Case Report

Case report: cotyledonoid dissecting leiomyoma in a 49-year-old woman

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Background: Cotyledonoid dissecting leiomyoma (CDL) is much less common than typical leiomyoma. Macroscopically, it displays multinodular, exophytic, placenta-like cystic masses and extends into the broad ligament, pelvic cavity, and retroperitoneal space. The seemingly malignant gross appearance of the tumor has perplexed gynecologists and pathologists; microscopically, it has no malignant characteristics, such as atypical cells, a high mitotic index, or tumor necrosis. To date, only a few cases of CDL have been reported. Here, we report a case of CDL, highlighting its gross and histological appearance, and present a review of the literature.

Case Description: A 49-year-old woman presented with a history of progressive constipation of 6 months' duration and a palpable left lower abdominal mass of 1 month's duration. Transvaginal ultrasound revealed a bulky uterus containing 2 subserosal fibroids measuring 9.9 cm × 6.9 cm × 6.3 cm and 8.1 cm × 6.6 cm × 6.8 cm, respectively. An abdominal modified radical hysterectomy and bilateral salpingo-oophorectomy was performed. An intraoperative frozen section showed an angioleiomyoma with edema. However, the postoperative paraffin section confirmed a diagnosis of CDL. No abnormalities were observed at the 6-month follow-up visit.

Conclusions: Despite its seemingly malignant gross appearance, CDL, based on its microscopic appearance, is a rare benign tumor and has a favorable prognosis.

Keywords: Cotyledonoid; dissecting; gynecology; leiomyoma; case report

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Introduction

Leiomyoma is the most common uterine mesenchymal tumor. Cotyledonoid dissecting leiomyoma (CDL) is much less common than typical leiomyoma, which resembles a placental cotyledon (1). In 1975, CDL was initially described as "grape-like leiomyoma" and also became known as the Sternberg tumor (2,3). A previous article did not find that certain ethnicities were at higher risk and reported that CDL patients were between 21 and 73 years old (4). The clinical manifestations of CDL are similar to those of typical leiomyomas and include abnormal uterine bleeding (most frequently menorrhagia) and presence of a pelvic mass, which presents with symptoms such as constipation, palpable abdominal masses, and abdominal pain (5). Herein, we describe a case of CDL in a perimenopausal woman. We present the following article in accordance with the CARE reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-1521/rc).

Case presentation

A 49-year-old woman presented with a history of progressive constipation of 6 months' duration and a palpable left lower abdominal mass of 1 month's duration.

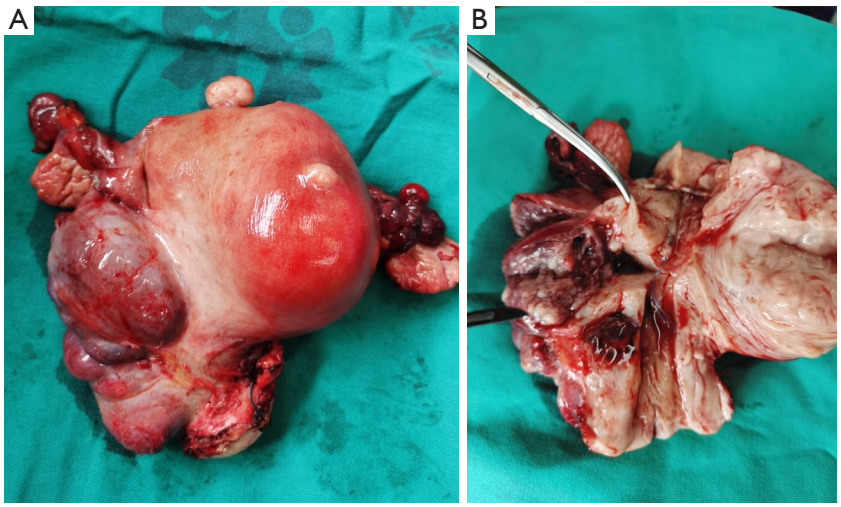

Figure 1 Gross images of CDL. (A) A brown placenta-like myoma, which has grown into the right broad ligament. (B) A tumor originating from the right cervical body junction presents placental cotyledon and papillary nodes in a cut section. CDL, cotyledonoid dissecting leiomyoma.

She was para 2 and had no abnormal uterine bleeding, dysmenorrhea, or abdominal pain. There was no significant past medical history. In addition, she had no history of cigarette smoking or alcohol consumption. Her body mass index (BMI) was 21.5 kg/m^2. A vagino-recto-abdominal examination revealed a bulky uterus the size of a 5-month pregnancy and no palpable abnormalities in the bilateral adnexa.

Transvaginal ultrasound revealed a bulky uterus containing 2 subserosal fibroids measuring 9.9 cm × 6.9 cm × 6.3 cm and 8.1 cm × 6.6 cm × 6.8 cm, respectively, as well as peripheral and internal probing blood flow signals. In addition, a cyst measuring 4.3 cm × 2.9 cm × 3.6 cm was seen in the left adnexa. An abdominopelvic contrast-enhanced computed tomography (CT) scan confirmed the presence of a right parametrial mass measuring 8.6 cm × 3.4 cm × 5.9 cm, located alongside the right cervical body junction margin. The CT scan also showed a left subserosal mass measuring 7.3 cm × 7.2 cm × 5.7 cm and a cyst in the left adnexa measuring 3.9 cm × 2.8 cm × 3.9 cm. There were no enlarged pelvic or para-aortic lymph nodes. Serum tumor markers levels were normal: cancer antigen 125 (CA125; 7.5 U/mL), CA19-9 15.3 U/mL, carcinoembryonic antigen (CEA; <0.5 ng/mL), and alpha-fetoprotein (AFP; 2.3 ng/mL). After counseling the patient, she opted for an abdominal modified radical hysterectomy and bilateral salpingo-oophorectomy.

During the surgery, the uterus was found to be irregularly enlarged, and multiple myomas were identified in the left anterior wall of the uterus (9 cm in diameter), uterine fundus (1 cm in diameter), and right cervical body junction (5 cm in diameter), which were brownish and grew into the right broad ligament (*Figure 1A*). A cyst (measuring 3×2 cm) was also found in the left ovary. Macroscopically, the mass located in the right cervical body junction presented placenta-like and papillary nodes on the inside (*Figure 1B*). An intraoperative frozen section showed an angioleiomyoma with edema. However, the postoperative paraffin section confirmed the diagnosis of CDL. Microscopically, the tumor grew in parauterine tissue (*Figure 2A*). The CDL showed cell islands, which were surrounded by angioedema stroma (*Figure 2B*). The smooth muscle was surrounded by a rich collagen and hyaline degeneration matrix (*Figure 2C*). Tumor cells were mild, with a cigar-shaped nucleus feature (*Figure 2D*).

Immunohistochemically, the tumor cells stained strongly positive for Wilms tumor protein 1 (WT-1), estrogen receptor (ER; *Figure 2E*), desmin (*Figure 2F*), caldesmon (*Figure 2G*), and vimentin. There was also heterogenous positivity for CD10 and progesterone receptor (PR; *Figure 2H*). In addition, the tumor cells were negative for cyclin D1, calretinin, p53, p16, CA125, Fli, D2-40, CK5/6, CD31, and CD34. Ki67 expression was less than 5% (*Figure 2I*). The patient was well after the operation. There was no recurrence at the latest follow-up, which was 9 months after surgery. The constipation was alleviated, and

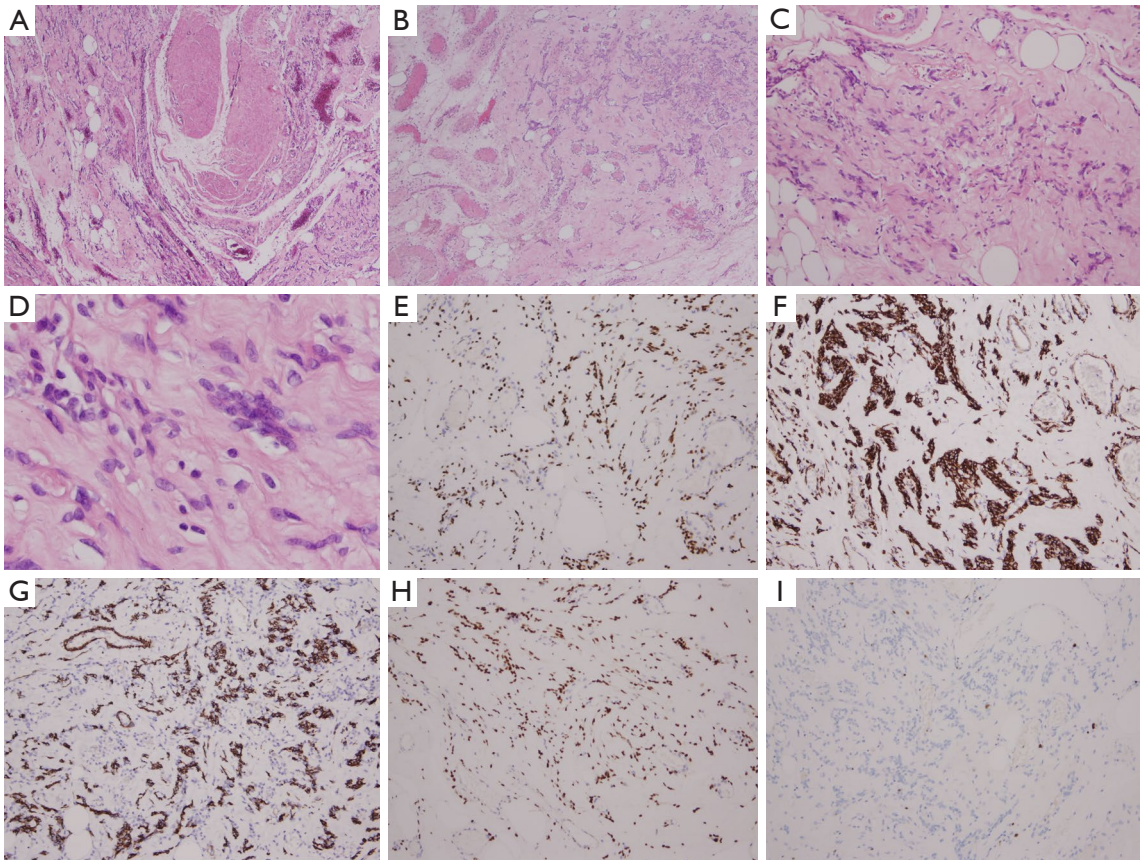

Figure 2 Histopathological images of CDL. (A) The tumor grew in parauterine tissue (HE, ×40). (B) Cell islands were surrounded by angioedema stroma (HE, ×40). (C) Smooth muscle was surrounded by a rich collagen and hyaline degeneration matrix (HE, ×100). (D) The tumor cells were mild, with a cigar-shaped nucleus (HE, ×40). (E) ER positive (based on IHC, ×10). (F) Positive for desmin (IHC, ×10). (G) Positive for caldesmon (IHC, ×10). (H) PR positive (IHC, ×10). (I) Ki67 expression was less than 5% (IHC, ×10). CDL, cotyledonoid dissecting leiomyoma; HE, hematoxylin and eosin; ER, estrogen receptor; IHC, immunohistochemistry; PR, progesterone receptor.

the patient was satisfied with the treatment.

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was provided by the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

CDL is a rare form of leiomyoma, with an appearance similar to that of placental cotyledons; its clinical manifestations include abnormal uterine bleeding, constipation, palpable abdominal masses, and abdominal pain (1). The patient in this study had experienced progressive constipation for 6 months. The tumor size of CDL has been found to vary between 4 and 43 cm, and the size decreases with increasing age, likely due to the hormone depletion (6).

Several reports have described CDLs as grossly multinodular, exophytic, placenta-like cystic masses, with extensions into the broad ligament, pelvic cavity, and retroperitoneal space. Saeki *et al.* described a polypoid CDL which showed exophytic growth, was multinodular, and had a grape-like appearance; the tumor originated from the myometrium and dissected the uterine wall. There was no clear boundary between the CDL and myometrium on the cut surface (7). Regarding tumor markers, serum CA125 levels of CDL cases have been reported as being slightly increased or within normal limits (6).

Due to its gross appearance, the differential diagnosis of

CDL is a challenge for both gynecologists and pathologists. It should be considered when differentiating between benign (including typical leiomyomas and those with cystic or hydropic degeneration) and malignant (including uterine sarcoma, myxoid lesions, and low-grade endometrial stromal sarcoma) tumors. Cystic or hydropic degeneration is prominent accumulation of intercellular fluid, which becomes extensive over time (8). However, cystic or hydropic degeneration does not dissect intramural tissues to appear as extramural cotyledonoid components (8). Gynecologists may consider the possibility of malignancy during surgery due to the appearance of CDL. Thus, intraoperative frozen sections are useful for distinguishing CDLs from myxoid lesions and uterine sarcomas. The microscopic characteristics of CDL usually do not display signs of malignancy (such as atypical cells, a high mitotic index, or tumor necrosis) (9). Morphologically, the dissecting growth pattern and frequently high vascularity of CDL within intramural tissue is similar to that of myxoid low-grade endometrial stromal sarcoma (10). Vessels in stromal tumors typically appear as many thin-walled arterioles, whereas those in CDLs are thicker and unevenly distributed (9). The immunohistochemistry of most low-grade endometrial stromal sarcomas is desmin-negative, caldesmon-negative, and CD10-positive, contrary to that of typical smooth muscle neoplasms (11). In addition, myxoid lesions are a concern in the differential diagnosis. Myxoid leiomyomas are macroscopically limited, and microscopically, myxoid materials separate spindle cells (9). In contrast to classical leiomyosarcomas, myxoid leiomyosarcomas, like CDL, may not also present with tumor cell necrosis, atypical cytology, and prominent mitotic activity. They can only be distinguished from benign myxoid leiomyomas on the basis of the myxoid, nonedematous characteristics of their intercellular material and lymphovascular invasion (12). The etiology of CDL remains unclear. Interestingly, Roth *et al.* asserted that the origin of CDL was the corpus uteri (1). The myometrium extends along the muscular vessels into the broad ligament. Subsequently, venous drainage of the tumor becomes congested in the extrauterine environment. In the cotyledonoid context, the combination of widespread muscular fibers, slender fibrous matrix, and vascular congestion presents a placenta-like or grape-like appearance.

Previous studies have reported that most patients with CDL undergo hysterectomy (5,7). Given the good prognosis of myomectomy in previous reports, a pregnant patient willing to undergo the procedure may be considered for fertility-sparing surgery (9,13). A CDL growing in the myometrium appears as a capsule and displays a cleavage plane, which makes it possible to perform a myomectomy. Complete excision is important because tumor regrowth has been reported (9,13). However, more data are needed to clarify the safety of myomectomy. Interestingly, hormonal therapy was administered before surgery in one study. In particular, Saeki *et al.* reported that a nulliparous 31-year-old woman with CDL was administered a gonadotropin-releasing hormone-analog, which resulted in a slight reduction in tumor volume, as confirmed by magnetic resonance imaging (MRI) (7). Ulipristal acetate, a selective PR modulator, was administered before surgery to control uterine bleeding in another patient with CDL. Furthermore, Raga *et al.* observed a response of CDL to ulipristal acetate similar to that of typical leiomyomas (reduction in the volume of tumor and vascularization of tumor) (14).

Microscopically, CDL usually does not display malignant characteristics, such as atypical cells, a high mitotic index, or tumor necrosis. Previous studies have shown that there was no tumor recurrence or metastases during follow-up (ranging from 1 month to 41 years) (5,15). In conclusion, despite its seemingly malignant gross appearance, based on microscopic appearance, CDL is a rare benign tumor with a favorable prognosis.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-1521/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tcr.amegroups.com/article/view/10.21037/tcr-22-1521/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research

committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was provided by the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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