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Uterine Leiomyomas with Perinodular Hydropic Degeneration
- A Report of Two Cases -

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Hydropic degeneration is a frequent degenerative change in otherwise typical uterine leiomyomas. Very rarely, however, a significant amount of edema fluid accumulates around the fascicles of neoplastic smooth muscle bundles and forms the characteristic multinodular growth pattern that is called perinodular hydropic degeneration of leiomyoma (PHDL). The gross findings, showing a vague worm-like appearance and very rarely having an extrauterine extension, and the microscopic features, showing perinodular retraction artifacts forming pseudovascular spaces, make it difficult to differentiate the tumor from intravenous leiomyomatosis or myxoid leiomyosarcoma. We described two cases of leiomyomas showing perinodular hydropic degeneration (PHD), a condition that has rarely been described in English literature, and discussed the mechanism of forming "extrauterine extension" or cotyledonoid features. One of our cases showed the typical features of cotyledonoid dissecting leiomyoma, the other showed those of intramural dissecting leiomyoma. An awareness of the gross and microscopic findings of PHDL is important not to overdiagnose a benign smooth muscle neoplasm as a more aggressive type of tumor. It is thought that intramural dissecting leiomyoma, cotyledonoid dissecting leiomyoma, and PHDL are not distinct, but closely related subtypes showing different phases of evolutionary changes.

Key Words : Uterine Neoplasms-Leiomyoma

Leiomyoma is a uterine neoplasm in which degenerative changes, such as hyaline fibrosis, hydropic change, cystic degeneration, and hemorrhage frequently occur. Varying degrees of hydropic change are observed in more than 50% of the cases.[1] Perinodular hydropic degeneration of uterine leiomyoma (PHDL) refers to a very rare, but characteristic pattern of degeneration in which a multinodular growth pattern is formed by the accumulation of edema fluid around the fascicles of neoplastic smooth muscle bundles and may cause problems in the differential diagnosis from intravascular leiomyomatosis (IVL) or myxoid leiomyosarcoma.[1,2] Multinodularity of the intrauterine component of the leiomyoma and hydropic changes in the surrounding connective tissue can be seen in several variants of leiomyomas, such as PHDL, infiltrating leiomyoma, cotyledonoid dissecting leiomyoma, and intravenous leiomyomatosis. However, the rarity of the documented cases means that the clinical and pathological significances of the lesion are not well recognized to the pathologists. We describe two such cases, one of which has the typical features of cotyledonoid dissecting leiomyoma. As far as we know, it has not been described in Korea and ours is the third report in English literature that describes an extrauterine extension or cotyledonoid feature of leiomyoma with perinodular hydropic degeneration.

CASE REPORTS

Case 1

The patient was a 35-year-old woman, gravida 1, para 0, who presented with a palpable abdominal mass with chronic menorrhagia. A transvaginal ultrasonography showed complex hypoechoic multiple nodules on the left adnexal region and within the adjacent myometrium. The patient underwent a total abdominal hysterectomy with left salpingo-oophorectomy. The uterus measured 10 × 8 × 5 cm and weighed 150 g. Multiple exophytic, papillary, or multinodular beaded masses projected from the left cornual portion of the uterus and the mass was connected to

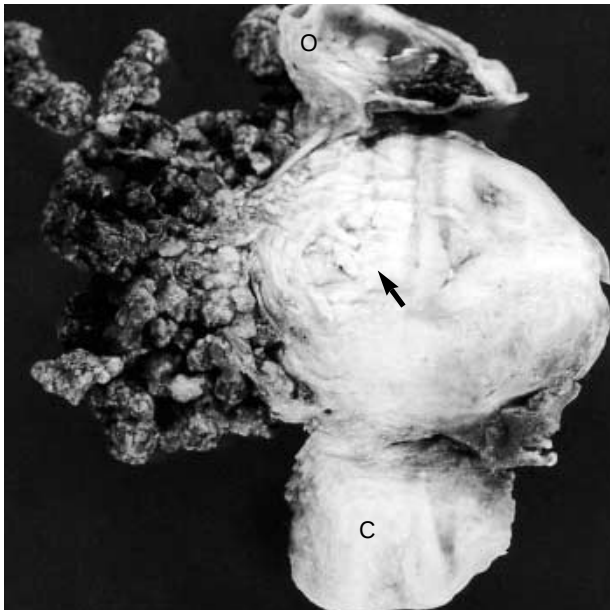

Fig. 1. Cut surface of the entire uterus shows multinodular or papillary exophytic masses projecting in the right cornual portion. Adjacent myometrium has an ill-defined intramural mass which is confirmed as an adenomatoid tumor (arrow) and intramural component of leiomyoma. C; uterine cervix, O; ovary.

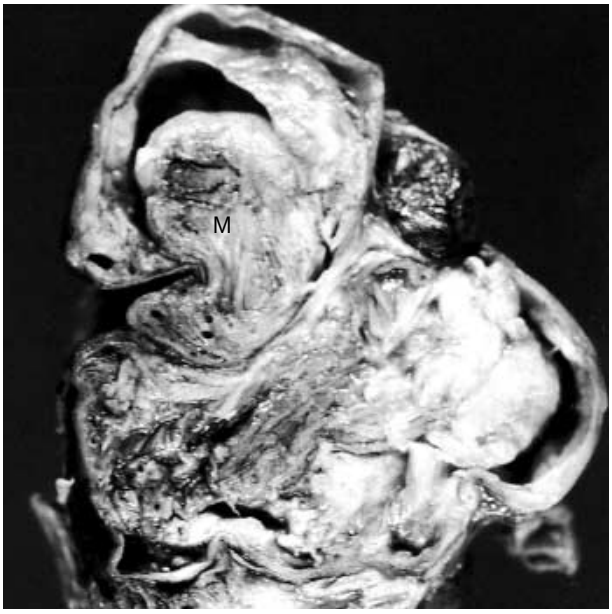

Fig. 2. Cut surface of the mass which forms a protruding mass above the serosal surface of the fundic myometrium. The mass (M) is reminiscent of worm-like mass of intravascular leiomyomatosis due to perinodular accumulation of edematous fluid.

an ill-defined intramural mass in the adjacent myometrium, measuring about 3.0 × 2.5 × 2.0 cm (Fig. 1, arrow). A serosal covering was not identified on the multinodular masses. Within the myometrium, there was an intramural myoma, measuring 3.5 × 3.0 × 3.0 cm. The left ovary, measuring 5 × 4 × 2 cm, adhered to the multinodular masses and it had a cyst with a smooth inner surface. The left salpinx revealed a hydrosalpingeal change with adhesion to the ovarian surface.

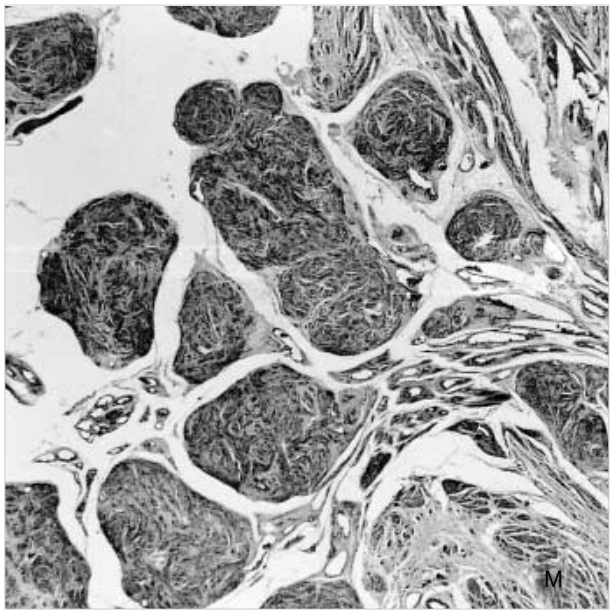

Fig. 3. Photomicroscopic findings shows innumerable nodules composed of mild to moderate hyalinized smooth muscle bundles projecting from the normal myometrium (M). Hydropic changes within the nodules are rarely present.

Case 2

The patient was a 46-year-old woman who presented with abdominal discomfort and vaginal bleeding. The preoperative clinical impression was a retroperitoneal tumor. The uterus, weighing 400 g and measuring 11 × 13 × 6 cm, showed a subserosally protruding, lobulated, partly cystic mass on the left lateral wall. The mass measured 11 cm in the largest dimension and the cut surface revealed several worm-like masses growing into the cystic spaces (Fig. 2). The serosal surface of the mass was smooth.

Both patients received total hysterectomies and they are doing well postoperatively during follow-up periods of 16 and 21 months. They did not receive any other treatments after surgery.

Histologically, the innumerable nodules in case 1 and the worm-like masses in case 2 were composed of mild to moderate hyalinized smooth muscle bundles, but were rarely hydropic within the nodules. Nuclear atypia, pleomorphism, or mitotic

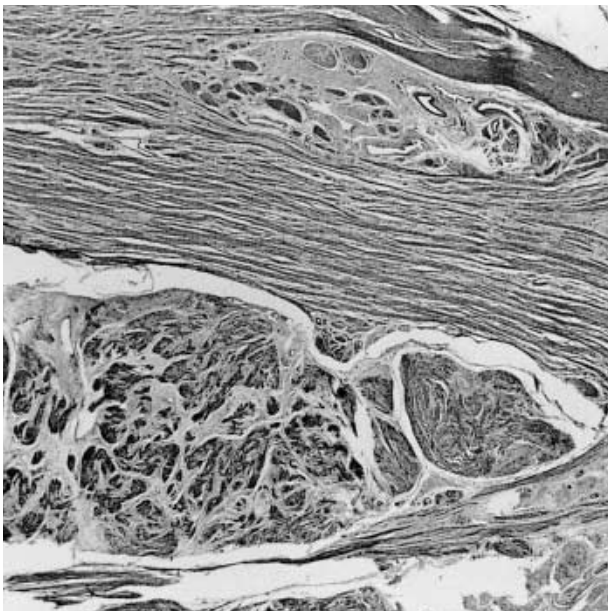

Fig. 4. Intramural dissecting mass underneath the projecting mass also shows retraction artifact around the nodule.

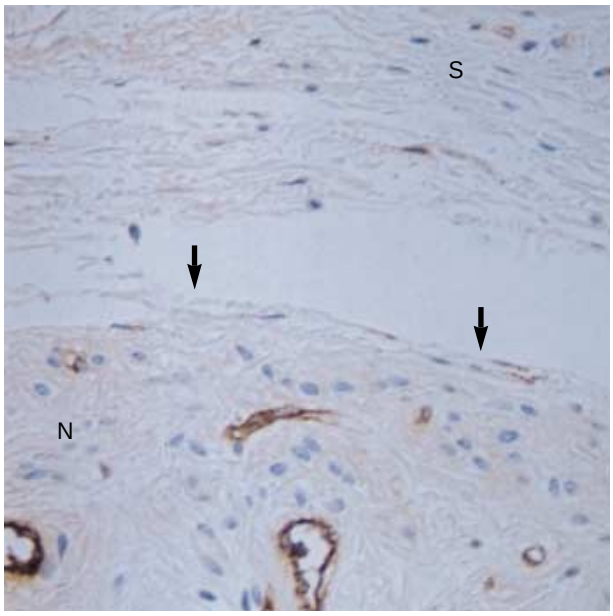

Fig. 5. Immunohistochemical stain for factor VIII does not demonstrate endothelial cells around the nodules (arrows). N: nodule, S: surrounding tissue.

activity were not identified in the constituent cells. Each nodule was detached from the intervening vascularized hydropic stroma by retraction artifacts that produced pseudovascular spaces around the nodules (Fig. 3). In case 1, similar myometrial nodules were identified within the adjacent myometrium as well as outside of the serosal surface, which also had retraction artifacts from the surrounding normal myometrium (Fig. 4). However, endothelial cells were not identified around the nodules on immunohistochemical staining for factor VIII-related antigen (1:600, Dako, Carpinteria, U.S.A.) and CD34 (1:2,500, Immunotech, Marseille, France) (Fig. 5). The intervening connective tissue between the nodules were loose and edematous and contained many dilatated vascular spaces, but intra-or extracellular mucin was not identified on alcian blue and colloidal iron stains. The nodules did not show infiltrative growth in any portion. In case 1, there was an adenomatoid tumor in the adjacent normal myometrium that was thought to be incidentally associated (Fig. 1, arrow).

DISCUSSION

Intramural dissection refers to an unusual growth pattern of leiomyoma with infiltration of blood vessels or the myometrium. In the literature, there are several variants of leiomyomas having poorly demarcated margins with intramural dissecting patterns at the periphery. Infiltrating leiomyomas have been described to indicate the leiomyomas that extend beyond the corpus with pushing margins and microscopic patterns of intramural dissection, most often into the broad ligament but also into other contiguous structures.[3] It was mentioned that they never detach themselves from the uterus and are differentiated from the leiomyosarcoma. However, their microscopic features are poorly documented in the literature and therefore differences from imtramural dissecting leiomyoma can not be clearly defined. Intramural dissecting leiomyoma is an intrauterine tumor having an irregular elongated focus of intramural dissection but lacking the features of intravenous leiomyomatosis or multinodular hydropic degeneration.[4] Cotyledonoid dissecting leiomyoma is a very rare uterine smooth muscle tumor with intramural dissection and characteristic gross findings in which an exophytic bulky tumor resembling placental tissue extends from the uterine wall into the broad ligament and pelvic cavity as in case 1.[5,6] Those three entities do not usually form hydropic tissue around the dissecting mass. In contrast, PHDL refers to a rare, but characteristic pattern of degeneration in which a multinodular growth pattern is formed by the accumulation of edema fluid around the fascicles of neoplastic smooth muscle bundles, and may cause problems in the differential diagnosis from IVL or myxoid leiomyosarcoma.[1,2] Case 1 in our study has features of both cotyledonoid dissecting leiomyoma and PHDL, case 2 shows features of both intramural dissecting leiomyoma and PHDL.

The mechanisms of forming the peculiar gross findings and perinodular fluid collection in case 1, which we call extrauterine extension, have not been fully understood. Because hyaline and cystic degenerations in the leiomyomas are frequently accompanied by hydropic degeneration,[2] it is presumed that the accumulation of a large amount of fluid around the subserosal multinodular myomatous masses (Fig. 4) and the subsequent degeneration or rupture of the overlying serosa may expose the preformed multinodular mass into the pelvic cavity, reminiscent of the extrauterine extension of the mass. Our assumption can be supported by the histological findings of retraction artifacts around the intramural dissecting masses in case 1 (Fig. 4) and perinodular cleft-like spaces containing fluid in case 2 (Fig. 2). Therefore, we thought that intramural dissecting leiomyoma, cotyledonoid dissecting leiomyoma, PHDL and possibly infiltrating leiomyoma are not separate, but closely related subtypes showing different evolutionary changes and it is important to examine the tissues at the interface between the grossly evident uterine tumor and the surrounding myometrium to identify if there is any intrauterine dissecting pattern.

The biologic behavior of the tumor cannot be clearly estimated because there have been only a few reports in the literature. Clement *et al*. presented 10 uterine leiomyomas with hydropic changes that created problems in the differential diagnosis.[2] The clinical features and the follow-up results were uneventful within a mean follow-up period of 3.8 years.[2] Coad *et al*., on the other hand, suggested a more aggressive behavior in a case of PHDL that showed extrauterine extension.[1] However, the patient showing extrauterine extension in our study, and those in the literature, are doing well postoperatively without evidence of recurrence, though the follow-up periods are not long as yet to form a positive conclusion. We believe that various gross and microscopic appearances can be formed according to the extent of hydropic and hyaline degeneration and that PHDL may produce even more worrisome gross features mimicking an invasion of the adjacent organs. However, extrauterine extension *per se* does not seem to be related to the prognosis or biologic behavior of the patient.

The presence of an extrauterine extension, such as a vague worm-like appearance and a perinodular retraction forming pseudovascular spaces in PHDL, closely mimics the gross and microscopic findings of intravenous leiomyomatosis. Intramural dissection can also be seen in cases of IVL, however, PHDL should be clearly differentiated from IVL or myxoid leiomyosarcoma because of its different biologic behavior. In IVL, up to 20% of the cases may have a recurrence following hysterectomy.[7,8] Immunohistochemical stainings for the factor VIII-related antigen or for other endothelial markers confirm the absence of the endothelial cells around the nodules or within the pseudovascular spaces of PHDL in contrast to the presence of endothelial cells of IVL. Extension beyond the confines of the myometrium raises the possibility of a myxoid leiomyosarcoma. PHDL, though, does not form a gelatinous circumscribed mass, or myometrial or vascular invasion, which are characteristics of myxoid leiomyosarcoma. The term "hydropic degeneration" is often inappropriately confused as "myxoid" degeneration. The term "myxoid" degeneration has been described as collection of acellular material rich in acid mucin and has been regarded as a feature often encountered in women with leiomyomas who are pregnant or taking progestins.[2,9] The myxoid material is strongly positive with alcian blue and colloidal iron stains in contrast to the hydropic substance in PHDL that shows either negativity or weak positivity for alcian-blue stain.[10,11] According to these characteristics, myxoid degeneration of leiomyoma must be much less common than hydropic degeneration. Although the histologic findings of increased cellularity, pleomorphism, mitotic activity, and infiltrative growth usually make it possible to diagnose myxoid leiomyosarcoma, the tumor may have a very low mitotic rate and insignificant nuclear atypia in some cases.[10,11] Therefore, scrutinized examination for infiltrative growth, mucin staining for myxoid materials, and gross findings can be helpful for the differential diagnosis.

In conclusion, an awareness of the gross and microscopic findings of a variety of degenerative changes in uterine leiomyomas, especially PHDL, is thought to be important so as not to erroneously diagnose a benign smooth muscle neoplasm as a more aggressive type of tumor that may call for aggressive management.

REFERENCES

1. Coad JE, Sulaiman RA, Das K, *et al.* Perinodular hydropic degeneration of a uterine leiomyoma: a diagnostic challenge. Hum Pathol 1997; 28: 249-51.
2. Clement PB, Young RH, Scully RE. Diffuse, perinodular, and other patterns of hydropic degeneration within and adjacent to uterine leiomyomas. Problems in differential diagnosis. Am J Surg Pathol 1992; 16: 26-32.
3. Hendrickson MR, Kempson RL. Smooth muscle neoplasm. In: Hendrickson MR, Kempson RL. eds. Surgical Pathology of the uterine corpus. Philadelphia: WB Saunders, 1980; 468-529.

4. Roth LM, Reed RJ. Dissecting leiomyomas of the uterus other than cotyledonoid dissecting leiomyomas: a report of eight cases. Am J Surg Pathol 1999; 23: 1032-9.
5. Roth LM, Reed RJ, Sternberg WH. Cotyledonoid dissecting leiomyoma of the uterus. The Sternberg tumor. Am J Surg Pathol 1996; 20: 1455-61.
6. Roth LM, Reed RJ. Cotyledonoid leiomyoma of the uterus: report of a case. Int J Gynecol Pathol 2000; 19: 272-5.
7. Clement PB, Young RH, Scully RE. Intravenous leiomyomatosis of the uterus. A clinicopathological analysis of 16 cases with unusual histologic features. Am J Surg Pathol 1988; 12: 932-45.
8. Mulvany N, Slavin J, Ostor A, *et al.* Intravenous leiomyomatosis of the uterus: a clinicopathologic study of 22 cases. Int J Gynecol Pathol 1994; 13: 1-9.
9. Clement PB, Young RH, Scully RE. Nontrophoblastic pathology of the female genital tract and peritoneum associated with pregnancy. Semin Diagn Pathol 1989; 6: 372-406.
10. Kasahara K, Nishida M, Iijima S, *et al.* Uterine myxoid leiomyosarcoma. Obstet Gynecol 2000; 95: 1004-6.
11. King ME, Dickersin GR, Scully RE. Myxoid leiomyosarcoma of the uterus. A report of six cases. Am J Surg Pathol 1982; 6: 589-98.