Notes on the morphological features of cotyledonary dissecting leiomyoma, which is rare in clinical practice

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Abstract

Benign uterine leiomyoma (U.LMA) and malignant uterine leiomyosarcoma (U.LMS), which are both uterine mesenchymal tumors, are distinguished by the number of cells with mitotic activity. However, uterine mesenchymal tumors contain tumor cells with various cell morphologies; therefore, making a diagnosis, including differentiation between benign tumors and malignant tumors, is difficult. For example, A cotyledonoid dissecting leiomyoma is a uterine leiomyoma with a very rare placental lobed tissue morphology that can be misdiagnosed as a malignant uterine leiomyosarcoma because of its rarity and characteristic appearance on gross examination. Similar to the detection of a suspicious malignant mass during MRI imaging examination by medical staff, healthcare professionals must understand the characteristic appearance of a cotyledonoid dissecting leiomyoma. Clinicians and pathologists must understand the oncologic features of cotyledonoid dissecting leiomyoma to prevent misdiagnosis of malignancy and consequent overtreatment.

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Editorial

Ye et al. reported the case of a 49-year-old woman with cotyledonoid dissecting leiomyoma diagnosed by surgical pathology using a paraffin-embedded postoperative tissue section [1]. In routine gynecologic practice, uterine smooth muscle tumors are among the most common gynecologic tumors. Uterine leiomyoma is a benign smooth muscle tumor that arises from the myometrium and accounts for approximately 75% of all uterine tissues removed from patients [2]. Uterine smooth muscle tumors occur mainly in women of reproductive age, and the prevalence of uterine leiomyoma in women up to the age of 50 years is approximately 70% [2][3]. However, its incidence is low in postmenopausal women. Uterine leiomyoma proliferation affects the secretion of female hormones, and the size of uterine leiomyomas varies slightly depending on the sexual cycle. Uterine leiomyoma has a histomorphology similar to that of lipoleiomyoma, intravenous leiomyoma, and leiomyoma with bizarre nuclei [4][5][6][7]. A cotyledonoid dissecting leiomyoma is a uterine leiomyoma with a very rare placental lobed tissue morphology [2] that can be misdiagnosed as a malignant uterine leiomyosarcoma because of its rarity and characteristic appearance on gross examination.

In one such case, contrast-enhanced computed tomography (CT) revealed a mass that was continuous with the muscular layer of the uterine corpus, suggesting that it arose from there [8]. However, there was no infiltration of tumor cells into the vein and myometrium. Therefore, a benign leiomyoma growing outside the uterus and exhibiting a morphology similar to that of the placental leaf is called a cotyledonoid dissecting leiomyoma [8].

A uterine leiomyoma, which extends into the uterine smooth muscle layer and broad ligament as well as extrauterinally in a beaded manner, is accompanied by marked edematous changes and macroscopically resembles a placental lobe cotyledon. Such uterine leiomyomas are, therefore, called cotyledonoid dissecting leiomyomas [4][8][9].F

Ye H et al. reported the case of a 49-year-old woman with cotyledonoid dissecting leiomyoma diagnosed by surgical

pathology using a postoperative paraffin-embedded tissue section [1]. The patient presented with a history of progressive constipation that lasted for 6 months and a palpable left lower abdominal mass since 1 month [1]. She exhibited neither pelvic nor para-aortic lymph node enlargement. Serum tumor markers, namely, cancer antigen (CA) 125, CA19-9, carcinoembryonic antigen (CEA), and alpha-fetoprotein (AFP) levels, were normal. Transvaginal ultrasonography revealed a massive mass comprising two subserous fibroids measuring 9.9 × 6.9 × 6.3 cm and 8.1 × 6.6 × 6.8 cm with peripheral and internal probing blood flow signals [1]. Rapid examination using intraoperative frozen sections revealed an angioleiomyoma with edema [1]. Truncal CT performed 6 months after surgery revealed no abnormal findings.

Recently, we encountered a case of cotyledonoid dissecting leiomyoma. In November 2020, a 57-year-old woman visited a hospital because of abnormal vaginal bleeding, and the development of a chocolate cyst was suspected. Magnetic resonance imaging (MRI) revealed a mass in the patient's pelvis (Figure 1) that could not be adjudged as malignant or benign. However, ovarian cancer was suspected because a solid component was identified on the MR image. Therefore, the patient was referred to our hospital that has a gynecological team for thorough examination. Transvaginal ultrasonography revealed a solid mass measuring 115 mm × 57 mm with an indistinct margin in the right ovary. The area of origin of this mass suggested ovarian cancer or a retroperitoneal tumor. In March 2021, the patient underwent a simple hysterectomy and bilateral salpingectomy. A degenerative uterine leiomyoma measuring 110 mm × 80 mm was found growing within the broad ligament attached to the right round ligament. No gross abnormalities were observed in the bilateral fallopian tubes and ovaries. The surgical pathological examination of the resected tissue demonstrated a cotyledonoid dissecting leiomyoma. There was no evidence of malignancy in the endometrial tissue, cervical tissue, or bilateral oviduct tissue. The patient is currently being followed up on an outpatient basis. Similar to the detection of a suspicious malignant mass during MRI by our medical staff, other healthcare professionals must understand the characteristic appearance of a cotyledonoid dissecting leiomyoma.

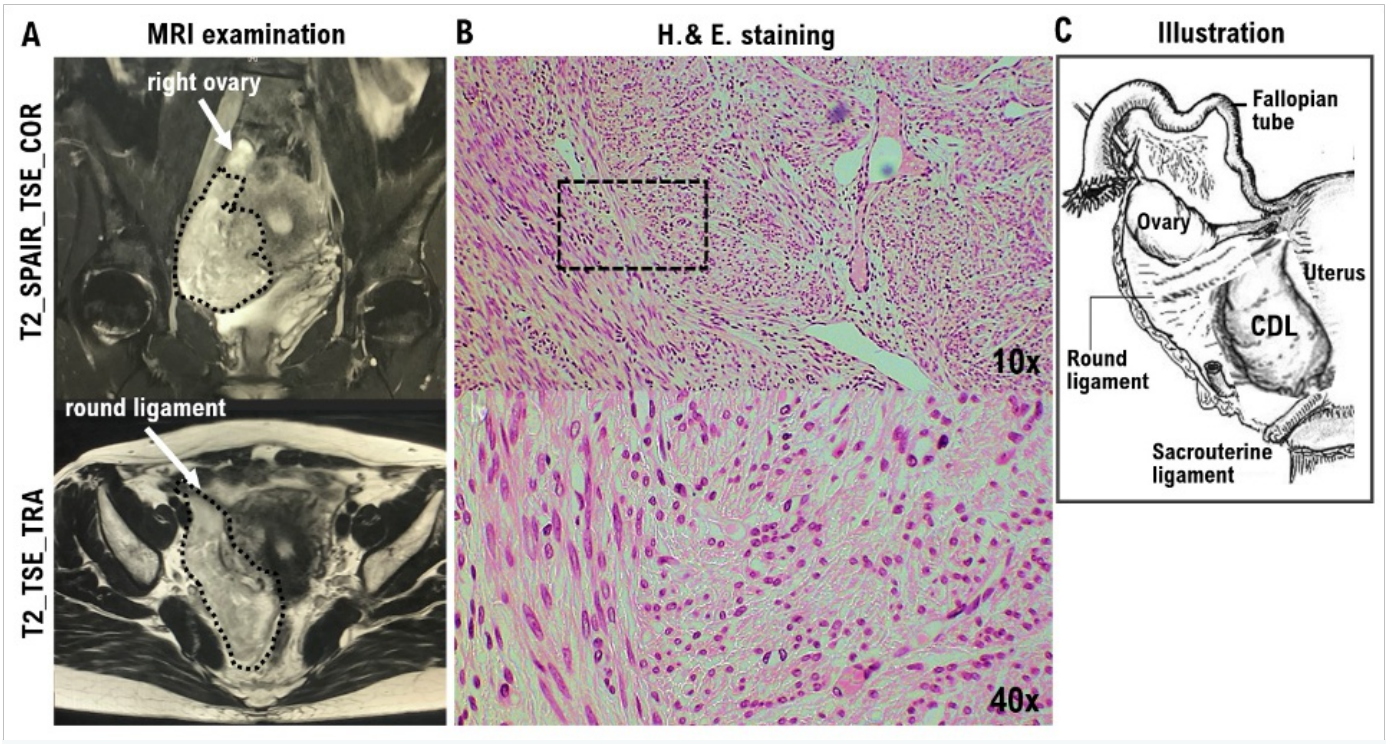

Figure 1. Morphological characteristics of a cotyledonoid dissecting leiomyoma observed on MRI and histopathological examination.

(A) Results of MRI. The T2W1 image shows a continuous, low-to-high-intensity mass lesion originating within the right muscle layer of the uterine corpus, extending outward into the uterus. The mass (encircled by a dotted line) is present between the round ligament (white arrow) and uterine artery and is enclosed by a membrane. The right ovary (white arrow) present superior to the mass is normal. The images suggest that the mass may be a degenerative uterine leiomyoma growing from within the myometrium into the broad ligament. The leiomyoma measures approximately 20 mm in size on the posterior wall of the uterine fundus. No lesions are seen in the ovaries. Significant lymphadenopathy or ascites is absent. **(B)** Results of histopathological examination. A soft mass approximately 120 mm in size is seen protruding from the uterine serosal surface. The cut surface of the mass is grayish white and multinodular and demonstrates a proliferation of smooth muscle cells having an island-like/alveolar-like morphology with edematous stroma. Marked infiltration of these smooth muscle cells into the uterine smooth muscle layer is observed. There is also evidence of infiltration of some proliferating smooth muscle cells into the blood vessels. No severe nuclear atypia or mitotic cells are observed. On the basis of these findings, a diagnosis of cotyledonoid dissecting leiomyoma can be considered. Surgical pathological examination reveals no malignant findings in cervical and fallopian tube tissues. Upper panel; Magnification 10, Lower panel; Magnification 40. **(C)** Illustration of the gross findings of the patient's cotyledonoid dissecting leiomyoma.

MRI, magnetic resonance imaging; H&E, hematoxylin and eosin; CDL, cotyledonoid dissecting leiomyoma

A cotyledonoid dissecting leiomyoma is an extremely rare benign uterine tumor. Its appearance on gross examination during surgical treatment is often misinterpreted as malignancy, which may result in overtreatment. Serum tumor markers such as CA125 and CA19-9 levels are elevated in many cases of gynecologic malignancies [10][11]. On the contrary, uterine leiomyomas, which are benign tumors, demonstrate normal results for serum tumor marker levels. Unnecessary surgical procedures, i.e., total abdominal hysterectomy (TAH) and bilateral salpingo-oophorectomy (BSO), can be avoided in patients of reproductive age if medical staff are aware of and experienced in recognizing the appearance and characteristics of cotyledonoid dissecting leiomyomas.

All cotyledonoid dissecting leiomyomas reported to date were clinically diagnosed as benign tumors, and only one

recurred after initial partial resection [12]. This was observed in a 33-year-old woman who underwent an incomplete resection to preserve fertility, and recurrence was reported 5 years after the initial surgical intervention [12]. However, tumor recurrence has not been reported in cases where complete resection (hysterectomy) for cotyledonoid dissecting leiomyoma was performed. In the case reported by Ye H et al., no evidence of recurrence was observed in the patient 18 months after hysterectomy. Recently, cases of epithelioid cotyledonoid dissociative leiomyoma variants and cotyledonoid dissecting leiomyomas with intravenous leiomyomatosis were also reported [13][14]. Histologically, the neoplastic smooth muscle cells of cotyledonoid dissecting leiomyomas form disorganized bundles, contrary to the organized pattern observed in common uterine leiomyomas [15].

In many cases, differentiating between uterine leiomyoma and uterine leiomyosarcoma is difficult. Uterine leiomyoma is the most frequently occurring uterine sarcoma and accounts for 1%–2% of all uterine malignant tumors [8]. Most uterine leiomyosarcomas occur in women aged >40 years. Unlike uterine benign smooth muscle tumors, uterine leiomyosarcomas are frequently observed in postmenopausal women [16]. In uterine mesenchymal tumors that develop from the uterine smooth muscle layer, the rapid growth of the tumor does not immediately suggest the development of uterine leiomyosarcoma. However, in postmenopausal women who are not undergoing hormone replacement therapy, malignancy should be suspected by medical staff when uterine mesenchymal tumors are growing or recurring. However, in the case reported by Ye H et al., neither an epithelioid pattern nor an intravascular neoplastic component was observed [1]. Therefore, recurrence after surgical treatment will presumably not occur in this patient.

In conclusion, a cotyledonoid dissecting leiomyoma is a rare variant of uterine leiomyoma[15][17]. Its gross appearance and ultrasonographic features may indicate malignancy. Furthermore, it demonstrates >10 increases in mitotic activity/10 high-power fields, tumor cell necrosis, and no evidence of cellular atypia. Thus, histologically, cotyledonoid dissecting leiomyoma is a benign tumor. To date, recurrence and metastasis have not been reported in a majority of the cases. Therefore, in clinical practice, prognosis is considered favorable. Clinicians and pathologists must understand the oncologic features of cotyledonoid dissecting leiomyoma to prevent misdiagnosis of malignancy and consequent overtreatment.

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Institutional Review Board Statement: This study was reviewed and approved by the Central Ethics Review Board of the National Hospital Organization Headquarters in Japan (Tokyo, Japan) on November 08, 2019 and Shinshu University (Nagano, Japan) on August 17, 2019, with approval codes NHO H31-02 and M192. The completion numbers for the authors are AP0000151756, AP0000151757, AP0000151769, and AP000351128. As this research was considered clinical research, consent to participate was required. After briefing regarding the clinical study and approval of the research contents, the participants signed an informed consent form.

Informed Consent Statement: The applicable for studies involving humans. We have obtained Informed Consent Statements from people participating in clinical studies.

Data Availability Statement: The study did not report any data.

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