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Leiomyomatosis peritonealis disseminata (LPD): five case reports and review of the literature

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Summary

Purpose of investigation: Leiomyomatosis peritonealis disseminata (LPD) is a special type of leiomyomatosis with an unclear pathogenesis. *Materials and Methods:* The authors investigated five LPD patients who were treated at the Fudan University Shanghai Cancer Center (Shanghai, China) from 2012 to 2016. They reviewed the medical history, preoperative examination, intraoperative manifestation, and postoperative pathologic results. *Results:* The five LPD patients were all in reproductive age and four of them had a medical history of laparoscopy for uterine fibroids. Two of them had pathologic results of mitotically active leiomyoma. All the conditions may have contributed to the development of LPD. *Conclusion:* The use of laparoscopic power morcellation, active proliferative status of the uterine fibroids, and hormone in female patients may help cause LPD. The present study may improve our understanding of the disease.

Key words: Leiomyomatosis; Peritonealis; Disseminata.

Introduction

Leiomyomatosis peritonealis disseminata (LPD) is a special type of leiomyomatosis. Accurate diagnosis is often difficult prior to the surgery because diagnosis relies on medical history, preoperative examination, observations during surgery, and pathological results. As yet, the pathogenesis is poorly understood. It has been reported that the majority of LPD patients have previously been exposed to laparoscopic power morcellation during myomectomy or subtotal hysterectomy [1]. The Food and Drug Administration (FDA) also indicated that the use of laparoscopic power morcellation may contribute to the development of LPD [2]. Because the etiology of LPD remains unclear, there is no standard treatment for LPD. The present study analyzed five LPD patients who were treated in Fudan University Shanghai Cancer Center (Shanghai, China) from 2012 to 2016 to improve our understanding of this disease. Written informed consents were obtained from the patients.

Materials and Methods

Case 1: A 31-year-old female (gravida 3, para 1, aborta 2) underwent laparoscopic myomectomy in 2004 and cesarean section in 2005 in local hospital. The authors do not know the details of the two surgeries and the postoperative pathologic report of the laparoscopic myomectomy. In June 2014, MRI found some masses in the right lower abdomen and pelvic cavity. CT also found the tumor in the hepatorenal recess (Figure 1). The patient presented with no specific symptoms. In addition, cancer antigen 125 level of 34.18 U/ml (normal range, < 35 U/ml), cancer antigen 199 level of 3.26 U/ml (normal range, < 27 U/ml), carcino-embryonic antigen level of 0.72 ng/ml (normal range, < 5.20), and an α-fetoprotein level of 2.83 ng/ml (normal range, < 10 ng/ml) were all within normal range. Based on the clinical manifestations and auxiliary examinations, an exploratory laparotomy was performed in 2014. During the surgery, all of the leiomyoma on the abdominal wall, omentum, pelvic peritoneum, hepatorenal recess, and the surface of intestine and mesentery were removed. Because the patient requested to preserve fertility, the uterus and bilateral adnexa had been retained. The blood loss is 700 ml and the blood infusion of red blood cell suspension was two units during the operation. Postoperative pathology determined a diagnosis of LPD. Immunohistochemical staining revealed the resected tissues to be positive for h-caldesmon, desmin, α-smooth muscle actin (SMA), and negative for DOG-1, S-100, CD117, and CD34, with a Ki-67 labeling index of 5-10%. The patient was monitored by follow-up every three months. At the time of writing, the patient remained symptom-free for 34 months without any evidence of recurrence.

Case 2: A 33-year-old female (gravida 3, para 1, aborta 2) underwent cesarean section in 2007 and laparoscopic myomectomy in 2011 in a local hospital. The postoperative pathology report: mitotically active leiomyoma. In September 2014, ultrasound found some masses in the abdomen and pelvic cavity. The patient presented with no specific symptoms. In addition, cancer antigen 125 level was slightly elevated to 47.78 U/ml (normal range, < 35 U/ml) and the other tumor markers were within normal range. During the operation, all of the leiomyoma on the abdominal and pelvic peritoneum were removed and hysterectomy and bilateral

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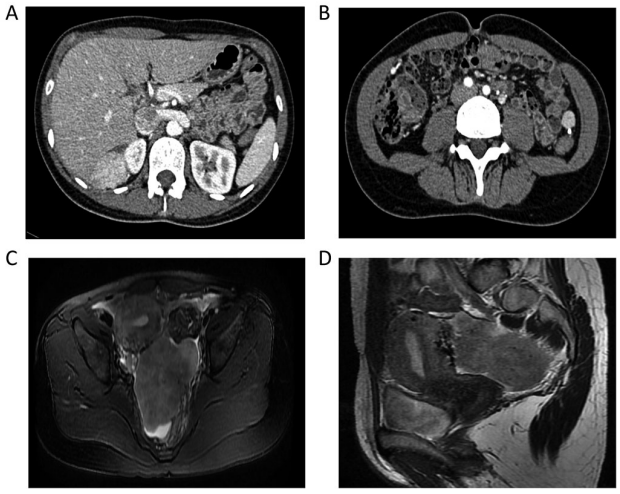

Figure 1. — CT and MRI view of case 1. (A) transverse view of CT of the upper abdomen before treatment. (B) Transverse view of CT of the middle abdomen before treatment. (C) Transverse view of MRI of the pelvic cavity before treatment. (D) Sagittal view of MRI of the pelvic cavity before treatment.

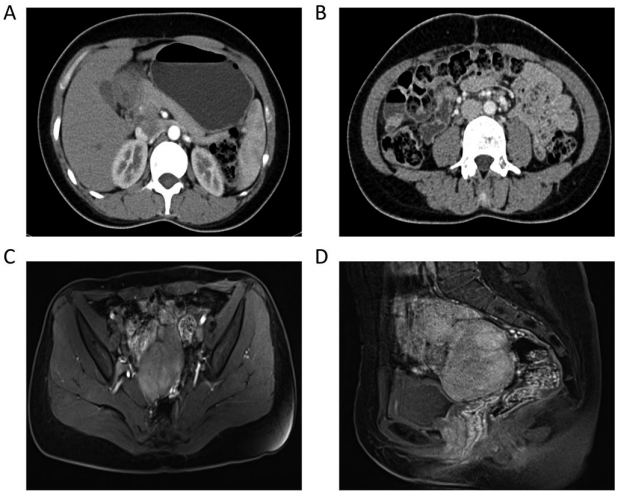

Figure 2. — CT and MRI view of case 4. (A) Transverse view of CT for the upper abdomen before treatment. (B) Transverse view of CT of the middle abdomen before treatment. (C) Transverse view of MRI of the pelvic cavity before treatment. (D) Sagittal view of MRI for the pelvic cavity before treatment.

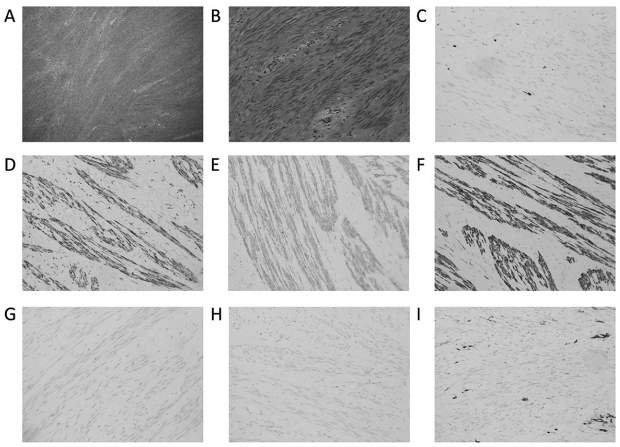

Figure 3. — Post-operative pathological analysis to determine a diagnosis of leiomyomatosis peritonealis disseminata. Hematoxylin and eosin staining at (A) ×40 magnification and (B) ×200 magnification. Positive immunohistochemical staining for (C) Ki67 (positive rate, < 5%). (D) h-caldesmon, (E) α-SMA, (F) desmin, and negative immunohistochemical staining for (G) DOG-1, (H) CD117 and (I) CD34 x200 magnification.

salpingo-oophenrectomy were performed concurrently. The blood loss was 500 ml and the blood infusion of red blood cell suspension was two units during the surgery. Postoperative pathology determined a diagnosis of LPD with occasional mitosis and no necrosis. The patient remained symptom-free for 31 months without any evidence of recurrence.

Case 3: A 48-year-old female (gravida 5, para 2, aborta 3) underwent laparoscopic subtotal hysterectomy because of uterine fibroids in 2006 in local hospital. The authors do not know the postoperative pathologic report. In 2014, ultrasound found some masses in the pelvic cavity. The patient presented with a progressive stomach ache. In addition, cancer antigen 125 level was slightly elevated to 54.30 U/ml (normal range, < 35 U/ml) and the other tumor markers were within normal range. The surgery was performed in October 2014. All of the leiomyoma on the omentum and pelvic cavity were removed and residual trachelectomy and bilateral salpingo-oophorectomy were performed concurrently. The blood loss during the operation was 250 ml without blood infusion. Postoperative pathology determined a diagnosis of LPD. The patient remained symptom-free for 30 months without any evidence of recurrence.

Case 4: A 37-year-old female (gravida 2, para 1, aborta 1) underwent cesarean section in 2002 and laparoscopic myomectomy in 2014 in local hospital. The postoperative pathology report: mitotically active leiomyoma. In May 2015, ultrasound found some masses in the pelvic cavity. The patient received laparoscopic debulking surgery including hysterectomy and bilateral salpingectomy in a local hospital. In April 2016, a gynecological ultrasound revealed an about 7.0-cm mass in the pelvic cavity. CT of the upper abdomen did not find any mass. MRI of the lower abdomen and pelvic cavity found a 6.9×5.9-cm mass in the pelvic cavity (Figure 2). All the tumor markers were all within normal range. An exploratory laparotomy was performed in 2016 in the present hospital. During the surgery, the pelvic mass near the rectum was removed. The blood loss during the operation was 50 ml without the blood infusion. Postoperative pathology determined a diagnosis of LPD. Immunohistochemical staining revealed the resected tissues to be positive for desmin, h-caldesmon, α-SMA, and negative for DOG-1, CD117, and CD34, with a Ki-67 labeling index of < 5% (Figure 3). Until now, the patient remained symptom-free for 12 months without any evidence of recurrence.

Case 5: A 32-year-old female (gravida 2, para 1, aborta 1) received cytoreductive surgery in 2008 because of LPD. It was reported that the masses in the abdominal and pelvic cavity and the uterus and bilateral adnexa were removed at the same time. In April 2012, a gynecological ultrasound revealed the masses in the abdominal and pelvic cavity. All the tumor markers were all

within normal range. An exploratory laparotomy was performed in 2012 in the present hospital. During the surgery, all of the leiomyoma on the omentum, the appendix, the terminal ileum, and the other abdominal and pelvic cavity were removed and an end-to-end ileocolic anastomosis were performed concurrently. The blood loss during the operation was 300 ml without the blood infusion. Postoperative pathology determined a diagnosis of LPD. Immunohistochemical staining revealed the resected tissues to be positive for desmin, ER, PR, and negative for CD10, h-caldesmon, α-SMA, CD117, and CD34. Until now, the patient remained symptom-free for five years without any evidence of recurrence.

Discussion

Willson and Peale [3] reported the first case of LPD in 1952. Although LPD is benign, it exhibits recurrent and malignant tendencies [4-10]. LPD lesions always appear at the omentum, small intestine, colon, uterus, ovary, oviduct or pouch of Douglas with no clinical symptoms. Previous studies hypothesize that the use of laparoscopic power morcellation may enable the fragments to spread and cause LPD [1, 11]. In this study, the four patients had a surgical history of laparoscopy for uterine fibroids, in which laparoscopic power morcellation was used. However, the last patient developing LPD without this history showed that the causes of LPD were complex and multifactorial.

The pathologic report in case 2 or 4 showed that the leiomyoma during laparoscopy was mitotically active. The authors also found a Ki-67 labeling index of 5-10% in case 1 and < 5% in case 4. Therefore the authors suggest that adaptation and multiplication of the uterine fibroids are also important.

LPD often occurs in women of reproductive age. The condition of LPD may be affected by estrogen and progesterone levels [12]. It was reported that estrogen and progesterone may differentiate the fibroblast-like cells into smooth muscle-like cells and decidua-like cells [13]. Hormonal stimulation is a promoter of the process for subperitoneal mesenchymal stem cells that undergo metaplasia and differentiation to smooth muscle, fibroblasts, myofibroblasts, and decidual cells [14]. Therefore, the majority of studies suggest that women of reproductive age should undergo lesion excision and omentectomy followed by ovarian ablation or suppression, such as gonadotropin-releasing hormone agonists (GnRH-a) [15], or aromatase inhibitors [16] or megestrol acetate [17]. A study has reported that GnRH-a therapy following surgery can prevent new lesions [18]. Other studies have shown that the tumor may regress post partum[19, 20].

So far, LPD is not diagnosed during surgery by frozen section. There is no standard for the diagnosis of LPD, which often depends on medical history, preoperative examination, intraoperative manifestation, and postoperative pathology. Moreover, the pathogenesis of LPD remains poorly understood and no standard treatment exists for LPD. So individualized treatments have been considered. For those patients who do not desire to bear children, total abdominal hysterectomy, omentectomy, salpingo-oophorectomy, or debulking should be the most appropriate alternatives [21, 22]. In this study, except for case 1 who retained the uterus and bilateral adnexa and case 4 who retained the ovaries, the other three patients all received hysterectomy and bilateral salpingo-oophorectomy. For those patients with distant metastasis who cannot undergo surgery or malignant transformation, ovarian suppressin or systemic chemotherapy may be considered [15, 23]. Although LPD has malignant tendency [4-10], there have been no malignant transition in our five cases until now. One study reported that LPD is sometimes associated with endometriosis [12]; a possible explanation is that the two diseases may be derived from the same cellular origin [23, 24]. However, there were no endometrial lesion in the present five patients.

Conclusion

In conclusion, the diagnosis of LPD is rare and difficult. The majority of LPD patients have a medical history of laparoscopy for uterine fibroids. The pathology of some uterine fibroids is mitotically active leiomyoma. The use of laparoscopic power morcellation may contribute to the development of LPD. In women of reproductive age, hormonal stimulation is also a promoter for LPD. So far, there is no standard treatment for LPD. Individualized treatments have been considered, including total abdominal hysterectomy, salpingo-oophorectomy, omentectomy, or debulking surgery, followed by ovarian suppressin or systemic chemotherapy. In general, the prognosis of most LPD patients is good as the minority become malignant.

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