Leiomyomatosis peritonealis disseminata with malignant degeneration. A case report

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Summary

Leiomyomatosis peritonealis disseminata (LPD) is an uncommon condition characterized by multiple nodules of smooth muscle within the peritoneal cavity. It usually occurs during reproductive age, and is especially associated to exogenous and endogenous exposure to female gonadal steroids. A limited number of cases of malignant transformation have been reported in the literature. We report a case of leiomyomatosis peritoneais disseminata with sarcomatous degeneration in a 37-year-old nulligravid patient with no exposure to exogenous estrogen or progesterone, revealed by increased abdominal perimeter. The imaging techniques showed occupation of the entire peritoneal cavity by bulky solid masses. The patient underwent a total hysterectomy with bilateral salpingo-oophorectomy and tumoral mass resection. The histopathologic diagnosis was leiomiomatosis peritonealis disseminata with leiomyosarcomatous degeneration. The patient was given systemic chemotherapy with tumoral progression, and died 24 months after the initial diagnosis.

Key words: Leiomyomatosis peritonealis disseminata. Sarcomatous degeneration.

Introduction

Leimyomatosis peritonealis disseminata (LPD) is a rare entity characterized by the presence of multiple leiomyomas throughout the peritoneal cavity. It is usually diagnosed in advanced stages of the disease, being discovered incidentally during regular follow-up, surgery or imaging examinations. Because of the peritoneal dissemination of the tumorous nodules, the macroscopic appearance can mimic peritoneal carcinomatosis.

The pathogenesis of the LPD remains unknown. It is considered to originate from metaplasia of subperitoneal mesenchymal cells that usually pursues a benign course. Estrogen and progesterone receptor expression has been found in 92% of LPD cases. These receptors may serve as targets for steroids to stimulate tumor growth, and make this pathology a typical disorder appearing during reproductive age. Malignant degeneration is a rare condition (2-5%) that implies a poor prognosis.

We present a case of a woman with a sarcomatous degeneration of a LPD, associated with endometriosis.

Case Report

A 37-year-old nulligravid woman was referred to our emergency service for evaluation of increased abdominal perimeter. Her medical history was remarkable for a phlebite in the right leg one year before. She had no history of exposure to oral contraceptive agents.

On physical examination, she had an increased abdominal circumference with important collateral circulation, and a large abdominal mass that occupied the whole abdominal cavity. Gynecologic examination was difficult due to the size of the mass; the uterus and ovaries were not palpable. The parametrium were not infiltrated. Edema was present in both legs, but was more significant in the right one. General blood and urine analysis was normal. Abdominal ultrasonography (US) showed a heterogeneous solid mass that occupied the abdominal cavity, with calcium in the right flank, displacing the intestinal structures. There was a right chronic hydronephrosis and ectasia of the left kidney due to ureteral compression/entrapment. The uterus and ovaries were of normal size. There was no ascites. Tumor markers were within normal range, except CA 125 = 56.9 U/ml. Thorax radiology and mammography were normal.

Computed tomography (CT) scan revealed occupation of the entire peritoneal cavity by bulky solid masses with abundant and large calcifications in the right hemiabdomen. The pouch of Douglas was occupied with rectal left displacement. A normal uterus was displaced forward, and intestinal structures displaced upwards. There was left kidney ectasia (degree II) due to ureteral lumbar compression and atrophic parenchyma of the right kidney with important functional alteration due to terminal hydronephrosis, with ureteral compromise at the sacrum level. A right iliofemoral venous thrombosis was suspected and confirmed by echo Doppler.

The patient underwent laparotomy: the surgical procedure included total hysterectomy with bilateral salpingo-oophorectomy, tumoral mass resection and presacral adenopathy dissection. Surgical findings were multiple intraabdominal bulky solid masses, the biggest measuring 30 cm depending on the uterosacral ligament and retroperitoneum (Figure 1). Two other bulky masses in both iliac fossae and both flanks were seen (Figure 2), the left one measuring 15-20 cm arising from the broad ligament and the retroperitoneum, with lipoid content that entrapped the sigma and the left ureter. The right one was of stony consistency, arising from the broad ligament and retroperitoneum, of 10-15 cm, that entrapped the right ureter. Both ureters had significant dilatation. Other multiple solid nodules (leiomyomas/sarcomas) of 3-4 cm the disseminated in the parametrium were found. The uterus and both ovaries were of normal size and morphology. Uterosacral ligaments were adherent to the large tumoral mass. There were palpable iliac adenopathies, and palpable 2 cm presacral adenopathy. The right and the left tumors were not completely resectable, and the patient underwent suboptimal surgical cytoreduction, with residual tumor of 3 and 4 cm, respectively. The intraoperative

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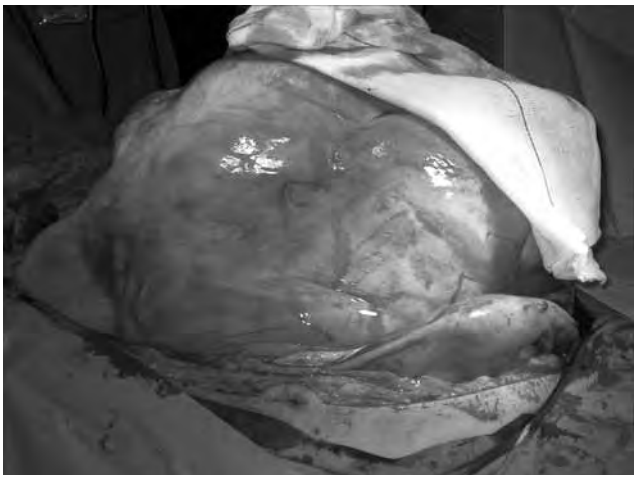

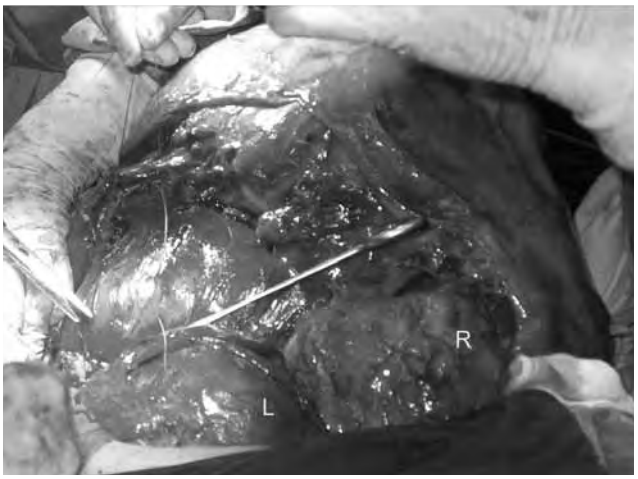

Figure 1. — Intraabdominal bulky solid mass of 30 cm depending on the uterosacral ligament and retroperitoneum. The uterus and both ovaries were of normal size and morphology.
Figure 2. — Two other bulky masses: the left one (L) measuring 15-20 cm with lipoid content. The right one (R) of stony consistency.

biopsy of the presacral adenopathy showed a malignant fusocellular anaplasic tumor, compatible with leiomyosarcoma. This was confirmed in the final anatomopathology examination.

The patient was transfused with seven units of packed red blood cells and three units of fresh-frozen plasma in the operating room, and was transferred to the intensive care unit.

On macroscopic examination the final pathology results showed endocervical endometriosis and an endocervical polyp, six nodular masses ranging in size from 4.5 cm to 17.5 cm, and a nodular mass 36 cm in diameter and 6700 g covered by serosa. The histopathologic microscopic diagnosis was leiomyomatosis peritonealis disseminata with leiomyosarcomatous degeneration and necrosis, multiple atypical mitosis (mitosis averaged more than 5 per 10 high power fields), with pleomorphic areas, mixoid areas, lipomatous metaplasia and bone metaplasia. There was no vascular infiltration. It was associated with endometriosis in one of the masses and cervical stroma. The immunohistochemical staining was positive for muscle-specific actin, caldesmon and CD10. The staining for AE1/AE3 and S100-protein was focally positive. Desmin was negative. Hormone receptors were positive for estrogen and progesterone.

The patient was given triptorelin to decrease hormonal stimulation to the masses, and avoid disease progression. She was only given one dose of 3.75 mg of triptorelin because of mass growth. One month after surgical treatment, magnetic resonance imaging (MRI) showed multiple pelvic masses measuring together 20 x 15 x 12 cm with a compressive effect. Palliative systemic chemotherapy with adriamicine was prescribed. Objective tumor response was achieved and sustained for six months. Despite chemotherapic treatment with five lines of agents (adriamycin, gemcitabine+DTIC, isophosphamide, yondelis and nexavar), the masses did not decrease in size. Ureteral entrapment required a nephrostomy and ureteral catheterism. The patient died 24 months after the initial diagnosis of LPD due to mass progression and massive rectorragia with cardiorespiratory and multiorganic failure.

Discussion

LPD is a rare disease described in 1952 by Willson and Peale [1]. The condition implies an important diagnostic and therapeutic challenge due to its low prevalence and absence of treatment guidelines. Since this pathology was described, it has been reported in less than 150 patients in the available literature.

The etiopathogenesis of LPD is unclear. This syndrome might be caused by a metaplasia of submesothelial and omental multipotential cells to fibroblasts, myofibroblasts [2-4], smooth muscle cells and decidual cells, in cases of hormonal stimulation and individual predisposition [5]. Estrogens and progesterone play an important role in the pathogenesis. An association with high levels of exogenous and endogenous female gonadal steroids has been found, as prolonged oral contraceptive use, pregnancy, functional granulosa cell tumors, ovarian stimulation or combined hormone replacement therapy use [6-9]. The association with endometriosis suggests that this disease may have a metaplastic origin. Our patient had endometriosis in one of the masses.

There could be some ethiopathogenic mechanisms yet unknown, since 3.9% of the described cases develop in postmenopausal women [3] without either combined hormone replacement therapy or concomitant pathology and in two previously healthy men [10]; there are also documented symptoms of LPD in patients with no uterus and no ovaries and a case of familial clustering [11].

LPD has a fast and indolent course until the characteristic symptoms of a usually bulky mass appear. The most common clinical signs are increasing abdominal perimeter and unspecific abdominal pain. The diagnosis of the retroperitoneal mass is done through physical and imaging examinations, in which it can mimic a peritoneal carcinomatosis. Cross-sectional imaging studies show numerous well-circumscribed solid masses in the peritoneal cavity that vary in size from several millimeters to many centimeters. The masses are often heterogeneous in CT attenuation and enhance similar to uterine leiomyomas. At MRI imaging, the masses are isointense relative

to muscle with T1-weighted sequences, heterogeneously enhanced following intravenous administration of gadolinium, and are low signal intensity with T2-weighted sequences. Anatomopathologic study confirms the diagnosis and rules out malignant degeneration.

Surgery is the mainstay treatment for LPD. It is also necessary to decrease estrogenic stimulus to the masses [3] by removing all existing hormonal treatment and using medical treatments as GnRH-analogues plus add back therapy, bilateral oophorectomy and, more recently, by the use of selective estrogen receptor modulators (SERMs) (5) and aromatase inhibitors (anastrozole) [12].

The prognosis of LPD is favorable in most cases, with spontaneous regression of the leiomyomas or regression following withdrawal of ovarian hormones or oophorectomy. This prognosis worsens in recurrent cases, and even more dramatically in those with sarcomatous degeneration (up to 2-5%) [10]. The interval of malignant transformation ranges from the time of diagnosis to eight years after the initial diagnosis, the average being 13 months in reported cases of the available literature [13].

LPD with a malignant transformation is a locally aggressive pathology, with a strong tendency to recur despite non-affected surgical margins. It can metastasize, especially to the retroperitoneal lymph nodes and lungs [14, 15]. The most frequent cause of death is disease progression with organ compression like the kidneys, liver or digestive organs, which leads to organic failure. In our case, the patient died due to mass growth and gastrointestinal bleeding with cardiorespiratory failure.

Up to this time, chemotherapy is administrated as a palliative treatment, without any existing standards of administration [16]. A close control of patients with LPD must be performed at six-month intervals because of the possibility of early recurrence or malignant degeneration [9, 14].

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