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Diffuse Leiomyomatosis of the Uterus
- A Brief Case Report -

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Diffuse leiomyomatosis of the uterus is a rare condition that is distinguished from the uterine leiomyoma due to the diffuse involvement of the myometrium by numerous, ill-defined, smooth muscle nodules. We present here a case of diffuse uterine leiomyomatosis in a 34-year-old woman. The hysterectomy revealed a symmetrically enlarged uterus containing numerous, small, ill-defined leiomyomatous nodules. Microscopically, the nodules were composed of compact fascicles and interweaving bundles of uniform benign smooth muscle cells. On the immunohistochemical staining, the progesterone receptor level was higher in the leiomyomatosis than in the adjacent normal myometrial tissue, but the estrogen receptor level and Ki-67 labeling index were equal in both areas. At the twelve months follow-up, this patient has been doing very well with no evidence of pelvic or intraabdominal recurrence of disease.

Key Words : Leiomyomatosis; Leiomyoma; Ki-67; Sex steroid receptor; Uterus

Diffuse uterine leiomyomatosis is a rare benign condition in which the uterus is symmetrically enlarged as a result of the involvement of the entire myometrium by innumerable, ill-defined, often small and confluent histologically benign smooth muscle nodules.[1] To the best of our knowledge, only 32 cases have been reported so far in the English literature.[2] Diffuse uterine leiomyomatosis has not yet been reported on in Korea. We herein report on a case of diffuse uterine leiomyomatosis with a review of the relevant literature.

CASE REPORT

A 34-year-old woman (gravida 2, para 2) presented with a seven-year history of lower abdominal discomfort and irregular menstruation. The patient's obstetrical history included two Cesarean sections that resulted in the delivery of two healthy full-term babies. The physical examination showed an enlarged uterus that was subsequently confirmed by ultrasound examination. There were no other abnormal findings of the pelvic and abdominal cavity on exploration, except for the enlarged uterus. A total abdominal hysterectomy was performed. On gross examination, the resected uterus was symmetrically enlarged; it measured 10 cm in length, 9 cm between the cornua and 7 cm anteroposteriorly, and the serosal surface had a bosselated appearance. The ectocervix, the squamo-columnar junction and the endocervix were unremarkable. The entire myometrium was diffusely thickened and almost completely replaced by large numbers of firm, poorly demarcated, confluent nodules ranging from 0.5 cm to 1.5 cm in diameter. The nodules were paler than the surrounding myometrium and they presented with a whorled or trabeculated appearance. No areas of necrosis or calcifications were identified. The outline of endometrial cavity was distorted by multiple submucosal nodules and it had a bosselated appearance, although the endometrium itself appeared normal on gross examination (Fig. 1). Microscopically, the nodules were composed of compact fascicles and interweaving bundles of plump uniform benign smooth muscle cells. The nodules blended with each other and merged imperceptibly with the surrounding less cellular normal myometrium. Clustered capillaries presented in the center of the nodules and the nodules were surrounded by hyalinized stroma. No cellular pleomorphism or abnormal mitotic figures

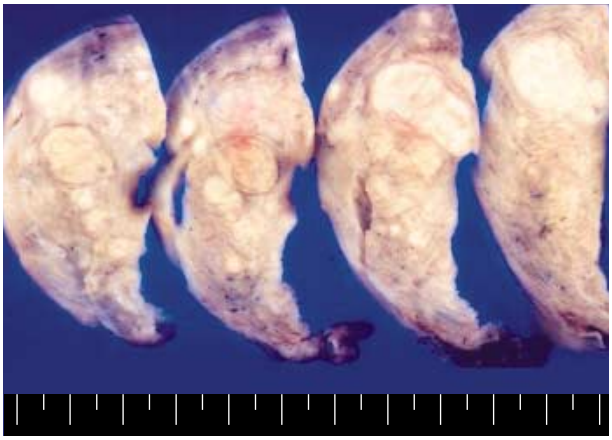

Fig. 1. The cut surface of a uterine wall shows numerous coalesced and ill-defined leiomyomatosis nodules replacing most of the myometrium.

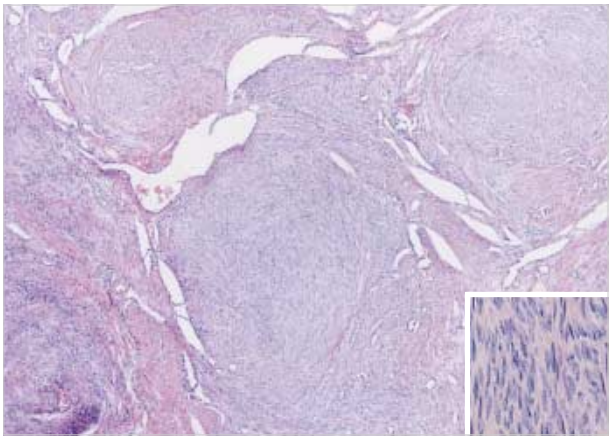

Fig. 2. The myometrium shows innumerable minute leiomyomatous lesions separated by a rather hyalinized stroma. High power view shows neither cellular atypia nor mitotic activity (inset).

were found, nor was any intravascular extension discovered (Fig. 2). The endometrium showed changes typical of the proliferative phase. On the immunohistochemical staining performed on ten different sections, the progesterone receptor (PR) (1:50, Dako, Carpinteria, CA, USA) level was higher in the leiomyomatosis than in the adjacent normal myometrial tissue (Fig. 3), whereas the estrogen receptor (ER) (1:50, Dako, Glostrup, Denmark) was negative, and the Ki-67 (1:200, Dako, Glostrup, Denmark) labeling index was less than 5% in both areas. At the twelve months follow-up, the patient has been doing very well with no evidence of pelvic or intraabdominal recurrence of disease.

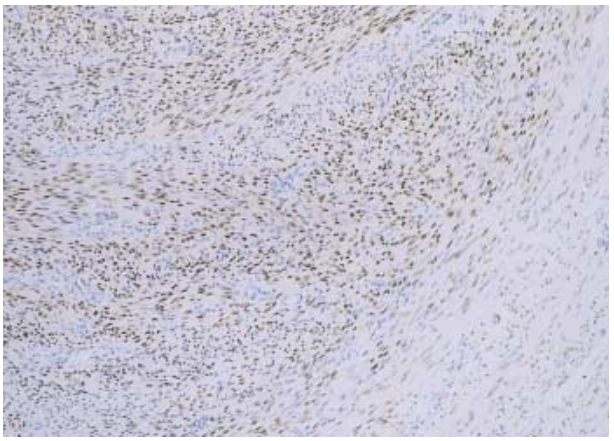

Fig. 3. On immunohistochemical study, the progesterone receptor level is higher in the leiomyomatosis (left) than in the adjacent normal myometrial tissue.

DISCUSSION

There are only 32 well-documented cases of diffuse uterine leiomyomatosis in the English literature.[2] All the reported cases of diffuse leiomyomatosis were in women of reproductive age from 22 to 38 years, as in the present case. Similar to uterine leiomyomas, patients with leiomyomatosis presented with menorrhagea, dysmenorrhea, abdominal pain, infertility, and pelvic pressure. Although some of these lesions may be associated with parametrial and ovarian involvement, diffuse uterine leiomyomatosis is usually confined to the uterus, and this case represents an example of diffuse and uniform involvement of the entire myometrium by multiple leiomyomas. All the cases of diffuse leiomyomatosis showed no evidence of recurred disease after hysterectomy, even though there are cases of leiomyomatosis exhibiting concomitant parametrial, pelvic and bilateral ovarian involvements.[3]

The differential diagnosis of leiomyomatosis includes multiple leiomyomas, intravascular leiomyomatosis and endometrial stromal sarcoma.[1,4,5] Leiomyomatosis can be distinguished from leiomyoma due to the uniform symmetrical involvement of the entire myometrium by smooth muscle nodules without distinct borders between the nodules, whereas cases of multiple leiomyomas tend to have asymmetrical involvement of the uterus and sharp circumscription of the individual leiomyomas. Intravascular leiomyomatosis has a creamy to yellow color, and there are intravascular extensions of worm-like smooth muscle tumor having multinodular irregular or indistinct margins. Intravascular leiomyomatosis can be distinguished histologically from diffuse leiomyomatosis by the presence of some or all of the neoplastic smooth muscle within the vascular channels. Endometrial stromal sarcoma is characterized by its invasive growth having an abrupt transition with the normal myometrium, and it has a sheet-like, rather than fascicular, growth pattern. In contrast to diffuse leiomyomatosis, small neoplastic cells with round to oblong nuclei

and scant cytoplasm separate the thick walled vessels. In addition, endometrial growth and intravascular growth are usually present.

Both leiomyoma and diffuse uterine leiomyomatosis are thought to be neoplastic processes. However, the pathogenesis of diffuse leiomyomatosis, like the usual uterine leiomyomas, is far from clear. Individual uterine leiomyomas have been recognized as a monoclonal neoplasm on the basis of analysis of glucose-6-phosphate dehydrogenase isoenzymes.[6] Mulvany *et al*.[4] have suggested that it is difficult to conceive of the independent and synchronous origin of numerous nodules of the diffuse leiomyomatosis, and a field effect via the increased concentration of ERs and PRs is more likely. However, Baschinsky *et al*.[5] have reported that various tumor sites within the diffuse uterine leiomyomatosis were of different clonal origin, and this supports the independent origin of the neoplastic clones. They suggested that diffuse uterine leiomyomatosis may be an exuberant example of multiple uterine leiomyomas budding into each other and blending imperceptibly to the extent that the single nodules could not be readily identified by gross examination.

The concentration of ERs and PRs in leiomyoma cells is variable during the menstrual cycle. Nisolle *et al*.[7] have reported that ERs and PRs were significantly higher in leiomyoma than in the adjacent myometrium, and the difference of the proliferation index (Ki-67) was not significant during the proliferative phase. In the present case, however, the ER level was equal in both areas. The results suggest that diffuse leiomyomatosis lesions may be under the influence of progesterone, which may play a major role in their growth. All the reported patients have undergone hysterectomy, despite that these patients were in the third or fourth decades of life, because the innumerable nodules with unclear margination preclude the possibility of myomectomy. The use of an antiprogestin agent may be proposed as a treatment for diffuse leiomyomatosis. The distinction from uterine leiomyomas rests, not only upon the macroscopic and microscopic appearances, but possibly also on pathogenesis and the certainly of their treatment.

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