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CASE REPORT

Leiomyomatosis Peritonealis Disseminata Associated with Endometriosis

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ABSTRACT

Leiomyomatosis peritonealis disseminata (LPD) is a rare disease, characterized by the presence of multiple smooth muscle tumour nodules scattered over the abdominopelvic viscera and peritoneum which occurs mostly in women of reproductive age. Approximately 55 cases have been reported in the world literature so far. LPD is a benign condition and mostly asymptomatic for which conservative management is indicated. However, 8 cases of them were complicated by sarcomatous degeneration. Because LPD has a definite malignant potential, extensive sampling of the lesions and careful follow-up should be recommended. An aggressive surgical approach seems to be necessary in some cases especially in the cases who have symptoms and no dramatic response to conservative treatment. The case of a 35 year-old woman is presented. The patient's history revealed prolonged exposure to oral contraceptives, for 18 years, with first presentation of pelvic endometriosis. Six years later, LPD and endometriosis were diagnosed by diagnostic laparoscopy with histological examination due to recurrent chronic pelvic pain. Eight months of GnRH analog treatment and 2 years of follow-up were performed. Finally, total abdominal hysterectomy with debulking of culdesac, bilateral salpingo-oophorectomy, omentectomy had to be done due to the recurrence of severe chronic pelvic pain. Pathologic studies showed an admixture of leiomyomatosis peritonealis disseminata (LPD) and endometriosis. The association with endometriosis suggests that LPD may be derived from subcoelomic mesenchyme through a metaplastic process.

Key words: Leiomyomatosis peritonealis disseminata (LPD), endometriosis

Leiomyomatosis peritonealis disseminata (LPD), also known as diffuse peritoneal leiomyomatosis, is a rare disease of unknown cause, characterized by the presence of multiple smooth muscle tumour nodules scattered over the abdominopelvic viscera and peritoneum which occurs mostly in women of reproductive age, especially with pregnancy or associated with prolonged exposure to oral contraceptive agents but rarly in postmenopausal ones. All but one of the patients were women.[1] There is a very high association with excess exogenous and endogenous female gonadal steriods, specifically estrogen and progesterone. LPD appears to be derived from subcoelomic mesenchyme through a

metaplastic process[2] or from the Mullerian epithelium, which is distributed throughout the subperitoneal mesenchyme seems possible in histogenesis.[3] An unusual predilection or selective sentivity of subperitoneal mesenchymal cells to estrogen and progesterone may account for development of this entity.[2,3] Approximately 55 cases have been reported in the world literature so far. Conservative treatment with long-term follow-up is recommended because generally LPD has generally indolent clinical course and undergo spontaneous regression.[3-7] After reviewing literature, 8 cases of malignant degeneration of this disease, including the only male patient, have been reported.[1,8-13] Extensive sampling of the lesions should be recommeded. An aggressive surgical approach seems to be necessary in some cases. We reported a LPD patient associated with endometriosis, normal levels of estrogen and progesterone, with 2 year follow- up and had to be finally operated by aggressive surgery.

Case Report

A 35-year old female who was gravida 0 with a history of good health most of her life, presented to her physician in the year of 1990 complaining of dysmenorrhea after on contraceptive pills for 11 years, lately with minipills. Pelvic endometriosis stage I. was diagnosed and electro-coagulated by laparosocpy. She came to her physician again in February 1997 with an experience of 2-year severe chronic pelvic pain. Innumerable grey-white tumour nodules ranging from 0.5 to 5 cm in diameter were found covering the peritoneal surface of abdominal cavity, small intestine, colon, mesentery, omentum and the surface of uterus and adnexal structures by second laparoscopy. Leiomyomatosis peritoneal disseminata associated with endometriosis was diagnosed by histologic examination, without high levels of estrogen and progesterone. Conservative treatment and closed follow-up are performed, IUD was applied intead of contraceptive pills. However, after 6 month follow-up she had no relief of her symptoms and no regression of leiomyomatosis peritonealis disseminata proved by the third laparoscopy. GnRH analog treatment was considered in September 1997. With a good result, no symptoms of pelvic pain after 1 month of treatment with no severe side effects. GnRH analog was continued until April 1998. Minimal regression of LPD was found on the fourth laparoscopy. One month later in July 1998, her disease progressed as manifested by recurrent chronic pelvic pain and could not be inhibited by anti-analgesic drugs (NSAID). After counselling, we began 3-month GnRH analog pre-operative treatment in October and total abdominal hysterectomy with debulking of cul de sac, bilateral salpigo-oophorectomy, omentectomy had to be performed in January 1999. Tumor removal was subtotal.

With operative findings, innumerable grey-white tumour nodules ranging from 0.5 to 5 cm in diameter were seen covering the peritoneal surface of abdominal cavity, small intestine, colon, mesentery, omentum and the surface of uterus and adnexal structures, including in cul de sac (Fig. 1-3).

Not only was peritoneal surface involved, muscular layers in many areas of intestines were involved as well. In addition, a lot of endometriotic spots could be found between tumour nodules on almost all organs mentioned. Malignancy degeneration could not be excluded by frozen sections of the ometum. Nevertheless, due to innumerable nodules being in muscular layers of intestines and severe bleeding, almost all tumour nodules attached to intestinal wall, mesentery, and parietal peritonium were not removed. Histologically, all sections were composed of proliferating smooth muscle cells with rod-like nuclei showing extremely rare mitotic figures without cytologic atypia, confirming a diagnostic of LPD. Endometrium without atypia and stroma with haemosiderin macrophages were also found on almost all sections including occasional endometrial glands and stroma within smooth muscle nodules. She was discharged following an unevenful recovery. Every 6-month follow-up by clinical symptoms, CA-125 and CT scan were planed.

Fig. 1.

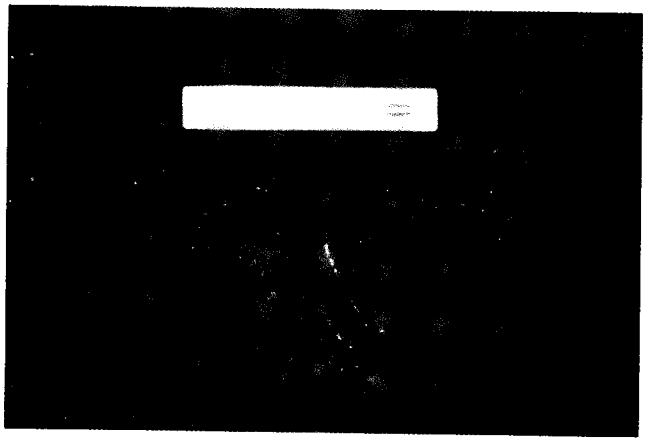

Fig. 2.

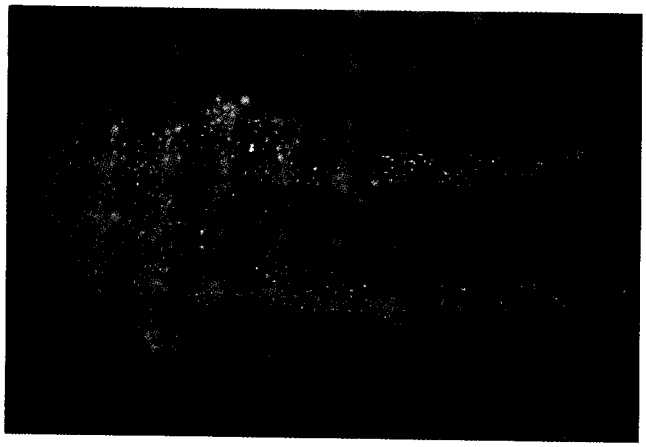

Fig. 3.

Discussion

The benign tumours of leiomyomatosis peritonealis disseminata must be differentiated from peritoneal metastasis of malignant tumours in order to avoid overtreament with a radical operation. This patient is the first LPD associated with endometriosis seen in our clinic, an incidental finding during diagnostic laparoscopy for suspicious of pelvic endometriosis. Biopsies were done with suspicious of peritoneal metastasis of malignancy. The association with endometriosis suggests that LPD may have a metaplastic origin from subcoelomic mesenchymal cells. This association however has been found in the literture in only a few cases.[14-17] LPD has almost always been associated with conditions characterized by high levels of circulating estrogen, such as pregnancy, as well as in women with granular cell tomours[2] and in those using oral contraceptives. The presented case further confirms the association between prolonged exposure to oral contraceptives and LPD. However, the serum estrogen and progesterone levels determined in our patient did not reveal any abnormal change. An unusual sensitivity of subperitoneal mesenchymal cells in this patient to estrogen and progesterone may account for development of this entity.[2, 3, 14] One of interest in this case is innumerable tumour nodules found in muscular layers of intestines as well. There have been only few cases of intestinal wall involvement reported in literature.[18, 19] Immunohistologic examinations comfirmed the myocytic character of the lesion and substantiated the hormonal influence on growth and regression of LPD nodules by detection of estrogen and progesterone receptors in the tumour cells.[20] To our knowledge, LPD is a benign condition and mostly asymptomatic for which conservative management is indicated.[3-7] After removal of hormonal stimulation, LDP spontaneously resolves.[2, 5, 7, 21] Many cases of LPD have regressed at postpartum period, after bilateral oophorectomy, or after treatment of GnRH analog.[22] Conservative tratment and 6-month follw-up in this case were performed, IUD instead of contraceptive pills, but her symptoms and status of

disease did not regress. The association with endometriosis might be the cause of her symptoms. GnRH analog was a another one considered on her as suggested by previous author.[22] Unfortunately, she was free of symptoms during 8-month GnRH analog treatment, there was just only minimal regression of LPD. Furthermore, 1 month after stop of treatment, her disease progressed, as manifested by recurrent chronic pelvic pain and could not be managed by NSAID. Since LPD has a definite malignant potential, the onset of sarcomatous degeneration of LPD could occur at a distance of 8-24 months from the initial diagnosis.[8] In addition to a recent report in 1998 which showed a patient who experienced sarcomatous transformation after having diagnosed as LPD for 11 years.[9] A close long-term follow-up is desirable. In practice, there are no firm guidelines in the literature with regard to the management of these patients. GnRH analog could not be applied to relieve her symptoms again for a long time. It could not seem to relieve her symptoms with further conservative treament. Non-invasive investigations such as an increase of CA 125,[8] ultrasound, CT scans and MRI may be helpful for early sarcomatous degeneration detection. Most radiologists have no familiarity with its imaging features, though. Moreover, it must be emphasized that malignant degeneration could only be excluded by extensive sampling of the lesions and by the favourable clinical outcome. After counselling, aggressive surgery was considered to exclude malignant degeneration, to eliminate her symptoms and to eliminate hormonal stimulation of tumor growth.[13, 23] One month after surgery, the patient free of symptoms. Although a report showed LPD could have been aggravated by estrogen replacement therapy in postmenopausal patient,[22] we prefer to apply estrogen replacement therapy preventing hypoestrogenism in this patient after 6 months of surgery. Every 6-month CA-125 and CT scan follow-up for signs and symptoms of progression and sarcomatous degeneration are planned.

In conclusion, because LPD is an uncommon benign disease, There is no firm guidelines in literature with regard to the management of these patients. However conservative treatment, is recommended with close long-term follow-up. It must be differentiated from peritoneal metastasis of malignant tumours in order to avoid overtreatment with a radical operation. With high malignant potential, variation of pathological and clinical courses, lines of managment seem to depend on many factors such as age, associated causes, symptoms, severity, histology, responses of treatments and follow-up ability. Extensive sampling of the lesions or aggressive surgical approach may be necessary especially in the cases who have symptoms or do not dramatically respond to conservative treatment.

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