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CASE REPORT

Leiomyomatosis Peritonealis Disseminata with Features of Carcinomatosis on Laparoscopy

A case report

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وُرامٌ عَضَلِيٌّ أَمْلَس صفاقي منتشر مع صفات سرطانية عند تنظير البطن

تقرير حالة

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الملخص: الوُرامٌ العَضَلِيٌّ الأَمْلَس الصفاقي مرض نادر يتميز بتكاثر العقيدات الحميدة تحت الصفاق وتتكون أساسا من خلايا العضلات الملساء الحميدة، والتي تحاكي السرطان الصفاقي بالعين المجردة . هذا وصف لحالة امرأة عمرها 43 عاما كانت تشكو من غزارة الطمث مع ضغط وآلام في الحوض. أظهرت الموجات فوق الصوتية لمنطقة الحوض وجود أورام ليفية رحمية وكيس مبيضي. كان من المقرر أن يجرى لها استئصال الرحم مع البُوق والمَبيْض الأيسر لتخفيف الأعراض. شوهدت صورة سرطان صفاقي عند التنظير وتم أخذ خزعات متعددة أثناءه وأحيلت المريضة إلى فريق الأورام النسائية. أجريت الجراحة النهائية وكان التشريح المرضي النهائي متسقا مع الوُرامٌ العَضَلِيٌّ الأَمْلَس الصفاقي بدون وجود دلائل سرطانية. لم تعطى الهرمونات البديلة بعد الجراحة. ولو أن شكل الوُرامٌ العَضَلِيٌّ الأَمْلَس الصفاقي بالعين المجردة يشبه السرطان . لكن عادة ما يتبع مساق حميد بعد الجراحة . راجعنا الأدبيات الطبية المنشورة بمختلف المصادر باستعمال مفاتيح الكلمات لمعرفة العلاج الحالي للورام العَضَلِيٌّ الأَمْلَس الصفاقي واختطار تحوله إلى ورم خبيث. يعتبر تشخيص الوُرامٌ العَضَلِيٌّ الأَمْلَس الصفاقي تحد. ولو أن تحوله إلى مرض خبيث نادر لكنه يمكن أن يحصل. خاصة ان الهرمونات تلعب دورا مهما في إمْراض الوُرامٌ العَضَلِيٌّ الأَمْلَس الصفاقي . ولهذا يجب متابعة المرضى بعد الجراحة بعناية إذا كانوا يعالجون بالهرمونات البديلة. لأن هذه الأورام يمكن أن تنمو من جديد وتسبب أعراضا. أو تتحول إلى أورام خبيثة.

مفتاح الكلمات: الوُرامٌ العَضَلِيٌّ الأَمْلَس الصفاقي، السرطان الصفاقي، التحول السرطاني، تقرير حالة.

ABSTRACT: *Leiomyomatosis peritonealis disseminata* (LPD), also known as diffuse peritoneal leiomyomatosis, is a rare disease characterised by subperitoneal proliferation of benign nodules mainly composed of benign smooth muscle cells, macroscopically mimicking peritoneal carcinomatosis. We report a 43 year-old woman who presented with menorrhagia, pelvic pressure and pain. Ultrasound of the pelvis showed uterine fibroids and an ovarian cyst. She was scheduled to have a laparoscopic hysterectomy and left salpingo-oophorectomy for symptomatic relief. A picture of carcinomatosis was seen on laparoscopy so multiple biopsies were taken and the patient was referred to the gynaecological oncology team. Definitive surgery was performed and final pathology was consistent with LPD with no evidence of malignancy. No hormone replacement therapy was offered after surgery. Macroscopically, LPD has features of malignancy; it usually pursues a benign course. To review current management of LPD and the risk of malignant transformation, we conducted a search in Medline, EMBASE, and the Cochrane Database of systematic reviews using the keywords: leiomyomatosis peritonealis disseminata, management and malignant transformation. LPD is a diagnostic challenge. Although rare, malignant transformation can occur since hormones play an important role in the pathogenesis of LPD, following surgery, patients should be followed carefully if they are on hormone replacement as these tumours could re-grow and cause symptoms or transform to malignancy.

Keywords: *Leiomyomatosis Peritonealis Disseminata*; Peritoneal carcinomatosis; Malignant transformation; Case report

A 43 year-old woman presented with increasing menorrhagia, pelvic pressure, and pain. An ultrasound of the pelvis showed multiple small uterine fibroids with a dominant intramural fibroid measuring 5cm in diameter and a 3cm left ovarian cyst with a solid component and normal Doppler. The cancer antigen 125 (CA 125) was 32 iu/ml. Her her menstrual cycle was regular with menorrhagia. There was no history of oral contraceptive use. She was para 2, with unremarkable past medical, surgical and family history. The endometrial biopsy was consistent

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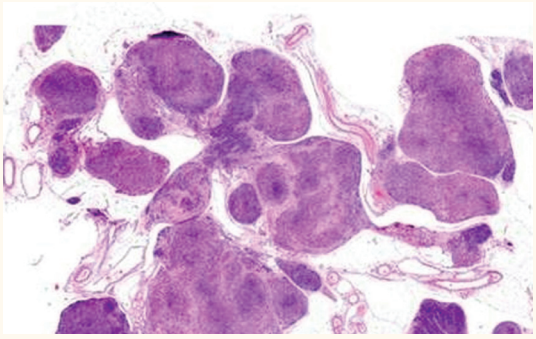

Figure 1: Multiple small nodules of mature smooth muscle surrounded by omental fat

with a proliferative phase endometrium. She was scheduled to undergo a laparoscopic hysterectomy and left salpingo-oophorectomy for symptomatic relief. Laparoscopy revealed a uterus enlarged with fibroids, and the left ovary contained a 3cm cyst with a smooth surface. The omentum was vascular and thick, covered by numerous nodules of variable sizes ranging from 2mm to 1cm. These nodules were also found in the posterior cul-de-sac and under the diaphragm. Because disseminated malignancy was suspected, biopsies were taken from the peritoneal and omental lesions. Definitive surgery was postponed to a later date and the patient was transferred to the gynaecological oncology team. The histopathologic examination was consistent with *Leiomyomatosis peritonealis disseminata* (LPD) [Figure 1]. A computed tomography scan was suggestive of peritoneal nodules. No ascites, no pulmonary or hepatic nodules were seen; there were no enlarged retroperitoneal lymph nodes. The patient subsequently underwent total abdominal hysterectomy (TAH), bilateral salpingo-oopherectomy (BSO), omentectomy and excision of all grossly visible peritoneal lesions [Figure 2]. Final histological examination confirmed the diagnosis of LPD, uterine fibroids, and dermoid cyst in the left ovary. Estrogen receptors (ER) were positive and progestin receptors (PR) were negative in the nodules.

Discussion

LPD was first described in 1952 by Willson and Peale[1] and was identified as a pathological entity in 1965 by Taubert et al.[2] The aetiology of LPD is unknown, but it is thought to originate from metaplasia of submesothelial, multi-potential mesenchymal cells.[3] An association with high levels of exogenous and endogenous female gonadal steroids, e.g. in pregnancy and prolonged exposure to oral contraceptive agents, has been found indicating that estrogen and progestins do play an important role in the pathogenesis of LPD.[4] Both ERs and PRs have been described in tumour cells.[5] Although LPD is most common in females of reproductive age, cases have been reported in postmenopausal women. [6-9] Recently, familial clustering of LPD has been reported, proposing an autosomal-dominant model with varying degrees of penetrance.[10] LPD has also been reported in men [11, 12] and in association with Currarino syndrome.[13] Patients usually present with nonspecific abdominal problems, such as abdominal discomfort or pain, rectal or vaginal bleeding or a mass in the lower abdomen as in our case. The condition presents a multiple, firm, round, white-to-gray nodules ranging in diameter from 0·5 cm to 10 cm lining the peritoneal surface. The cut surface resembles uterine leiomyoma with firm, white and whorled architecture.[14] Microscopically, the round nodules of LPD consist of mature fusiform smooth muscle cells. These cells are arranged in interdigitating fascicles. Often the nodules lack mitotic figures or the mitotic index (MI) is less than 3/10 high power field (HPF). Cellular atypia, nuclear polymorphy, hyperchromasia, and tumour cell necrosis are absent in LPD while a leiomyosarcoma has a higher MI and shows nuclear atypia, tumour necrosis, and infiltrative growth into adjacent structures/organs. Immunohistological staining is typical of smooth muscle tumours with expression for vimentin, desmin, smooth muscle actin, and muscle-specific actin.[15] Some rare cases of malignant transformation in patients suffering from LPD have been reported and the incidence is unknown. Results presented in the literature are conflicting as to whether malignant transformation is related to estrogen stimulation or not, the majority of cases having no association with hormonal stimulation.[16-20] In a review of 103 case reports, Beckers described six cases with malignant leiomyosarcoma diagnosed shortly after the diagnosis of LPD was made.[3, 21] Surprisingly, none of these patients had been exposed to exogenous estrogen and none had uterine leiomyomas. Beckers hypothesised that LPD without exogenous or increased endogenous estrogen exposure, and without expression of ER and PR in the LPD

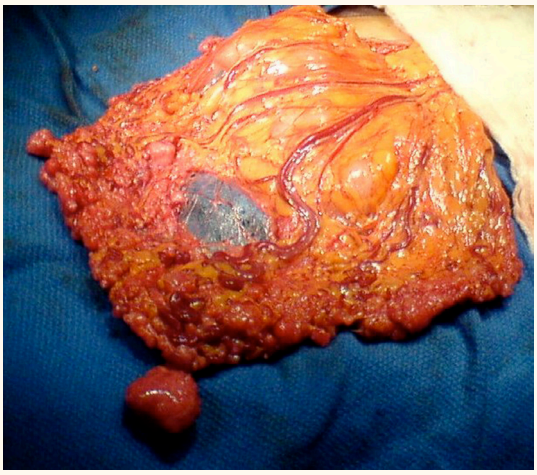

Figure 2: Vascular omentum with multiple nodules

nodules, may represent a different entity carrying a higher risk of malignant transformation and so will need a more aggressive approach.

Imaging studies have not been of great help for the diagnosis of LPD. Ultrasound, computed tomography or magnetic resonance imaging can show the soft tissue masses along the subperitoneal surface and mesentery that resemble peritoneal carcinomatosis, but biopsy is essential for histopathologic diagnosis. Due to the high vascularity of these tumours, biopsies taken by laparoscopy need to be done with great care to ensure proper haemostasis, and furthermore to allow assessment of the extent of LPD and to exclude other diagnoses.[10] The therapy of this benign disease remains controversial and, so far, there are no firm guidelines in the literature with regard to the management of these patients. In women with reproductive desire, many authors advocate a conservative approach. Reducing exposure to estrogen is often sufficient to cause regression of LPD.[22] Regression of LPD was reported with hormonal therapy using gonadotropin-releasing hormone (GnRH) agonists,[23] megestrol acetate,[24] and danazol.[25] A TAH with unilateral or BSO is only recommended for symptomatic relief in patients who have completed their families or for postmenopausal patients. Recurrence of LPD has been reported even after a radical surgical approach.

Conclusion

LPD is a rare disease that clinically mimics peritoneal carcinomatosis on presentation. Diagnosis of LPD should be based on histopathological examination and imaging studies have a limited role in this regard. Due to the association of this rare disease with hormonal stimulation and the fact that there are no solid data to support the safety of hormone replacement therapy following TAH and BSO, patients should be followed carefully after surgery if they are on hormone replacement. This is because these tumors, though benign, could re-grow and cause symptoms or transform to malignancy. Although this clinical entity was described in the 1950s, there are as yet no firm guidelines for the management of these cases.

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