Original Article

Leiomyomatosis peritonealis disseminata coexisting with endometriosis within the same lesions: a case report with review of the literature

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Abstract: Leiomyomatosis peritonealis disseminata (LPD) is an extremely rare condition, which is characterized by the presence of multiple peritoneal and subperitoneal nodules composed of bland smooth muscle cells. Albeit extremely rare, coexistence of endometriosis within LPD lesions has also been reported. Herein, we report the seventh documented case of LPD coexisting with endometriosis within the same lesions and review the pathogenesis of this lesion. A 42-year-old Japanese female presented with an abdominal tumor. Computed tomography revealed a tumorous lesion in the right ovary and multiple small nodules in the abdominal cavity. Under a clinical diagnosis of ovarian cancer with peritoneal dissemination, resection of these lesions was performed. Histopathological study of the disseminated peritoneal nodules revealed proliferation of interlacing bundles of spindle cells with eosinophilic cytoplasm and bland cigar-shaped nuclei. Mitotic figures were hardly seen. The peritoneal nodules of the rectum had cystic cavities within the spindle cell bundles, and endometrial glands and stroma were present around the cystic cavities and spindle cells. The resected tissues of the ovary and cecum showed the same histopathological features. Accordingly, a diagnosis of LPD with endometriosis within the same lesions was made. A possible origin of LPD is thought to be the submesothelial multipotential stem cells, also referred to as the secondary müllerian system. The presence of endometrial tissues within LPD lesions, as seen in the present case, also support this hypothesis because endometrial tissues are also derived from the müllerian system.

Keywords: Leiomyomatosis peritonealis disseminata, endometriosis, peritoneum, ovary

Introduction

Leiomyomatosis peritonealis disseminata (LPD), also referred to as disseminated peritoneal leiomyomatosis, is an extremely rare condition, which is characterized by the presence of multiple peritoneal and subperitoneal nodules composed of bland smooth muscle cells occurring mainly in the reproductive-aged females [1]. This disease was first described by Willson and Peale in 1952 [2], and later designated as LPD by Taubert et al. in 1965 [3]. Since then, less than 150 cases have been reported in the English literature [1]. Albeit extremely rare, coexistence of endometriosis within LPD lesions has also been reported, and only 6 cases have been documented in the English literature [4-8]. Herein, we report the seventh documented case of LPD coexisting with endometriosis within the same lesions, and review the clinicopathological features and pathogenesis of this extremely rare lesion.

Case report

A 42-year-old Japanese female (2 gravida and 2 partus), who was not taking oral contraceptives, presented with an abdominal tumor at an outpatient clinic. Physical examination revealed an immovable tumor in her abdominal cavity. Laboratory tests demonstrated elevated serum CA125 (567 U/mL; range <34) and CA19-9 (193 U/mL; range <36) levels. Contrast-enhanced computed tomography showed a cystic lesion containing solid area with enhance-
ment in the right ovary and multiple small nodules with enhancement in her abdominal cavity. According to these results, ovarian cancer with peritoneal dissemination was suspected clinically, and subsequently, she was referred to our hospital for surgery.

Intraoperative examination revealed that the right ovarian tumor, measuring 12 cm in diameter, was strongly adhered to the cecum, and innumerable small nodular lesions, measuring 1 to 30 mm in diameter, were present in the mesentery, omentum, peritoneum, Douglas's...
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pouch, and serosal surface of the small intestine, large intestine, and rectum. Total hysterectomy and bilateral salpingo-oophorectomy with resection of the ascending colon and some of the disseminated nodules were performed.

Histopathological examination of the resected disseminated nodules revealed well-circumscribed multiple nodular lesions, measuring 1 to 25 mm in diameter, in the peritoneum (Figure 1A). These nodules were composed of proliferation of interlacing bundles of spindle cells with eosinophilic cytoplasm and bland cigar-shaped nuclei without conspicuous nucleoli (Figure 1A, 1B). Mitotic figures were hardly seen (<1/10 high-power fields). Most of these lesions were comprised of smooth muscle component, however, two nodules from the rectum, measuring 25 x 25 mm and 25 x 15 mm in diameter, had cystic cavities with hemorrhage within the smooth muscle nodules (Figure 1C). Endometrial tissues were present around the cystic cavities and within the bundles of smooth muscle cells in these two lesions (Figure 1C, 1D). Endometrial tissues were composed of endometrial gland as well as endometrial stroma (Figure 1D, 1E). The nuclei of the endometrial glandular cells were pseudostratified, however, no nuclear enlargement was noted (Figure 1E). Moreover, the nuclei of the endometrial stroma were also bland (Figure 1E).

The resected specimens of the ovary also demonstrated multiple nodules composed of proliferation of interlacing bundles of spindle cells with eosinophilic cytoplasm and bland cigar-shaped nuclei. Mitotic figures were hardly seen (<1/10 high-power fields). Some of these nodules had endometrial tissues within the spindle cell bundles and cystic cavities with hemorrhage. Endometrial tissues were composed of endometrial glands without atypia and endometrial stroma.

The cecum had multiple nodular lesions composed of bland interlacing bundles of spindle cells from the serosa to the muscularis propria (Figure 1F). Some nodules of the cecum also had endometrial glands and stroma.

Multiple leiomyomas were observed in the uterine corpus, and no endometrial tissues were present within these leiomyomas. The uterine cervix had no neoplastic lesions.

Immunohistochemical studies were performed using an autostainer (Ventana) by the same method as previously reported [9-12]. Desmin and alpha-smooth muscle actin were diffusely positive for spindle cells of the disseminated nodules of the peritoneum, ovary, and cecum, but negative in the endometrial glands and stroma (Figure 2A). Estrogen and progesterone receptors were diffusely expressed in the spindle cells and endometrial glands and stroma. CD10 was expressed in the endometrial stroma, but not in the endometrial glands and spindle cells (Figure 2B). Ki-67 labeling index was 1.5% in the spindle cell component.

According to these results, an ultimate diagnosis of LPD coexisting with endometriosis within the same lesions was made.
Discussion

LPD is an extremely rare benign condition of unknown etiology. A possible origin of the smooth muscle cells in LPD is thought to be the submesothelial multipotential cells, however, it has not been clear whether the stimuli to induce smooth muscle differentiation is hormonal, genetic, or both [1]. The submesothelial multipotential cells have also been referred to as the secondary müllerian system, which lacks organization of the fallopian tubes, uterus, and upper vagina, although it seems to maintain its ability to differentiate into specialized epithelia or stroma of the müllerian system in the adult life [4-6]. Tavassoli and Noris reported the largest case series of LPD [7]. They studied 20 cases of LPD, and speculated that LPD occurs due to an unusual predisposition, or selective sensitivity of subperitoneal mesenchymal stem cells undergoing smooth muscle metaplasia [7]. This hypothesis is persuasive because LPD occurs exclusively in the reproductive-aged females [1], and some cases of this disorder are found after prolonged use of oral contraceptives [7, 13], hormonal replacement therapy [14], or tamoxifen use [15], during pregnancy [7, 16], and in the presence of an estrogen-secreting tumor [2, 17]. Moreover, the results of positive immunoreactivity for estrogen and progesterone receptors in the smooth muscle cells of LPD, as also seen in the present case, and the cases of spontaneous regression of LPD after discontinuation of hormonal agents or after pregnancy further support this hypothesis [1, 18, 19]. These results suggested that an increased sensitivity to estrogen in susceptible patients predisposes them to the development of LPD [1].

The peculiar histopathological finding of the present case was the presence of endometrial tissue within LPD. Most of the LPD lesions of the present case lacked endometrial tissues, however, nodules in the rectum, ovary, and cecum had endometrial tissues within the smooth muscle cell bundles, and moreover, the lesions in the rectum and ovary had cavities with hemorrhage and endometrial tissues within the smooth muscle cell bundles. To the best of our knowledge, only six cases of LPD with endometriosis within the same lesions have been reported in the English literature [4-8], although some cases of LPD without endometrial tissues within the lesions but accompanied by endometriosis of the ovary have been documented [20, 21]. Table 1 summarizes the clinicopathological features of the previously reported cases of this condition as well as the present one. Kuo et al. reported the first case of this lesion in a 30-year-old female in 1980 [8]. In the series by Tavassoli and Norris, one of 20 patients with LPD had endometriosis within smooth muscle nodules [7]. All patients were of reproductive age (range from 32 to 42 years). No differences in the clinicopathological features of LPD with or without endometriosis were present.

The concise mechanism of the presence of endometrial tissues within LPD lesions has been unresolved. However, the most persuasive hypothesis is that submesothelial multipotential stem cells can differentiate to not only smooth muscle cells but also endometrial glands and stroma [7]. In addition, an extremely rare case of LPD with endocervicosis has also been documented by Liu et al. [22]. Endocervicosis is a rare lesion characterized by the presence of mucinous endocervical-type glands, and is usually found in the urinary bladder. In their case, endocervical type glands were present within most areas (approximately

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age</th>
<th>Location</th>
<th>Reference</th>
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<tbody>
<tr>
<td>1</td>
<td>32</td>
<td>Pelvic and abdominal peritoneal surfaces, omentum, and left ovary</td>
<td>[4]</td>
</tr>
<tr>
<td>2</td>
<td>41</td>
<td>Peritoneal surfaces and omentum</td>
<td>[4]</td>
</tr>
<tr>
<td>3</td>
<td>41</td>
<td>Peritoneal surfaces, and serosal surface of the bowel and the uterus</td>
<td>[5]</td>
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<tr>
<td>4</td>
<td>32</td>
<td>Peritoneal surfaces, omentum, and serosal surface of the intestine</td>
<td>[6]</td>
</tr>
<tr>
<td>5</td>
<td>33</td>
<td>Omentum</td>
<td>[7]</td>
</tr>
<tr>
<td>6</td>
<td>30</td>
<td>Peritoneum, mesentery, and small and large intestines</td>
<td>[8]</td>
</tr>
<tr>
<td>Present Case</td>
<td>42</td>
<td>Peritoneum, mesentery, the serosal surface of the small and large intestines, and ovary</td>
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80%) of the LPD lesions [22]. This case also supports the hypothesis that submesothelial multipotential cells (secondary müllerian system) are origins of LPD because endocervical tissues are derived from the müllerian system.

Endometriosis is defined as the presence of endometrial tissue outside the endometrium. It usually consists of endometrial glands and stroma, however, smooth muscle is occasionally present in endometriotic lesions [23]. Extensive amounts of smooth muscle in endometriosis have been referred to as endometrometriosis or “uterus-like masses”, when they demonstrate a central cavity lined by endometrial tissue [23, 24]. The frequent locations of endometrometriosis are the ovary (42%), uterus (25%), and broad ligament (13%). The abdominal cavity is an exceptional location of this entity [23]. The ovarian lesion of the present case resembled “uterus-like masses” because abundant endometrial tissues were present within the smooth muscle bundles and had cavities with hemorrhage.

In addition, although LPD is a benign condition, only a few cases of LPD with malignant transformation (leiomyosarcoma) have been reported [1, 25]. Therefore, extensive histopathological examination is needed to diagnose LPD.

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