INTRODUCTION

Low-grade endometrial stromal sarcoma (LGESS) is rare and accounts for 0.2%–0.4% of uterine malignancies [1,2]. LGESS with intravascular extension to the inferior vena cava (IVC) or to the heart is extremely rare. It is estimated that only 26 cases have been reported in the world, and it has never been reported in Korea. We treated a patient with LGESS and IVC extension and report our experience here.

CASE

A 60-year-old female presented with left leg edema. She had a history of total hysterectomy with right salpingo-oophorectomy in 2002, with final diagnoses of leiomyoma of the uterus and a mucinous cystadenoma of the right ovary. She visited a local clinic, and computed tomography (CT) was performed. On CT scan, multiple masses were found around both external iliac veins (EIVs), with
Endometrial Stromal Sarcoma with IVC Extension

Fig. 2. Preoperative T1-weighted magnetic resonance imaging with fat suppression image after contrast injection. (A) Pelvic masses around external iliac vein (EIV, arrowheads) and artery (arrows). Boundary between mass and EIV appears to fuse, indicative of direct vascular invasion. (B) Tumor mass (arrows) within left common iliac vein is identified.

Fig. 3. Macroscopic and microscopic findings of the surgical specimens. (A) Two pelvic masses and inferior vena cava (IVC) mass were obtained. (B) Tumor cells show bland ovoid to spindle nuclei with scant cytoplasm arranged concentrically around (H&E stain, x400). (C, D) On immunohistochemical analysis, tumor cells show cytoplasmic immunostaining for CD10 and nuclear immunostaining for β-catenin (C: CD10 immunohistochemistry, x400; D: β-catenin immunohistochemistry, x400).
suspected direct vascular invasion. The patient underwent pelvic mass biopsy and left salpingo-oophorectomy. The specimen was insufficient for a diagnosis and was then transferred to our hospital. A pathologic review was performed, and a hemangiopericytoma-like vascular pattern was observed. We attempted to perform an additional pathologic review of the specimens which were obtained in 2002, but they had already been disposed of. Ascending venography was attempted through the femoral veins, but was limited due to obstruction of both EIVs by the tumor mass (Fig. 1). Magnetic resonance imaging of the pelvis was performed. Both EIVs were directly invaded by the tumor, and the tumor extended beyond the convergence of the common iliac veins (Fig. 2). During the operation, huge retroperitoneal masses were found: the right side mass was 8 cm and the left side mass was 6 cm in diameter. The masses were rubbery with yellow color. The mass margins were well-capsulated, but were hardly fixed to the EIVs. The mass in the IVC extended to 3 cm below the hepatic vein convergence to the IVC. The tumor-free IVC segment was too short to apply a vessel clamp. Instead, we encircled the IVC for 2 times with a long tape and then pulled it gently to control the IVC temporarily. Through a transverse incision on the proximal IVC, the tumor was identified from its proximal end. The tumor had a few dense and worm-like appearance adhesions to the intima of the IVC, and direct invasion to the IVC was absent. The tumor was easily peeled off from the IVC with gentle retraction and was removed completely. The patient recovered without complications, and she was discharged at postoperative day (POD) #13.

The pelvic masses were pathologically diagnosed as LGESS. The mitotic index was 12 per 10 high power fields (HPFs). The tumor cell showed a diffuse, strong cytoplasmic immunoreactivity for CD10 and nuclear immunoreactivity for β-catenin, estrogen receptor (ER), and progesterone receptor (PR), but they were completely negative for smooth muscle actin (Fig. 3).

A follow-up CT scan was performed on POD #7. Two remnant tumor masses were identified on the posterior side of the left EIV, with diameters of 3 cm and 2.5 cm. Additional surgery had a very high risk of vessel injury, so we decided to treat the remnant lesions with adjuvant therapy. The patient received radiotherapy over the left pelvic cavity for two months. Hormonal therapy (Letrozole; Femara; Novartis Pharmaceuticals Corporation, Hanover, Germany) was continued for over 13 months, and the masses did not show any progression. This study was approved by the Seoul St. Mary’s Hospital institutional review board (IRB No. KC13ZISE0347).

DISCUSSION

The classification of ESS was proposed by Norris and Taylor in 1966. In this classification, if mitosis was observed in less than 10 cells per 10 HPFs, it was classified as low-grade ESS. If mitosis was observed in 10 or more cells per 10 HPFs, it was defined as high-grade ESS [3]. However, clinical outcomes were not well associated with mitotic activity [3-5]. In 2002, the World Health Organization classification divided ESS into LGESS and undifferentiated ESS (UESS) according to infiltration pattern and tumor morphology [2]. LGESS shows histologic characteristics of the non-neoplastic proliferative phase of endometrial stroma, small cells with scant cytoplasm, round to ovoid nuclei, plexiform vasculature, and infrequent mitotic figures. LGESS infiltrates myometrium in a ‘finger-like’ fashion. Conversely, UESS does not contain the normal proliferative endometrial stroma, and involves destructive infiltration of the myometrium and intratumoral necrosis [2-4].

The differentiation of LGESS from leiomyoma may be difficult. Only 10% of patients are diagnosed as LGESS before surgery, and there are many cases of false diagnosis even after a postoperative pathologic examination [5]. It is important to distinguish between LGESS and leiomyoma because leiomyoma is a benign disease, while LGESS is a malignant disease. While both tumors have well-circumscribed margins, LGESS has a soft and rubbery consistency with a yellow color, while leiomyoma has a firm, whirled and bulging appearance with a whitish color [6,7]. When accompanied by intravascular extension, both tumors are easily peeled from the vascular intima, show worm-like projections to the vascular wall, and can extend to the IVC or heart [6,8,9]. One different feature is that LGESS commonly infiltrates extraterine organs while intravascular leiomyomatosis rarely does [7,10]. The most important factor for distinguishing LGESS from leiomyoma is to precisely identify microscopic findings, and then we can obtain useful diagnostic information by incorporating a immunohistochemistry study. Several markers have been proposed as a tool of diagnosis for ESS, including vimentin, actin, and desmin. However, these markers have had heterogeneous outcomes and insufficient specificity. The useful markers for diagnosis of ESS are CD10 and β-catenin. LGESSs are usually positive for CD10 and both ER and PR. CD10, however, may also be positive in leiomyoma. For differential diagnosis, complementary usage of β-catenin can be helpful. Nuclear β-catenin is not expressed in normal endometrial stroma or uterine smooth muscle tumors. β-catenin is frequently expressed in ESS, especially in LGESS. Therefore, combination of CD10 and β-catenin for diagnosis of LGESS is very useful [11,12].
Most cases of LGESS have favorable outcomes, with a 5-year survival rate of 80%-90% after curative resection. However, recurrence is common even in early stages, estimated to be between 37%-60%, and the disease related death rate is reported to be 15%-25% [13,14]. The prognostic factors reported by previous studies have been controversial. Generally agreed prognostic factors are degree of differentiation and completeness of surgery. Other factors, such as tumor stage, vascular or lymphatic involvement, depth of myometrial invasion, steroid hormone receptor status, and application of adjuvant therapy have provided inconsistent results [3,14-17]. LGESS is a relatively favorable malignant disease, but it has high rate of recurrence, thus complete resection is mandatory. For successful management of LGESS, appropriate evaluations about tumor extent or metastasis must be checked, necessary procedures must be preceded, and exact planning of the operation must be established.

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