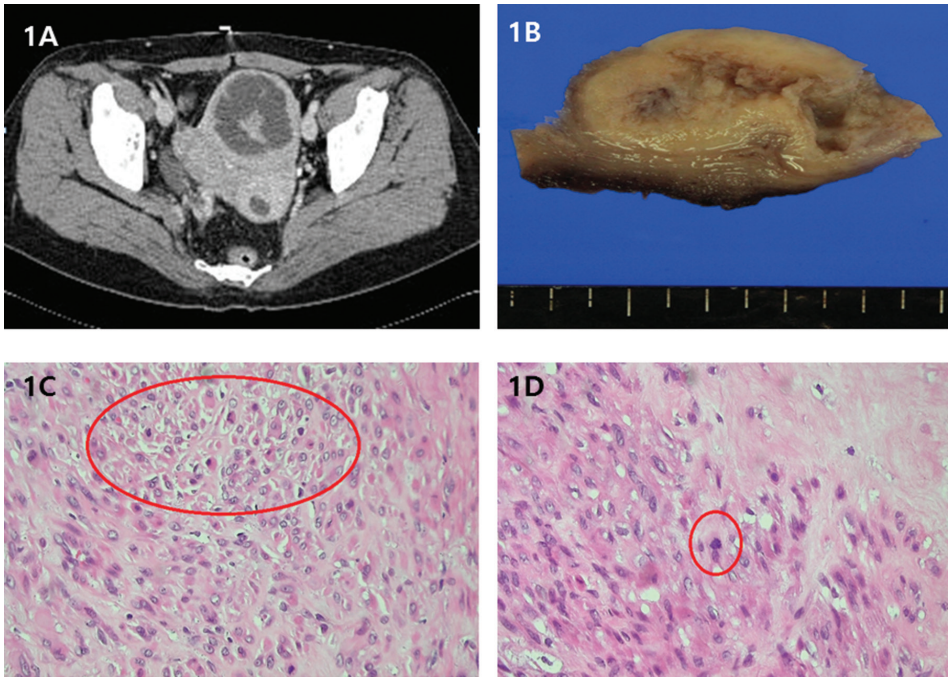

Fig. 1 **A.** *Abdominal and pelvic CT suggested a diagnosis of multiple uterine leiomyomas (6 cm, 5 cm, 3 cm) with secondary degeneration, intramural type.* **B.** *On gross examination, uterine mass was 6 cm, intramural, with a central irregular cystic lesion and clear serous fluid.* **C.** *On microscopic examination, coagulative tumor cell necrosis was present (hematoxylin and eosin, ×400).* **D.** *On microscopic examination, low mitotic count (<10/high power field) and diffuse moderate cellular atypia was present (hematoxylin and eosin, ×400)*

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Positron-emitting tomography-CT was performed postoperatively to evaluate for distant metastasis; there was no evidence of malignancy. The patient reported for a follow-up involving abdominal, pelvic and chest CT every 3 months. The patient showed no clinical evidence of tumor recurrence or metastasis 10 months after surgery.

Case 2

A 52-year-old Korean, menopausal woman (gravida 2, para 2) visited her physician due to a 2-month history of lower abdominal discomfort and a palpable mass. She never received hormone therapy and had no other gynecologic history. Transvaginal sonography showed an abnormal cystic uterus mass, and the patient was transferred to our hospital for further evaluation. On gynecologic examination, a soft and firm mass was palpable, which corresponded to about 10 weeks pregnant uterus. Serum hemoglobin was 12 g/dL; other laboratory parameters, including tumor markers (CA-125, CA 19-9) were non-specific. Transvaginal sonography revealed a well-circumscribed, approximately 10 cm uterine mass with cystic and solid components (Fig. 2A). We aspirated the cystic lesion under ultrasonographic guidance and cytologic results were negative for malignancy. Based on the presumed diagnosis of a degenerating cystic uterine leiomyoma, we performed total laparoscopic hysterectomy. Based on an intraoperative frozen pathology assessment, it was difficult to distinguish between malignant and benign lesion because the differentiation of the cells was very low and the shape of the cells was broken; therefore bilateral salphingo-oophorectomy was performed. During operation, no cancer cell spilled into the operative field.

Grossly, the uterus showed a 9 × 7 cm intramural mass with a soft and yellowish gray fish-flesh-like cut surface (Fig. 2B). On pathological examination, the uterine smooth muscle showed coagulative tumor cell necrosis, a high mitotic index (≥10/HPF), and diffuse mild cellular atypia (Fig. 2C, 2D). These findings were consistent with the diagnosis of uterine LMS.

Postoperatively, abdominal, pelvic and chest CT was performed to rule out metastasis. No significant findings were revealed and the patient was ultimately diagnosed with uterine LMS, staged as IB according to the FIGO classification. A follow-up abdominal, pelvic and chest CT was performed after 3 months. There was no clinical evidence of tumor recurrence at 1 year after surgery.

DISCUSSION

Uterine sarcomas are rare tumors that account for approximately 3% of all uterine malignancies[4]. The most common type of uterine sarcoma is LMS (63%), followed by low/high grade endometrial stroma sarcoma (21%) and undifferentiated uterine sarcoma[4]. Most uterine sarcomas occur in women over 40 years of age who usually present with abnormal vaginal bleeding, a palpable pelvic mass, and pelvic pain[1]. In menopausal women who are not on

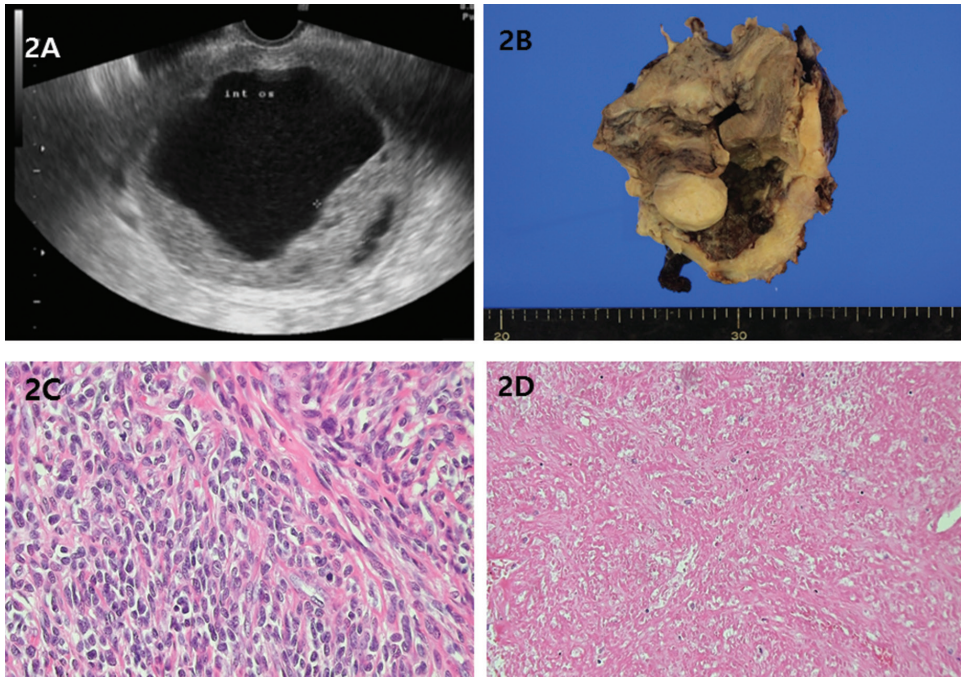

Fig. 2 **A.** *Transvaginal sonography revealed a well-circumscribed, approximately 10 cm uterine mass with cystic and solid components.* **B.** *Grossly, the uterus showed a 9 × 7 cm intramural mass with a soft and yellowish gray fish-flesh-like cut surface.* **C–D.** *The uterine smooth muscle showed coagulative tumor cell necrosis, a high mitotic index (≥10/HPF), and diffuse mild cellular atypia (hematoxylin and eosin, ×400)*

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hormonal replacement therapy and present with a rapid growth of a leiomyoma, malignancy should be suspected[1]. It is difficult to accurately differentiate LMS from leiomyomas because both tumors develop from uterine smooth muscle and the symptoms and signs are similar. The incidence of LMS found in women operated on for presumed uterine leiomyoma is approximately 0.5%[5].

Unlike uterine leiomyoma, LMS are characterized by aggressive nature, early dissemination, and poor prognosis. Importantly, the treatment methods differ. Minimally invasive procedures can now be used in leiomyoma treatment, while LMS is treated with total abdominal hysterectomy without morcellation to prevent tumor cell spreading throughout the pelvic cavity[1,6]. It was reported that the recurrence rate of the uterine sarcoma is increased three times or more when using the morcellation[7]. Also, patients undergoing intact removal of the uterus had significantly improved survival rates and decreased recurrence rates[8]. Thus accurate diagnosis and proper treatment are important. Many studies distinguishing LMS from leiomyoma preoperatively using radiological criteria, tumor markers, and cytology, as well as other factors have been reported. Exacoustos et al. reported that ultrasound findings, including a single and large diameter lesion greater than 8 cm, marked peripheral and central vascularity as well as cystic degeneration, were significantly associated with LMS[9]. However, these features were not observed in our two patients. Cho et al. reported that preoperative neutrophil-to-lymphocyte ratio (>2.1), large tumor size (>8 cm), and lower body mass index (≤20) could be useful for the discrimination of LMS from leiomyoma[10]. Goto et al. studied the relationship between magnetic resonance imaging-based and pathologic diagnosis in 130 patients with myoma and 10 patients with LMS. The results showed 3% false positive, 0% false negative, 100% sensitivity, 96.9% specificity, and 71.4% positive predictive value, 100% negative predictive value[12]. Dynamic magnetic resonance imaging enhanced with Gd-DTPA combined with serum determination of lactate dehydrogenase (LDH) and LDH3 seems to be useful in the preoperative differential diagnosis of uterine LMS from degenerated leiomyoma[12]. Transcervical needle biopsy using histopathologic scoring (mitotic index, cytologic atypia, coagulative tumor cell necrosis, variant, vascular extension, marginal infiltration) is a reliable diagnostic tool[12,13]. However, this test is limited because there is a restriction that the tumor should be involving or encroaching on the endometrium[13]. So the roles of these modalities in the preoperative prediction of LMS remain unclear, and there is no accurate diagnostic tool available.

In our cases, in the course of treating menopausal women with a uterine mass showing cystic change, we performed needle aspiration, sonography, CT, and serum tumor markers to differentiate uterine LMS from leiomyoma. All results were negative for malignancy, so we preoperatively presumed a diagnosis of benign uterine leiomyoma. However, LMS was diagnosed by final pathological examination.

In conclusion, uterine LMS is very difficult to distinguish from a degenerating cystic uterine leiomyoma, especially in the menopausal state. Until an accurate preoperative diagnostic modality becomes available, menopausal women with a cystic uterus mass diagnosed as uterine leiomyoma should be treated surgically as if they had a malignant diagnosis, in order to prevent tumor cells from spreading intraperitoneally.

Conflict of interest

The authors do not report any financial or personal connections with other persons or organizations, which might negatively affect the content of this publication and/or claim authorship rights to this publication.

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