A Case of Cotyledonoid-Dissecting Leiomyoma - The Utility of Laparoscopic Biopsy and Gonadotropin-Releasing Hormone Analogs

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ABSTRACT: Cotyledonoid-dissecting leiomyoma, a very unusual form of uterine leiomyoma, often leads to misdiagnosis as a malignant tumor. Here, we describe a case of a 45-year-old nulliparous woman who underwent a laparoscopic biopsy of a large pelvic mass consisting of multiple flaps. Histologically, the mass was composed of smooth muscle fascicle nodules separated by hydropic connective tissue, and exhibited extensive stromal hyalinization. The tumor was diagnosed as a cotyledonoid-dissecting leiomyoma based on the laparoscopic, pathological, and image findings. Prior to performing radical laparotomy, two courses of leuprorelin were administered in anticipation of tumor reduction and hypoperfusion, and the tumor size reduced remarkably. We demonstrated the utility of laparoscopic biopsy, considering its minimal invasiveness and diagnostic accuracy. Furthermore, the preoperative use of Gonadotropin-releasing hormone (GnRH) analogs to reduce surgical stress may be useful for treating cotyledonoid-dissecting leiomyomas.

KEYWORDS: Cotyledonoid-dissecting leiomyoma, gonadotropin-releasing hormone analog, hydropic degeneration, laparoscopic biopsy, stromal hyalinization

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Introduction

Cotyledonoid-dissecting leiomyomas are an unusual form of uterine leiomyoma with a characteristic external morphology and imaging findings.[1] Cotyledonoid-dissecting leiomyomas are typically multinodular and exophytic, resemble placental tissue, and sometimes extend into the pelvic cavity, enclosing existing structures.[2] However, ruling out the possibility of malignancy before pathological diagnosis may sometimes be difficult.

Generally, cotyledonoid-dissecting leiomyomas exhibit unique pathological findings that lead to accurate diagnosis. It shows irregular nodular dissection of bland smooth muscle cells within the myometrium and incorporates bulbous protuberances within the exophytic component. Perinodular hydropic degeneration and intravenous extension were occasionally observed. However, some histological variants, such as lipoleiomyomas and epithelioid cell variants, have been reported.[3-6] The origin of the smooth muscle can only be recognized using immunohistochemistry. Deciding an operative method based on intraoperative frozen sections involves the risk of overtreatment. As this tumor frequently affects females in their reproductive years, a careful therapeutic strategy for an accurate diagnosis is needed to avoid unnecessary invasiveness and maintain fertility.

Herein, we report a case of a large cotyledonoid-dissecting leiomyoma that was treated with a two-stage operation. We performed a laparoscopic biopsy and diagnosed the patient with a cotyledonoid-dissecting leiomyoma. Radical laparotomy was performed after tumor reduction with leuprorelin. In this case, we suggest the use of laparoscopic biopsy and GnRH analogs for treating cotyledonoid-dissecting leiomyomas.

Case Presentation

A 45-year-old nulliparous female with no significant medical history presented at a regular internal medicine outpatient clinic. The patient had no relevant family history. The patient did not receive medications associated with female hormones. Her chief complaints were abdominal distension and lower abdominal pain 3 months prior to presentation. The pain score was 3/10 on a numerical rating scale. Computed tomography (CT) with contrast enhancement revealed a $22 \times 20 \times 8$ cm pelvic mass. Existing structures, such as the bilateral internal iliac arteries, were surrounded by tumors (Figure 1a). Upon suspicion of malignant uterine lymphoma, she was admitted to our department. Her abdomen was distended and elastic, and mild tenderness was observed on internal examination. Transvaginal ultrasonography revealed a uniformly hypoechoic mass with relatively abundant blood flow in the lower abdomen. No normal uteri were observed. Magnetic resonance imaging (MRI) revealed a large pelvic mass in contact with the uterus that filled the entire pelvic cavity. The tumor mainly exhibited a low signal intensity compared to the muscle with a partially high signal intensity, similar to the partition wall (Figure 1b). Diffusion-weighted echo-planar MRI (DWI) revealed that the tumor mainly exhibited isosignal intensity compared to the myometrium. The serum CA-125 levels were slightly elevated (37.2 IU/mL). Laparoscopic biopsy was performed for the clinical

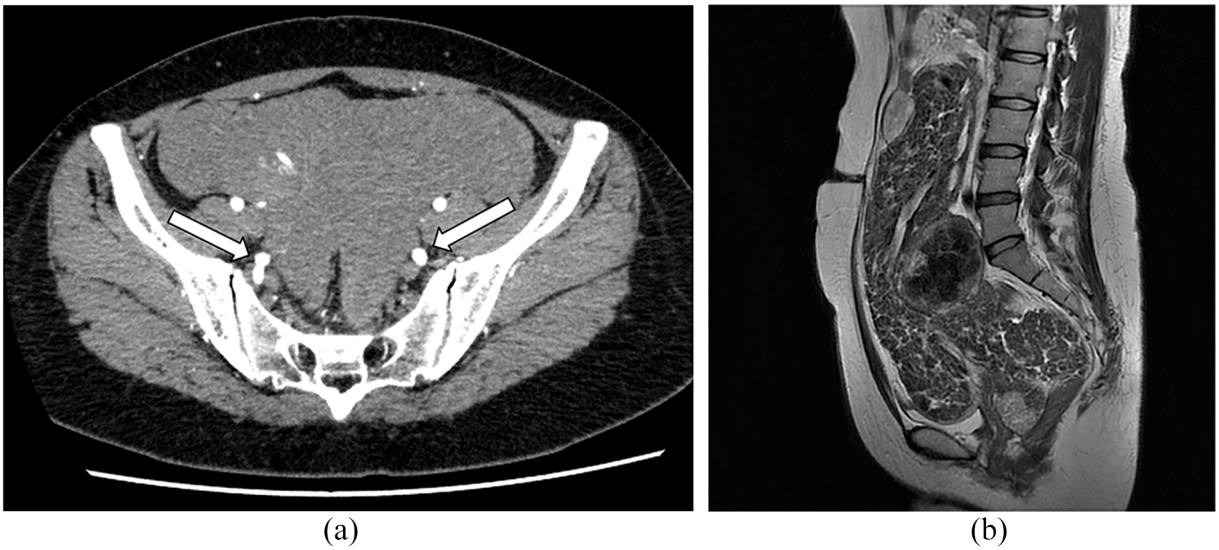

Figure 1. Preoperative findings: (a) Contrast-enhanced computed tomography revealing a $22 \times 20 \times 8\,cm^3$ pelvic mass with contrast enhancement. Existing structures such as the bilateral internal iliac arteries are surrounded by a tumor (arrow). (b) T2-weighted magnetic resonance imaging showing a large pelvic mass in contact with the uterus that filled the entire pelvic cavity. The tumor mainly shows low signal intensity compared to the myometrium and partially shows high signal intensity similar to that of the partition wall.

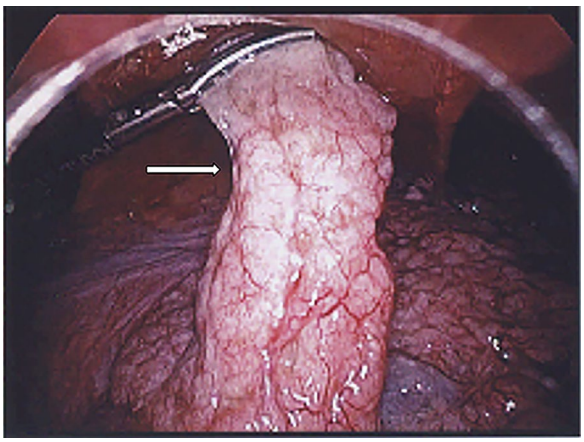

Figure 2. Laparoscopic findings. The mass is grayish-white in color and consists of multiple soft flaps (arrow).

diagnosis of malignant uterine lymphoma or sarcoma. There were no ascites. The mass was grayish-white in color and comprised multiple flaps (Figure 2). Microscopically, the biopsy specimen showed smooth muscle fascicles with hydropic changes similar to those observed in benign leiomyomas. Based on the laparoscopic, pathological, and imaging findings, the tumor was diagnosed as a cotyledonoid-dissecting leiomyoma. We discussed the treatment strategy in our department with cardiovascular surgeons and urologists. We concluded that a total abdominal hysterectomy with sufficient support from cardiovascular surgeons and urologists was the best option. However, a certain number of preparation days were required until the ideal surgery was performed. Two courses of leuprorelin were administered for tumor reduction and hypoperfusion in 1 trial, which was more effective than expected. The maximum tumor diameter was markedly reduced from 22 to 20 cm. Radical laparotomy revealed that the tumor was multinodular and exophytic, resembling placental tissue, and partially extended under the bilateral broad ligaments and into the abdominal cavity. The tumor surrounded the iliac vessels; however, gross examination revealed no evidence of intravenous leiomyomatosis. Total abdominal hysterectomy and left salpingo-oophorectomy were performed. After surgery, gynecological examinations and ultrasonography were performed every 3 months. Systemic computed tomography with contrast enhancement was regularly performed annually to detect tumor recurrence, including intravascular growth. The patient is alive and healthy 5 years after surgery.

Pathological findings

The mass was attached to the posterior uterine wall. The morphology consisted of bulbous protrusions (Figure 3a). Histologically, the tumor was lobular and multinodular with some areas of hemorrhage composed of smooth muscle fascicle nodules separated by hydropic connective tissue containing congested vessels (Figure 3b). Extensive stromal hyalinization was observed in the background (Figure 3c). Cellular atypia, mitotic activity, and coagulative necrosis were not observed. No intravascular growth patterns were observed. Our final diagnosis was cotyledonoid-dissecting leiomyoma.

Discussion

Cotyledonoid-dissecting leiomyomas, or Sternberg's tumors, were first described in 1996 by Roth et al.[1] David et al[7] first coined the term "grapelike leiomyoma" based on the overall description of the tumor in 1975. Buonomo et al[8] recently reported its clinical features from a review of 94 cases. The median patient age of these cases was 44 years (range 21-73). The most

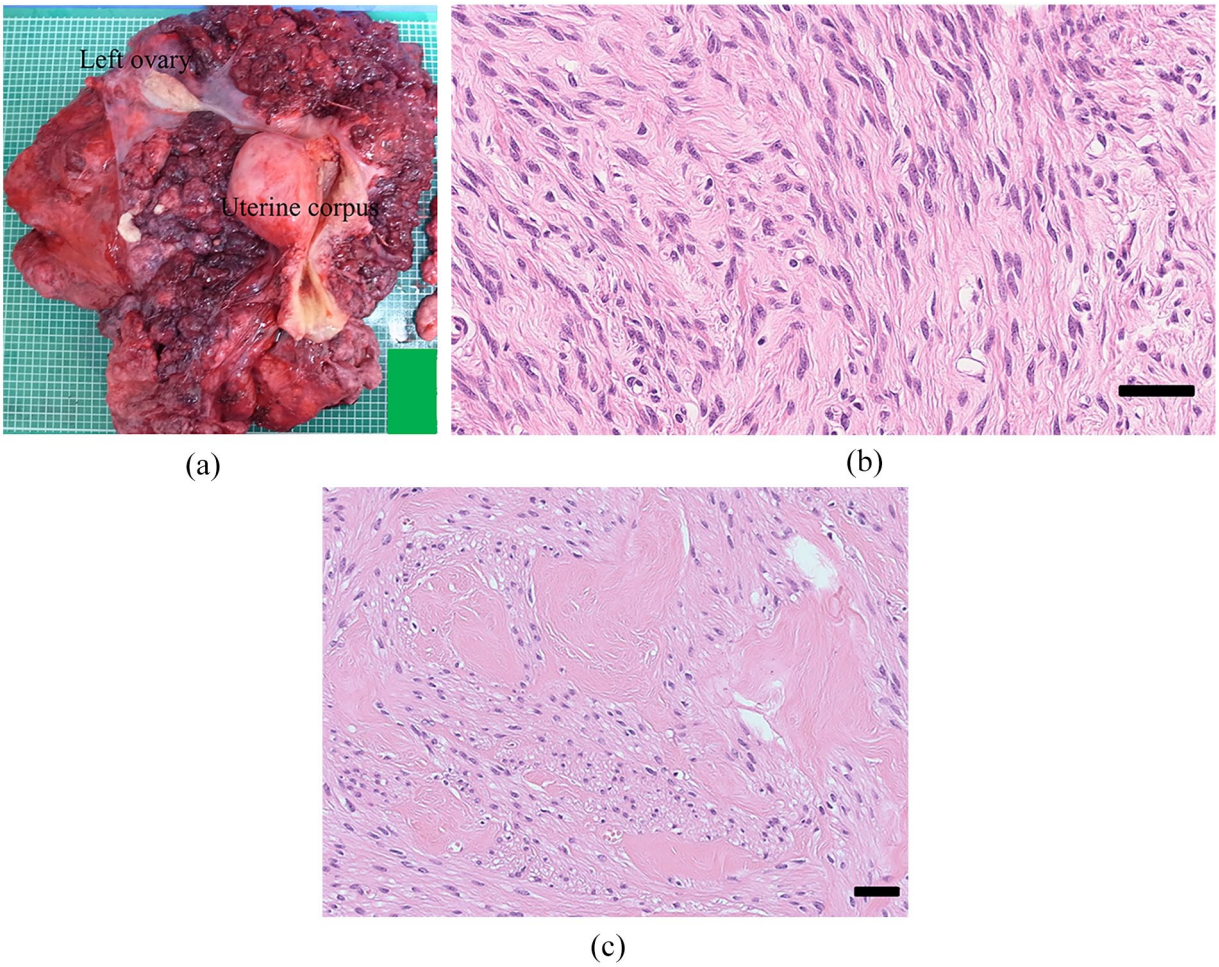

Figure 3. Pathological findings. (a) Overall findings: The mass was lobular and multinodular, with some areas of hemorrhage. (b) Hematoxylin and eosin staining: Scale bar, 50 μm. The tumor is composed of nodules of smooth muscle fascicles separated by hydropic connective tissue. (c) Hematoxylin and eosin staining: Scale bar, 50 μm. Extensive stromal hyalinization is present in the background.

common complaints were abdominopelvic masses, abnormal uterine bleeding, and pain. No obvious risk factors were identified in this study. The mean tumor size was 12 cm. Most were exophytic multinodular masses with a placenta-like color that protruded over the uterine serosa and entered the broad ligaments.

Contrary to the overall appearance, the pathological features include a lack of cellular atypia, mitotic activity, and coagulative necrosis. That is the best differentiation from other malignant tumors such as uterine sarcoma and smooth muscle tumor of uncertain malignant potential (STUMP).[2] Kim et al[9] reported the percentage of intravascular growth via histological assessment was 21.4% (9 of 42 cases).

In general, total hysterectomy was performed in patients who did not wish to have children, and no recurrence cases were observed. However, few patients who underwent conservative surgery experienced tumor recurrence.[10,11] As has been previously established, this tumor frequently affects females during their reproductive years. The tumor is usually large and shows gross findings resembling malignant uterine tumors such as leiomyosarcoma or endometrial stromal sarcoma. Clinicians must be aware of this rare disease and avoid overtreatment, which can damage fertility.[12]

Some reports recommend intraoperative frozen sections when selecting conservative surgery.[13] However, some histological variants of cotyledonoid-dissecting leiomyomas have also been reported. Fukunaga et al[3] and Blake et al[4] reported a lipoleiomyoma variant of cotyledonoid-dissecting leiomyomas. Soleymani et al[5] and Chawla et al[6] reported an epithelioid cell variant that showed epithelioid tumor cells with a pale eosinophilic cytoplasm and central bland nuclei. The smooth muscle origin was recognized only using immunohistochemistry. Based on morphological assessment, there is a wide range of differential diagnoses, including malignant tumors such as metastatic carcinoma, mesothelioma, melanoma, PEComa, and renal cell carcinoma. Therefore, an intraoperative frozen section is unlikely to aid in an accurate diagnosis and exclude its malignant potential. Laparoscopic biopsy is useful owing to its minimally invasive nature and diagnostic accuracy.[14]

Uterine leiomyomas express hormone receptors. Preoperative use of GnRH analogs for tumor reduction and hypoperfusion is common, especially in cases of conserving surgery or high surgical stress, such as those with a large tumor size.[15] Saeki et al[16] reported a successful conserving surgery case of a cotyledonoid-dissecting leiomyoma after

the administration of a GnRH agonist. In our case, leuprorelin was markedly effective for tumor reduction. Thus, the use of GnRH analogs appears to be effective in treating cotyledonoid-dissecting leiomyomas, which reflect the expression of hormone receptors.

Conclusion

We encountered a case of cotyledonoid-dissecting leiomyoma, a rare uterine tumor. Considering its minimal invasiveness and diagnostic accuracy, we demonstrated the utility of laparoscopic biopsy. We also demonstrated that the efficacy of GnRH analogs was similar to that in general leiomyomas. Our findings support the preoperative use of GnRH analogs to reduce surgical stress.

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Author Contributions

SK and AN contributed to the clinical management and drafted the original manuscript. KI contributed to the pathological diagnosis. DN supervised the preparation of this case report. All authors reviewed the manuscript draft and revised it critically on intellectual content. All authors approved the final version of the manuscript to be published.

Ethics

Due to because this is a case report, it is not covered by ethical guidelines.

Consent for Publication

Written informed consent was obtained from the patient for the publication of this case report and all accompanying images. A copy of the consent form is available upon request for a review by the journal editor.

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