Leiomyomatosis peritonealis disseminata: an additional case

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Summary

Leiomyomatosis peritonealis disseminata (PPD) is a rare smooth muscle tumour of women in the reproductive age. It is characterized by multiple small nodules on the peritoneal surface, mimicking a metastatic process. To date, about 100 cases have been reported in literature. The authors herein present an additional case consisting of multiple nodules located on the surface of the omentum, parietal peritoneum, as well as colon and rectum wall in a patient without signs of excess of estrogen, progesterone, or steroid hormones nor treated with hormones for any reason. The patient has been submitted to laparoscopic myomectomy few years ago. Microscopically, these nodules consisted of bundles of spindle-shaped smooth muscle cells (positive for smooth muscle actin, desmin, estrogen, and progesterone receptor). A brief review of the literature on the pathogenesis of the disease is also added.

Key words: Leiomyomatosis peritonealis disseminata; Pathogenesis; Behaviour.

Introduction

Leiomyomatosis peritonealis disseminata (LPD) is a rare disease of unknown etiology, more often benign, characterized by multiple smooth muscle tumors of varying sizes on the omentum and peritoneal surfaces grossly mimicking disseminated carcinoma [1]. A possible origin from submesothelial multipotential cells has been suggested, although it is not clear if the stimulus to smooth cell differentiation is hormonal, genetic or combined hormonal and genetic [2]. The condition is associated with high levels of exogenous and endogenous female steroids (e.g. pregnancy, prolonged exposure to oral contraceptives and/or combined hormonal replacement therapy, granulosa cell tumours of the ovary) [3, 4], indicating that estrogens and progestins may play an important role in the pathogenesis of LPD as they do in leiomyomata uteri. Most LPD cases are clinically benign, but in some instances they may progress, recur or (rarely) undergo malignant transformation [5]. About 103 documented cases were found in the literature: LPD patients are mainly females (n. 102) in the reproductive age [1, 6]. The authors present a case of LPD in a 32 year-old woman with a previous history of laparoscopic myomectomy supporting the iatrogenic theory.

Case Report

A 32-year-old female patient was admitted to the Department of Surgery of Siena University Hospital complaining of abdominal and pelvic pain. Physical examination revealed a firm hypogastric mass with a five-cm diameter. Abdominal ultrasound examination demonstrated the presence of numerous roundish peritoneal lesions of varying sizes connected with the muscular plane. Past medical history revealed a laparoscopic uterine myomectomy two years prior. There were no signs of excess of estrogen, progesterone or hormonal steroids, and the patient was not treated with hormones. Exploration laparotomy showed innumerable, firm, pale-grey, smooth nodules on the surface of the omentum, the parietal peritoneum, and on the muscular layer of colon and rectum wall. Excision of several of these masses was performed.

On macroscopic examination, all the lesions were similar. They were solid, firm and whitish, and ranged in size from 10 to 75 mm in maximum diameter (Figure 1). Nodules presented smooth external surface and pale, whorled cut surface. Pinpoint hemorrhages were found but there was no macroscopic evidence of necrosis. Microscopic examination showed well circumscribed nodules, embedded in fat tissue (Figures 2, 3). The nodules consisted of bundles of spindle-shaped smooth muscle cells, without atypia, necrosis, or mitosis (Figure 4). Some lesions showed extensive hyaline degeneration and foci of calcification. Immunostaining revealed positivity of neoplastic cells for smooth muscle actin (SMA) (Figure 5), caldesmon (Figure 6), desmin, HHF-35, estrogen (Figure 7) and progesterone receptors, and negativity for cytokeratins. Proliferative index (Ki-67) was about 8% (Figure 8). Cytological examination of the peritoneal liquid revealed only reactive mesothelial cells and foamy histiocytes. The final diagnosis was LPD.

Discussion

LPD is a rare condition which is known to often simulate intra-abdominal carcinomatosis. Firstly described by Wilson and Peale in 1952 [7], only in 1965 [1], the condition was named "leiomyomatosis peritonealis disseminata" and characterized as an entity related to uterine leiomyomas. Since then, 103 cases have been reported. Its exact pathogenesis remains obscure. The associations with pregnancy, prolonged oral contraceptive use, subserosal uterine leiomyomata, functional granulosa cell tumors, and endometriosis indicate hyperestrogenic states as a causal factor. Tavassoli and Norris [8] proposed that LPD is due to smooth muscle metaplasia of the sub-

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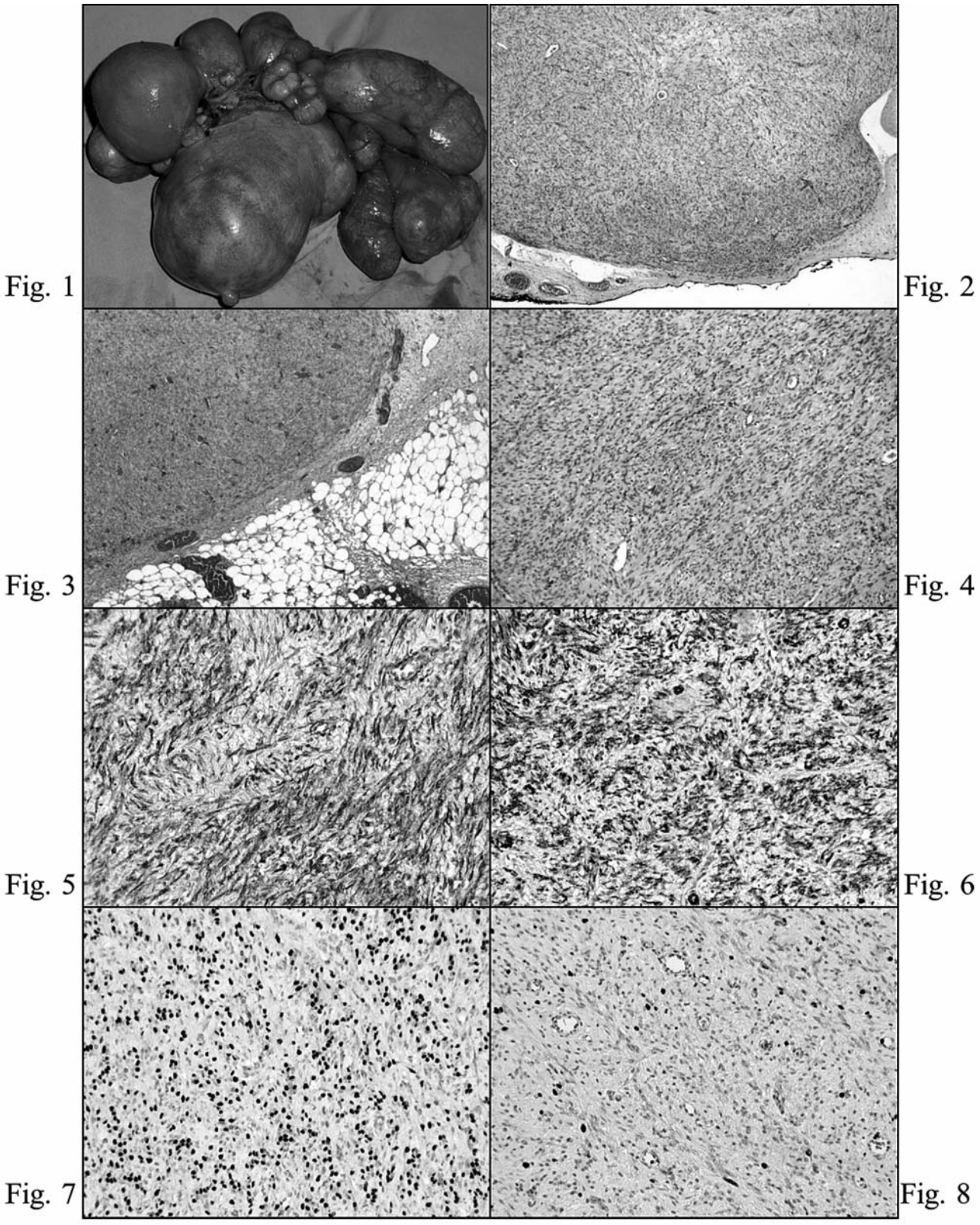

Figure 1. — Macroscopic appearance of the nodules
Figures 2-4. — Histologic aspect, leiomyomata
[2-4: Haematoxylin and Eosin; Original Magnification (OM), 2-3: x5; 4: x10; 4, bottom right x20].
Figure 5. — SMA stain, OM x20.
Figure 6. — Caldesmon stain, OM x20.
Figure 7. — ER stain, OM x20.
Figure 8. — Proliferation index (Ki-67), OM x20.

coelomic mesenchymal stem cells (the so-called pluripotent Mullerian stem cells), which are distributed throughout the subperitoneal mesenchyma, promoted by hormonal stimulation. Some authors have suggested that in case of individual predisposition (abnormality in chromosomes 17, 12, and 18) and hormonal stimulation, Mullerian stem cells proliferate along the line of myofibrous differentiation. In fact, pluripotent mesenchymal stem cells are capable of metaplastic change into leiomyocytes, myofibroblasts, endometrial stromal cells, and decidual cells [6]. Other papers suggest that LPD may be a result of fibrosing deciduosis under the influence of steroid hormones [9, 10]. However, decidual cells and fibrocytes are not always found in LPD nodules, therefore it may be concluded that fibrosis of decidual cells is a process not related to LPD. The reported cases of association between LPD and endometriosis, although few, favor a common origin for both the lesions. However, the mechanisms involved in this association are unknown. It is not clear whether the leiomyomatous nodules originate from foci of endometriosis, or if both the conditions are due to a common metaplastic phenomenon [1]. All these hypotheses do not explain the four cases of LPD in postmenopausal women without hormonal treatment and one case in a male patient. The identification of luteinizing hormone (LH) receptor in LPD nodules from a postmenopausal woman has suggested that the typical postmenopausal increase in LH levels might play a role in the pathogenesis of the condition [11]. Etiological mechanisms are still obscure in cases diagnosed in males and Halama *et al.* [12] hypothesized that LPD may represent an autosomal dominant condition with varying degrees of penetrance.

A possible iatrogenic cause for the disease has also been suggested [1], since increasing cases of LPD have been reported after laparoscopic myomectomy where the myoma was minced to be removed from the abdominal cavity. It is possible that fragments of the myoma, scattered in the peritoneal serosa, grow to become LPD. Miyake *et al.* [13] and Al-Talib *et al.* [2] supported this hypothesis because they found LPD nodules around the laparoscopy scar of a previous myomectomy in a patient who did not receive any hormonal treatment. These are findings in favour of an iatrogenic origin of LPD, as well as in the present case, since the patient did not show excess of estrogen, progesterone or steroid hormones and had no hormonal treatment. Malignant transformation of LPD and its metastases are uncommon and only ten cases (nine female, one male; 20-48 years of age) have been described so far [2]. None of these patients had been exposed to endogenous or exogenous estrogen, and none had uterine leiomyomas. All the patients presented multiple subperitoneal nodules. The nodules that Authors analyzed histologically did not show any signs of malignancy. However, some of the remaining nodules were leyomiosarcomas when analyzed four to 12 months later. Quade *et al.* [14] found molecular and cytogenetic features that indicate monoclonality of LPD nodules by analyzing 42 lesions of four patients in which the diagnosis of benignity was confirmed by an expert histopathologist. Monoclonality may indicate metastatic spread of a unicentric disease, but can also be the result of the selection of a clonal abnormality, as occurs in uterine leiomyomas [14, 15]. Malignancy is thought to be more common in LPD without exogenous or increased endogenous hormonal exposure and in tumours without expression of estrogen or progesterone receptors. The gross and microscopic findings in the present case exclude malignancy.

Due to the rarity of the condition, there are no definite guidelines on its management, however, it has been suggested that a rigorous sampling and a more aggressive approach should be preferable in higher risk groups. LPD detected incidentally carries an excellent prognosis and most cases regress after cessation of the estrogenic stimuli and only some require gonadotropin-releasing hormone agonists or surgical castration. In contrast, malignancy is an event predicting an early death despite multimodality combination therapy [16].

The present patient was treated with laparoscopic surgery of many of the greater nodules. One year after surgery she continues to be well.

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