

Disseminated Peritoneal Leiomyomatosis with Atypical Features and Comorbid Uterine STUMP: a Case Report and Review of the Literature

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Case Report

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Disseminated peritoneal leiomyomatosis (DPL) is a very rare benign disease, characterized by multiple solid subperitoneal or peritoneal smooth muscle nodules in abdominopelvic cavity and malignant transformation is extremely rare. Also, uterine smooth muscle tumors of unknown malignant potential (STUMP) is a rare tumor, which is regarded as subclassification in uterine smooth muscle tumors between benign and malignant criteria. Pathogenesis of DPL is uncertain, but increasing evidence of iatrogenic cause including laparoscopic myomectomy has been reported. We report a case of a 28-year-old female with previous history of laparoscopic myomectomy diagnosed with DPL with atypical feature and concurrent uterine STUMP using computed tomography (CT) and magnetic resonance imaging (MRI), as well as present a review of the literature.

Keywords: Magnetic resonance imaging; Leiomyomatsis; Smooth muscle tumor; Laparoscopy; Computed tomography

INTRODUCTION

Disseminated peritoneal leiomyomatosis (DPL) is a rare disease occurring mostly in women of childbearing age, featuring multiple solid peritoneal nodules mimicking peritoneal carcinomatosis (1). DPL itself is pathologically benign but its clinical presentation shows invasive behavior. Atypical histologic feature or malignant transformation of DPL is extremely rare. A smooth-muscle tumor of unknown malignant potential (STUMP) is a neoplasm within the uterus that does not fit the histologic diagnostic criteria of leiomyosarcoma, leiomyoma, or its variants, and only the outcome will confirm whether it is benign or malignant (2). Herein, we report a case of DPL with atypical features and concurrent uterine STUMP in a patient with a previous history of laparoscopic myomectomy, which was treated by surgery.

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CASE REPORT

A 28-year-old nulliparous woman was referred to our hospital for abdominal discomfort. The patient had a surgical history of laparoscopic uterine myomectomy at an outside hospital 3 and 5 years ago. She had no medical history of hormonal therapy. Serum CA-125 was elevated to 45.80 U/mL. Contrast-enhanced abdominal and pelvic CT scan revealed multiple solid masses of various sizes in the greater omentum and peritoneum. Also, there was a round, circumscribed enhancing myometrial mass in the uterine fundus (Fig. 1a). Although there was a moderate amount of ascites, no abnormal peritoneal thickening or abnormal lymphadenopathy was noted. Contrast-enhanced pelvic magnetic resonance imaging (MRI) revealed solid peritoneal masses that were hyperintense on T2-weighted images (Fig. 1b). A solid myometrial mass in the uterine fundus showed intermediate signal intensity on T2-weighted images (Fig. 1b). The peritoneal and uterine myometrial masses showed diffusion restriction on diffusion-weighted images (Fig. 1c, d) and homogeneous enhancement on dynamic contrast-enhanced images (Fig. 1e). Based on the imaging findings, we suspected disseminated peritoneal leiomyomatosis and a uterine leiomyoma of an atypical histologic type showing high cellularity or leiomyosarcoma. Open laparotomy was performed for the resection of the tumors. Microscopically, the myometrial, omental, and peritoneal masses showed moderate cellularity with no necrosis and consisted of intersecting fascicles of spindled cells. Tumor cells showed cytologically mild to moderate cellular atypia, and showed frequent mitoses (up to 6/10 high-power fields, mean 3/10 high-power fields) without an abnormal mitotic figure (Fig. 1f). By immunohistochemical stains, tumor cells were positive for SMA, and the Ki-67 proliferation index was 5% (Fig. 1g, h). The myometrial mass in the uterine fundus showed similar histopathologic features. The histopathologic features of the uterine and peritoneal masses showed the atypical smooth-muscle cell tumors described in the WHO classification based on tumor-cell necrosis and moderate to severe cellular atypia and mitotic count (3). The mass within the uterine myometrium was diagnosed as being STUMP based on the histologic findings. Since the diagnosis of STUMP is limited to the tumors within the uterus, the DPL with frequent mitoses was assigned for the multiple peritoneal masses based on the histological and clinical findings. The patient had no additional treatment after the surgery. CT performed a month after the surgery showed a small residual soft-tissue mass in a posterior cul-de-sac,

which was considered a residual tumor. A 20-month follow-up CT scan showed no interval change, suggesting a stable disease.

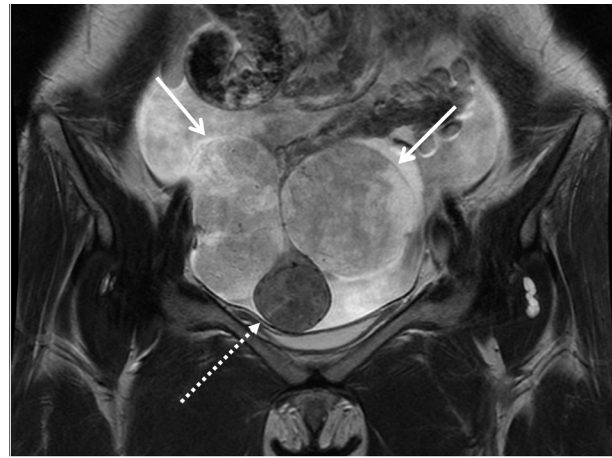
DISCUSSION

DPL is a rare disease showing multiple peritoneal nodules that often mimic peritoneal carcinomatosis (1). Since first described in 1952 by Wilson and Pearl, less than 150 cases of DPL have been reported in English-language literature. However, the incidence of DPL may be underestimated, because most cases are asymptomatic (4). The etiology of DPL is uncertain, and several theories have been proposed about the pathogenesis of this disease. Some authors suggest that this process is promoted by hormonal stimulation; this hypothesis is supported by the facts that DPL is common in women of reproductive age, during pregnancy, or after prolonged use of oral contraceptives (5). Recently, there have been increasing reports of iatrogenic dissemination after laparoscopic myomectomy, suggesting that morcellation is a contributing factor of DPL (6).

Although most of DPL is pathologically benign with a favorable prognosis, DPL with atypical histologic features or malignant transformation has been reported. Cytologic atypia, nuclear polymorphism, hyperchromasia, tumor-cell necrosis, and increased mitotic figures are histological signs of malignant transformation (7). Eighteen cases of DPL with malignant transformation have been reported in the English-language literature (8-12). Most of the patients were women of reproductive age (median age, 35.9 years old), but three patients were men. Most of the patients had no history of oral contraceptives. Clinical outcomes were not good; as nine out of the eighteen patients were dead during the median follow-up period of 15.6 months (except one patient with no data) because of the rapid progression of malignancy. There has been only one case reported showing DPL with atypical histopathologic features, in a 45-year-old woman with a previous laparoscopic myomectomy history (6), which showed radiological and histopathological findings similar to our case, in which the patient had comorbid uterine STUMP and a previous surgical history of repeated laparoscopic uterine myomectomy and no endogenous/exogenous hormone exposure. Taken all together, DPL with frequent atypia in our case possibly resulted from an atypical leiomyoma implanted as an iatrogenic cause. The report that atypical leiomyomas are more prone to peritoneal dissemination also supports this



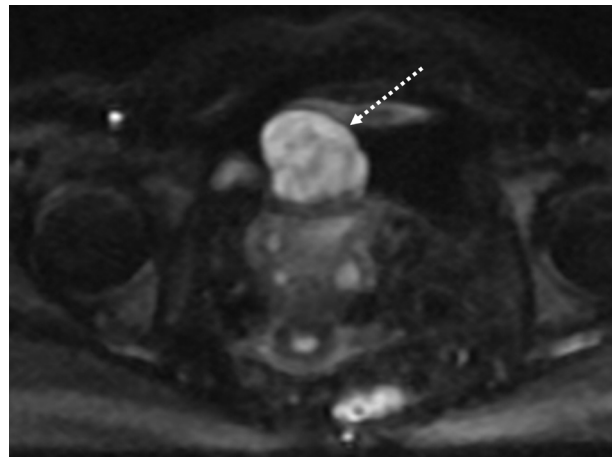
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b



c

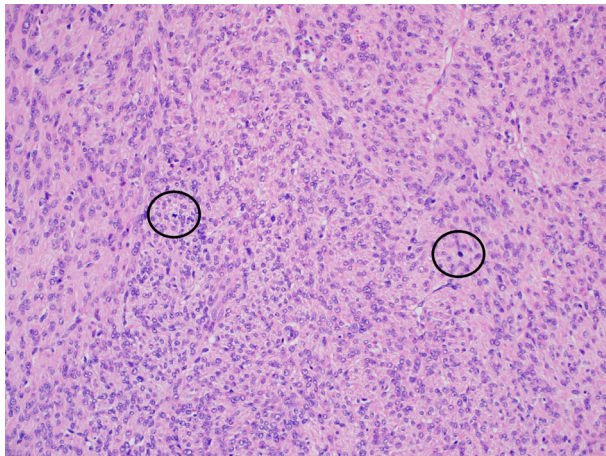


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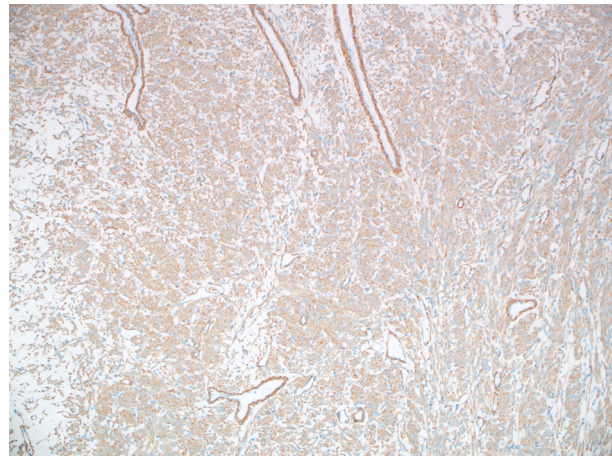


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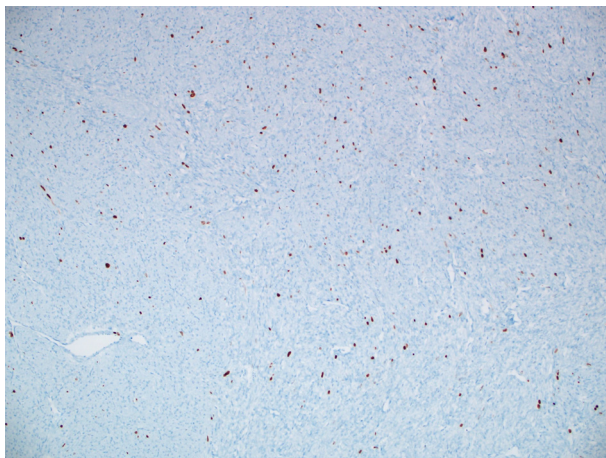
Fig. 1. Contrast-enhanced abdominal and pelvic CT scan (a) reveals intensely enhanced solid peritoneal masses in the right paracolic gutter (black solid arrow), on both sides of the pelvic cavity (solid white arrows with solid head) and myometrium of the uterine fundus (dashed white arrow). Coronal T2-weighted MR image (b) shows heterogeneously hyperintense solid peritoneal masses in the pelvic cavity (solid white arrows) and an isointense solid mass in the myometrium of the uterine fundus (dashed white arrow). Axial diffusion-weighted image at high b-value (1000 s/mm^2) showing hyperintensity of the peritoneal masses (c, solid white arrows) and the myometrial mass (d, dashed white arrow), suggesting high cellularity. Gadolinium-enhanced fat-suppressed T1-weighted coronal image shows homogeneous enhancement of the myometrial (e, dashed white arrow) and peritoneal masses (e, solid white arrows).



f



g



h

Fig. 1. Microscopically, spindle cells show cytologically mild to moderate cellular atypia with frequent mitoses (f, black circles) (Hematoxylin & Eosin, $\times 200$). Immunohistochemically, tumor cells disclose positive staining for SMA (g, SMA, $\times 100$), and the Ki-67 proliferation index is 5% (h, Ki-67, $\times 100$).

hypothesis (6).

Synonymous terms, such as atypical leiomyoma, atypical smooth-muscle neoplasm, or mitotically active leiomyoma, have been used for smooth-muscle tumors showing histologic features between those of leiomyoma and leiomyosarcoma, because of the characteristic histologic features and author preference. To prevent confusion caused by use of these terms, WHO classified smooth-muscle tumors that do not fit the diagnostic criteria of leiomyoma and leiomyosarcoma as STUMP for the lesions within the uterus, based on three histologic findings: tumor-cell necrosis, moderate-to-severe cellular atypia, and mitotic count (3). However, in general, the diagnosis of STUMP is limited to the uterine tumors, and there are no established criteria for the diagnosis of leiomyoma with atypical histopathologic features as STUMP. Therefore, we diagnosed the peritoneal masses as DPL with atypical histologic features based on

imaging and histopathologic features. Because uterine STUMPs are tumors of unknown malignant potential, for which only the outcome will confirm their benign or malignant nature (2), it can be assumed that DPL with atypical histopathologic features will have similar clinical outcomes. Thus, careful clinical management is needed. Imaging studies are important to assess the extent of the disease and the possibility of malignancy before surgery, as well as to prevent inadequate management leading to delay in diagnosis. Imaging findings of DPL are multiple, solid, and complex soft-tissue peritoneal or mesenteric masses similar to typical uterine leiomyomas, which appear as well-demarcated solid masses that are hypointense on T1- and T2-weighted MR images and homogeneous enhancement in dynamic contrast enhancement images (13). DPL with malignant transformation shows necrosis and hemorrhage within the peritoneal masses (10). Uterine STUMP usually

appears as a myometrial mass with T2 hyperintensity on MR imaging. DWI also provides useful information, as STUMP or malignant leiomyosarcoma could show diffusion restriction compared to their benign counterparts (13). When DPL or uterine leiomyoma with T2 high SI and diffusion restriction, an atypical histologic type of leiomyomas with high cellularity should be considered, as in our case. Since prognosis of DPL with malignant transformation is not favorable, early diagnosis and proper managements should be made, referring to clinical and radiologic features.

There is no established management protocol for DPL with atypical histopathologic features and uterine STUMP. However, therapy needs to be individualized according to the patient's age, hormonal and reproductive status, and symptoms. Treatment can be started by decreasing the estrogen concentration, either by discontinuing hormonal treatment or by administration of gonadotropin-releasing hormone (GnRH) or an aromatase inhibitor. Surgical approaches, including hysterectomy, salpingo-oophorectomy, omentectomy, or debulking surgery, can be a definite treatment (5). Although the prognosis of DPL is favorable, DPL with malignant transformation is a locally aggressive pathology with a strong tendency to recur despite complete excision. It can metastasize, especially to the retroperitoneal lymph nodes and lungs. Up to this time, palliative chemotherapy can be administrated in advanced diseases, without any existing standards of administration. A close follow-up for patients with DPL should be done at 6-month intervals because of the possibility of early recurrence or malignant degeneration (14). The reported recurrence rate for uterine STUMP is 7–27%. Tumor necrosis, degree of atypia, and mitosis are correlated with malignant behavior, and recurrence is observed in single or various combinations and degrees of those. Therefore, it is hard to predict the biological behavior, metastatic potential, or prognosis of STUMP. Reported survival outcome is good, with a five-year survival rate of 92–100% (15).

In summary, we described a rare manifestation of DPL with atypical features and comorbid uterine STUMP, stable at the 20-month follow-up after the surgery. It is important to identify patients with leiomyomas showing atypical features on preoperative imaging studies and to make appropriate treatment plans with close follow-up.

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368 e368

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