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Disseminated peritoneal leiomyomatosis: a case report and review of the literature

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Abstract

Disseminated peritoneal leiomyomatosis (DPL), also known as leiomyomatosis peritonealis disseminata, is a rare disease characterized by multiple benign smooth muscle tumors proliferating along the peritoneal surfaces. The cause of the disease is unclear, and possible factors include iatrogenic and hormonal stimulation. The patient was a 41-year-old Chinese woman with a history of laparoscopic myomectomy and subsequent pregnancy. Multiple abdominal masses were identified and required surgical intervention. The patient had no tenderness or other discomfort. The clinical and imaging diagnosis was gastrointestinal stromal tumor, but DPL was confirmed by postoperative pathological examination. The patient had a good prognosis, and no recurrence was observed during follow-up. Iatrogenic and hormonal stimulation leading to DPL is very rare, and we believe that multiple factors led to DPL in this case. Clinicians should be aware of such potential patients.

Keywords

Disseminated peritoneal leiomyomatosis, laparoscopy, hormone, misdiagnosis, case report, abdominal mass

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Introduction

Peritoneal disseminated leiomyomatosis (DPL) is a rare benign disease that is characterized by multiple smooth muscle tumors proliferating along the peritoneal surface. DPL was first reported by Wilson and Peale in 1952 and officially named by

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Taubert et al. in 1964.[1,2] The disease usually occurs in women of childbearing age but may also be seen in postmenopausal women and in men. The clinical manifestations are small nodules or several larger nodules diffusely distributed in the peritoneum. To date, approximately 200 cases have been reported worldwide. Owing to the rarity of the disease and the lack of typical clinical symptoms and signs, the misdiagnosis rate is extremely high. DPL is easy to misdiagnose as metastatic cancer, gastrointestinal stromal tumor (GIST), and mesothelioma. Currently, the pathogenesis of the disease remains unknown, but iatrogenic implantation (postoperative uterine leiomyoma),[3] hormonal effects,[4] heredity,[5] and peritoneal mesenchymal stem cell metaplasia[6]have been considered. In the past 20 years, with the application of laparoscopic surgery, the iatrogenic implant theory is being considered more often, and must be considered. However, this theory is based mainly on case reports, which are very rare. Persistent hormonal influence is also an important factor. Some patients have a history of ovarian tumors or are taking oral sex hormones, and after eliminating this exposure, the tumors stop growing or degenerate.[7] However, the disease progresses or relapses during pregnancy or pre-pregnancy, indicating that sex hormones may also be the cause. We searched the relevant literature and found that articles discussing a multifactorial theory are extremely rare. We report the recent diagnosis and treatment of a patient with a history of iatrogenic implantation and hormone exposure. Owing to the role of multiple factors, the risk of developing DPL was significantly increased, and we share the patient's detailed clinical data. By sharing this case and reviewing the relevant literature, we hope to enhance the level of understanding of DPL among clinicians and pathologists to reduce the misdiagnosis rate and the risk of DPL. We present the following case report in accordance with the CARE guidelines.[8]

Case presentation

A 41-year-old woman was referred to Yichang Central People's Hospital (Yichang, China) with unexplained pelvic and abdominal masses. The patient had normal menstruations, and she underwent laparoscopic myomectomy in our hospital 5 years earlier because of uterine leiomyoma. One year postoperatively, the patient became pregnant and underwent induced abortion. Ultrasonography revealed hypoechoic masses in the pelvic and abdominal cavities measuring 39×28 mm^2 and 111×83 mm^2, respectively (Figure 1). Contrast-enhanced computed tomography (CT) revealed a large mass in the left lower abdomen and soft tissue nodules in the muscular layer of the left lower abdominal wall (Figure 2). Lower abdominal magnetic resonance imaging (MRI) revealed long T1 and short T2 signals on T2-weighted images (T2WI) (Figure 3). Blood laboratory testing revealed abnormal carbohydrate antigen (CA)19-9 and CA125

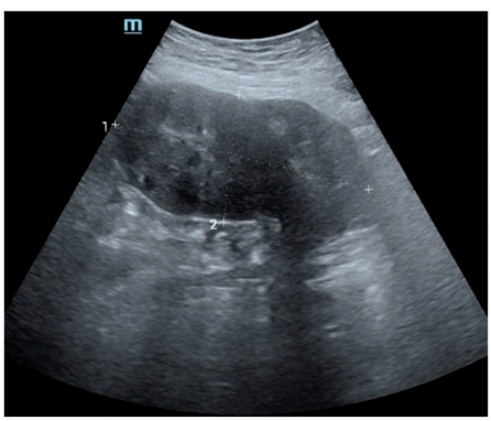

Figure 1. Lower abdominal ultrasonography showing a hypoechoic mass in the lower abdomen with a clear boundary and visible color Doppler blood flow signal.

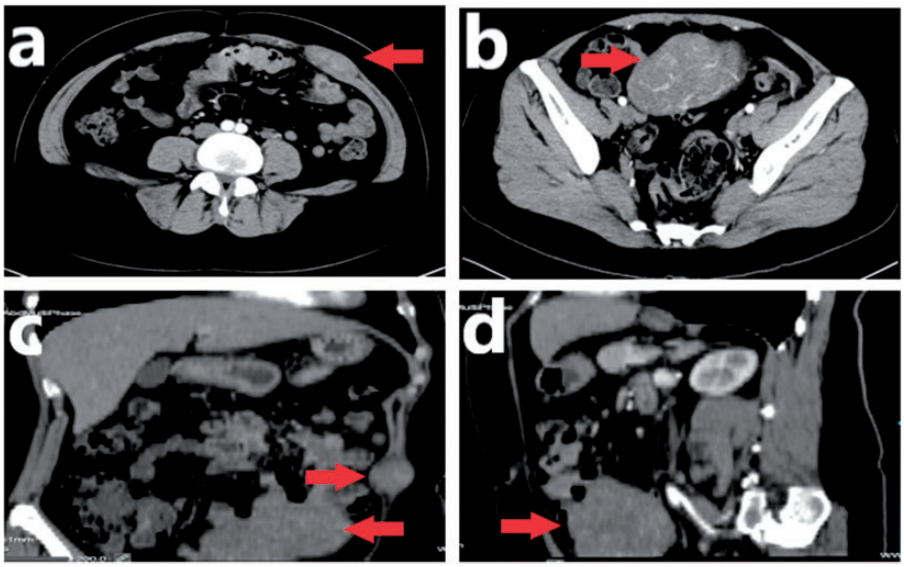

Figure 2. Lower abdominal enhanced computed tomography (CT); axial, coronal, and sagittal sections showing a large heterogeneous pelvic-abdominal mass lesion. The axial views (a, b) show two masses with clear boundaries, medium density, and abundant blood supply. The coronal view (c) shows two masses in the same plane. One large lump is indistinct from the surrounding intestine. The sagittal view (d) shows another large lump closely associated with the intestine. The red arrows indicate the mass(es) in each panel.

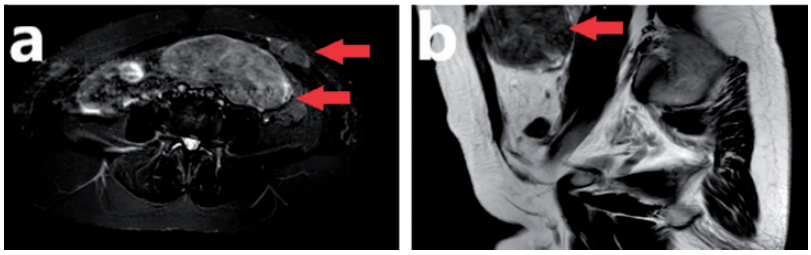

Figure 3. Lower abdominal magnetic resonance imaging showing a mass with long T1 and short T2 signals. The signals were not uniform, and the boundaries were clear on T2-weighted images; (a) axial view, (b) sagittal view. The red arrows indicate the mass(es) in each view.

concentrations; hormone levels were not tested. After a complete clinical investigation, the diagnosis was gastrointestinal stromal tumor (GIST), and the patient consented to undergo surgical treatment. Subsequently, diagnostic laparoscopy was performed, which identified a mass in the mesentery and another in the rectus abdominis. Frozen sections showed multiple spindle cells. Leiomyoma was considered, but peritoneal spread of GIST was difficult to rule out. Pathological examination of the specimens was performed after surgery. Gross findings (Figure 4a) indicated that the mesenteric and rectus abdominis masses comprised grayish-white nodules with intact surface capsules, and that the cross-section was grayish-white, solid, and moderate in texture. Microscopy (Figure 4b) revealed a fusiform structure composed of swirling smooth muscle cells. The spindle cells were uniform in size, and

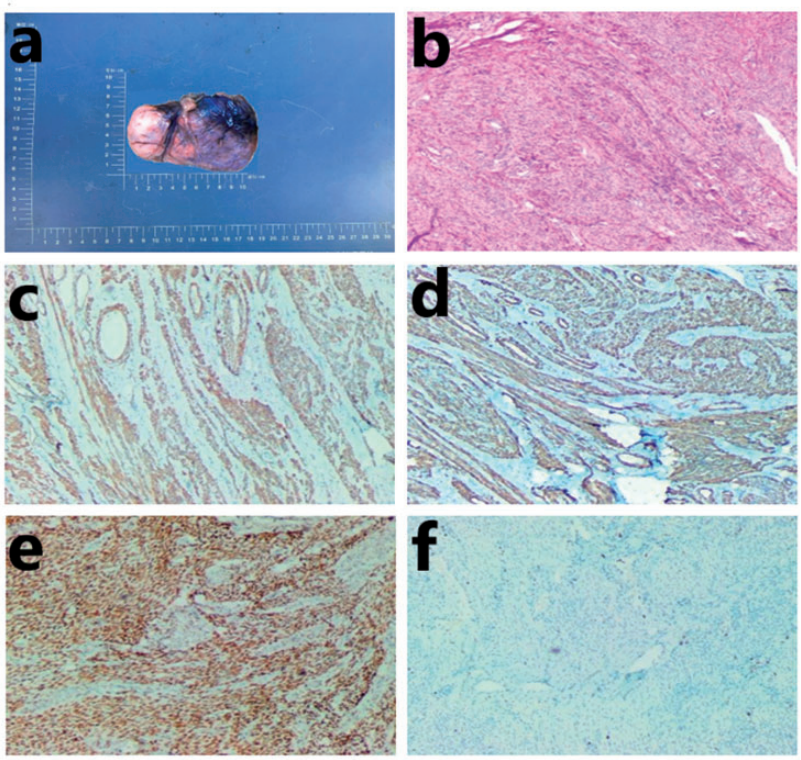

Figure 4. Histopathological findings (a) The excised specimens. (b) The fusiform structure is composed of smooth muscle cells, interwoven and arranged in a vortex pattern (hematoxylin and eosin; ×40 magnification). (c) Smooth muscle actin (SMA) expression was strongly positive. (d) H-caldesmon expression was strongly positive. (e) Estrogen receptor (ER) expression was strongly positive. (f) The Ki-67 index was <5%.

without atypia, nuclear division, or an invasive growth pattern. Immunohistochemical (IHC) staining showed that the spindle cells were positive for smooth muscle actin (SMA) (Figure 4c), desmin, H-caldesmon (Figure 4d), and estrogen receptor (ER) (Figure 4e); the Ki-67 index (Figure 4f) was <5%, and pan-cytokeratin (CK), cluster of differentiation (CD)34, CD117, and DOG-1 staining were negative. The diagnosis (abdominal cavity and rectus abdominis) was disseminated peritoneal leiomyomatosis. No further treatments were performed, and the patient was advised to check in regularly. She has been followed-up by telephone, and to date, there has been no recurrence (Table 1).

Table 1 Timeline of the patient's history and related treatment schedule.

Year	Event
2014	Laparoscopic myomectomy
2015	Pregnancy
2019	Multiple abdominal masses identified and surgical intervention performed
	Clinical misdiagnosis of gastrointestinal stromal tumor

Discussion

Reviewing the reported cases of DPL, most articles discussed a single factor leading to DPL. Some scholars believe that surgery

increases the risk of occurrence and spread of DPL.[9–11] Cases of multiple factors leading to DPL have been reported rarely. Our patient underwent laparoscopic myomectomy, and there was a possibility of tumor debris falling into the abdominal cavity during surgery. Less than 1 year after the operation, the patient became pregnant, and abortion was performed. Hormonal stimulation may also be an important cause of DPL. Laparoscopic surgery has been used to resect uterine leiomyoma for many years; the technique is mature, and the probability of DPL is very low. A recent paper highlighted the association between laparoscopic myomectomy and the incidence of DPL (0.12% to 0.95%).[12] However, the possibility of residual tissue falling into the abdominal cavity remains, which, coupled with hormone stimulation, leads to a significant increase in the incidence of DPL. The high ER expression in the tumor tissue of this patient confirmed that the abdominal tumor was affected by hormonal regulation. Some scholars have reported cases of DPL complicated with endometriosis or mesothelioma,[3,13] but this was not found in this case.

The clinical symptoms of DPL are usually atypical; blood tests have no specific indicators. Serological testing in our patient revealed elevated CA19-9 and CA125 concentrations, which were reported in previous cases.[14,15] The reason for these elevations is unclear. These indicators are specific clinical markers for digestive tract tumors and ovarian cancer. If the concentrations of these indicators are elevated, it is easy to consider abdominal metastatic cancer, leading to a misdiagnosis; a potential diagnostic trap. Most patients with DPL have no discomfort during gynecological examination. Occasionally, DPL may present as pelvic and abdominal pain or compression symptoms. DPL is diffusely distributed in the peritoneum, including the pelvic abdominal wall, greater omentum, intestinal serosa, mesentery, ovarian surface, uterus, and rectum. Most reports are characterized by diffuse small peritoneal nodules.[4] However, two large nodules are reported in this paper. The number and size of DPLs were not strictly defined in previous studies.

The preoperative diagnosis of DPL has always been a difficult problem, even intraoperatively. In this paper, GIST was diagnosed before and during the operation. The diagnosis was unclear until the final pathological diagnosis. Recently, Akamine et al. reported a case of GIST with DPL in which the authors encountered similar problems to those in our study.[16] Imaging features provide a crucial reference to make a clear diagnosis. On CT, masses in DPL are usually observed as well-circumscribed multiple nodules with contrast-enhancement compared with that of the myometrium or uterine fibroids. However, when necrosis, degeneration, or implantation of endometrial components occurs, enhancement is heterogenous, mimicking peritoneal carcinomatosis.[17] Although endometriosis was not present in this case, endometriosis also presents as multiple nodules with clear boundaries. Contrast-enhanced scans in DPL show moderate intensity, uneven density, and adequate blood supply. The superb contrast resolution and multiplanar capabilities of MRI make it particularly valuable for characterizing these tumors, which usually show low signal intensity similar to that of smooth muscle on T2WI. This feature helps differentiate DPL from peritoneal carcinomatosis (transferred or primary), which is usually T2-hyperintense. The MRI findings in this case were similar to those reported in the literature. Lower abdominal T2WI revealed a large heterogeneous pelvic-abdominal mass that appeared to be inseparable from the adjacent mesentery and omentum. A tortuous vascular pedicle was seen in the coronal views. Currently, the use of

positron emission tomography (PET)-CT in DPL is rare, and some scholars have reported that the lesions show strong uptake, with a maximum standardized uptake value (SUV) of 26.4.[18]

The main points in the pathological diagnosis of DPL are its multifocal nature (shown by imaging). Nodules consist of fusiform smooth muscle cells, occasionally containing fibroblasts and myofibroblasts, without atypia or mitosis (<1/50 per high power field (HPF)). The morphological arrangement is similar to typical uterine leiomyoma, which has a vortex pattern. Occasionally, DPL appears as an epithelial type, myofibroblast type, clear cell type, plexus type, or choroid type. The following differential diagnoses for DPL should be considered: (1) GIST, which is the most common mesenchymal tumor of the digestive tract, and which is characterized histologically by spindle cells, epithelioid cells, and occasionally, pleomorphic cells. IHC expression of CD117, CD34, and Dog-1 is also a feature. (2) Primary intraperitoneal leiomyosarcoma widely spread in the pelvic abdominal cavity. This sarcoma originates mainly from the retroperitoneum and is often located in the upper abdomen, mesenteric root, or near the retroperitoneum and is often accompanied by necrosis and cystic changes. Microscopically, sarcoma cells are poorly differentiated and have a high degree of atypia and numerous mitoses, which is very different from DPL. (3) Angiomyolipoma. This tumor is also benign, but vascular, adipose, and smooth muscle tissue can be seen histopathologically; no one tissue predominates. IHC indicates that vascular tissues are positive for CD-34, adipose tissue is positive for S-100, and smooth muscle cells are positive for SMA. (4) Multiple abdominal leiomyomas. These have no differences pathomorphologically, but can be distinguished mainly by medical history, hormone history, genetic history, and ER IHC status. Currently, there are no genetic differences.

There is no standard treatment for DPL. However, because of the rapid recovery and minimal trauma, laparoscopy should be the first choice for surgical diagnosis and treatment. For patients with fertility requirements, focal resection is feasible, and gonadotropin-releasing hormone agonists or aromatase inhibitors are used post-operatively.[4] For patients without fertility requirements, resecting the entire uterus, bilateral appendages, and the abdominal mass is feasible, and resecting the greater omentum is performed if necessary.[15] Recently, Benlolo et al. suggested that ulipristal acetate may be an effective, novel therapeutic option for managing DPL.[14] However, some scholars have suggested possible liver injury with this drug; therefore, it is necessary to closely monitor liver function.[19] Of concern with DPL is a tendency for recurrence and malignant transformation, with a reported risk of malignant degeneration of 2% to 5%.[20] Chiu et al. believe that several instances of huge tumors and recurrence are an indicator of malignancy.[21] However, the tumor sizes in our patient ranged from approximately 4 cm to 12 cm, and to date, there has been no recurrence or metastasis. The patient is satisfied with the treatment effect. DPL has a benign biological behavior, overall.

Conclusion

Through this case report, we hope to provide the following references for clinical practice: 1. Clinicians should take care during laparoscopic hysteromyoma resection to minimize the risk of residual tumor tissue falling into the abdominal cavity. 2. For patients with a history of fibroidectomy, hormonal stimulation should be minimized. If pregnancy is required, it should

be delayed to provide a preventive role. 3. For patients with uterine fibroids after surgery, the possibility of DPL should be considered in cases of abdominal soft tissue tumors, regardless of the duration. 4. For patients diagnosed with DPL, surgical resection should be as clean as possible to prevent the possibility of recurrence and malignant transformation.

Authors' contributions

XL and YH participated in the study design. XL wrote the manuscript. XL and YH participated in the literature search for the study and collected the images. QZ, LC, and YH revised the manuscript. All authors read and approved the final manuscript.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

Ethics and consent

Ethics committee approval was not required for this case report. Written informed consent from the patient for publication of this case report was obtained in accordance with the principles of the Declaration of Helsinki.

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