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Endometrial Stromal Sarcoma Arising from Endometrial Polyp: A Case Report

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Endometrial stromal sarcoma (ESS) is a rare malignant tumor of the uterus. We report an uncommon case of ESS composed of both low-grade ESS and high-grade ESS arising from an endometrial polyp. On the findings of magnetic resonance imaging and contrast computed tomography, a patient was suspected of having uterine malignant tumor. She underwent a total abdominal hysterectomy with bilateral salpingo-oophorectomy. Macroscopically, the tumor was a polypoid lesion in the uterine cavity. The tumor was an endometrial polyp with ESS components. ESS was composed of low-grade ESS and high-grade ESS. By immunohistochemistry, both an endometrial polyp and low-grade ESS showed a positivity for CD10, estrogen receptor (ER), and progesterone receptor (PR). However, high-grade ESS showed only a focal and weak CD10 positivity with no immunostaining for ER and PR. A focal or diffuse positivity for α-smooth muscle actin and desmin was noted in both low-grade and high-grade ESS. The positive rates of Ki-67 and p53 in high-grade ESS were elevated up to over 95%. She was diagnosed as having ESS in a stage IA. After surgery, she received no further treatment. She has been without recurrence for 4 years since an initial surgery. In conclusion, immunohistochemical analyses are useful for make an accurate diagnosis of ESS showing a transition from low-grade ESS to high-grade ESS in addition to the conventional method.

INTRODUCTION

Endometrial stromal sarcoma (ESS) is a rare malignant tumor of the uterus. Uterine sarcomas represent 8% of primary uterine malignancies, and ESS represent about 15% of uterine sarcomas (3,8). ESS was traditionally classified into two distinct subtypes, low-grade ESS and high-grade ESS according to the mitotic activity (15). Recently, the 2014 World Health Organization tumor classification system separates ESS into low-grade ESS, high-grade ESS, and undifferentiated uterine sarcoma (UUS) histologically, genetically, and clinically (13).

ESS is defined as endometrial stromal neoplasm that exhibits myoinvasion or intravascular growth (4). Low-grade ESS is composed of uniform, oval to spindle-sharped cells that resemble those of proliferative-phase endometrial stroma, whereas high-grade ESS lacks specific differentiation and bears no histological resemblance to endometrial stroma (18).

Genetically, low-grade ESS is shown to frequently contain chromosomal rearrangements that result in JAZF-SUZ12 fusion or equivalent genetic fusion (13), whereas high-grade ESS is defined by the presence of YWHAE-FAM22A/B fusions (13). In contrast, UUS is a tumor arising in the endometrium or myometrium with high-grade cytological features and with no specific type of differentiation (13). In the present case, we used a classification dividing ESS into low-grade ESS and high-grade ESS because we did not examine genetic type.

Herein, we report an uncommon case of an ESS independently composed of both low-grade ESS and high-grade ESS arising from an endometrial polyp. A spectrum of an endometrial polyp, through low-grade ESS, to high-grade ESS was assessed by a comparative pathological and immunohistochemical analyses.

CLINICAL CASE

A 67-year-old woman presented with abnormal genital bleeding of a few days' duration. Transvaginal ultrasound revealed the enlarged uterus with thickened endometrium. A magnetic resonance imaging (MRI) of the pelvis displayed a 7 cm-sized tumor protruding into the uterine cavity. The tumor with mixed low intensity and high intensity was noted on T2-weighted images (Figure 1A, B). The content of the tumor was mixed with low intensive and high intensive areas on diffusion-weighted (DW) images (Figure 1C). In a contrast computed tomography, the tumor filling in the uterine cavity was unevenly and lightly enhanced (Figure 1D). No

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metastatic lesion was found in the abdominal cavity on the images. Serum CA125 levels were elevated at 35.4 U/ml (normal range ＜35 U/mL). The cytology of the cervix was normal, but a biopsy of the endometrium could not be done due to the occlusion of the cervical os.

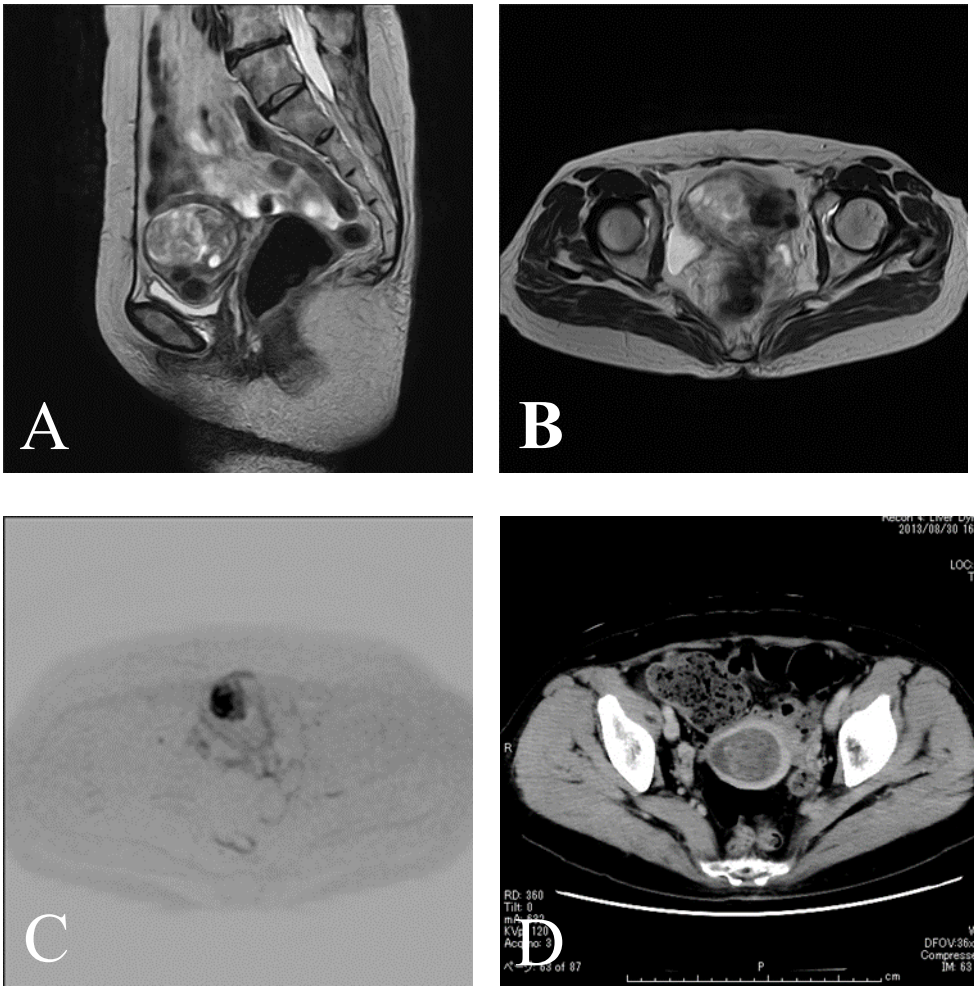

Figure 1. A magnetic resonance imaging of a 7 cm-sized tumor protruding into the uterine cavity on T2-weighted images. A) sagittal imaging, B) axial imaging, and C) a diffusion-weighted imaging, and D) a contrasted enhanced computed tomographic image of the tumor.

On the basis of the imaging studies, a preoperative presumptive diagnosis was a uterine malignant tumor. She underwent a total abdominal hysterectomy with bilateral salpingo-oophorectomy. Macroscopically, the uterus was enlarged, and a 70×50×30 mm polypoid mass was protruding into the uterine cavity. Pathological examination revealed ESS independently composed of both low-grade ESS and high-grade ESS in a direct continuity with an endometrial polyp (Figure 2A). The direct continuity between an endometrial polyp and low-grade ESS and that between low-grade ESS and high-grade ESS were histologically confirmed (Figure 2B, C). In an endometrial polyp, endometrial stromal cells were edematous and sparse in number, and the duct structure was kept. In low-grade ESS, spindle-shaped tumor cells similar to endometrial stromal cells proliferated (Figure 2D), and in high-grade ESS, tumor cells with cytologic atypia proliferated, and the necrosis was focally noted. Mitosis was not seen in low-grade ESS, but seen in high-grade ESS (Figure 2E, F).

Table I shows the differences in the histological and immunohistological findings among an endometrial polyp, low-grade ESS, and high-grade ESS. The lesion of high-grade ESS had more severe cytologic atypia and an increased mitotic index compared with the lesion of low-grade ESS. By immunohistochemistry, both an endometrial polyp and low-grade ESS showed a positivity for CD10 (Figure 3A, B), but high-grade ESS showed only a focal and weak CD10 positivity (Figure 3C). An endometrial polyp and low-grade ESS were immunopositive for estrogen receptor (ER) (Figure 4A, B), and progesterone receptor (PR) (Figure 4D, E). However, high-grade ESS were negative for ER and PR immunostaining (Figure 4C, F).

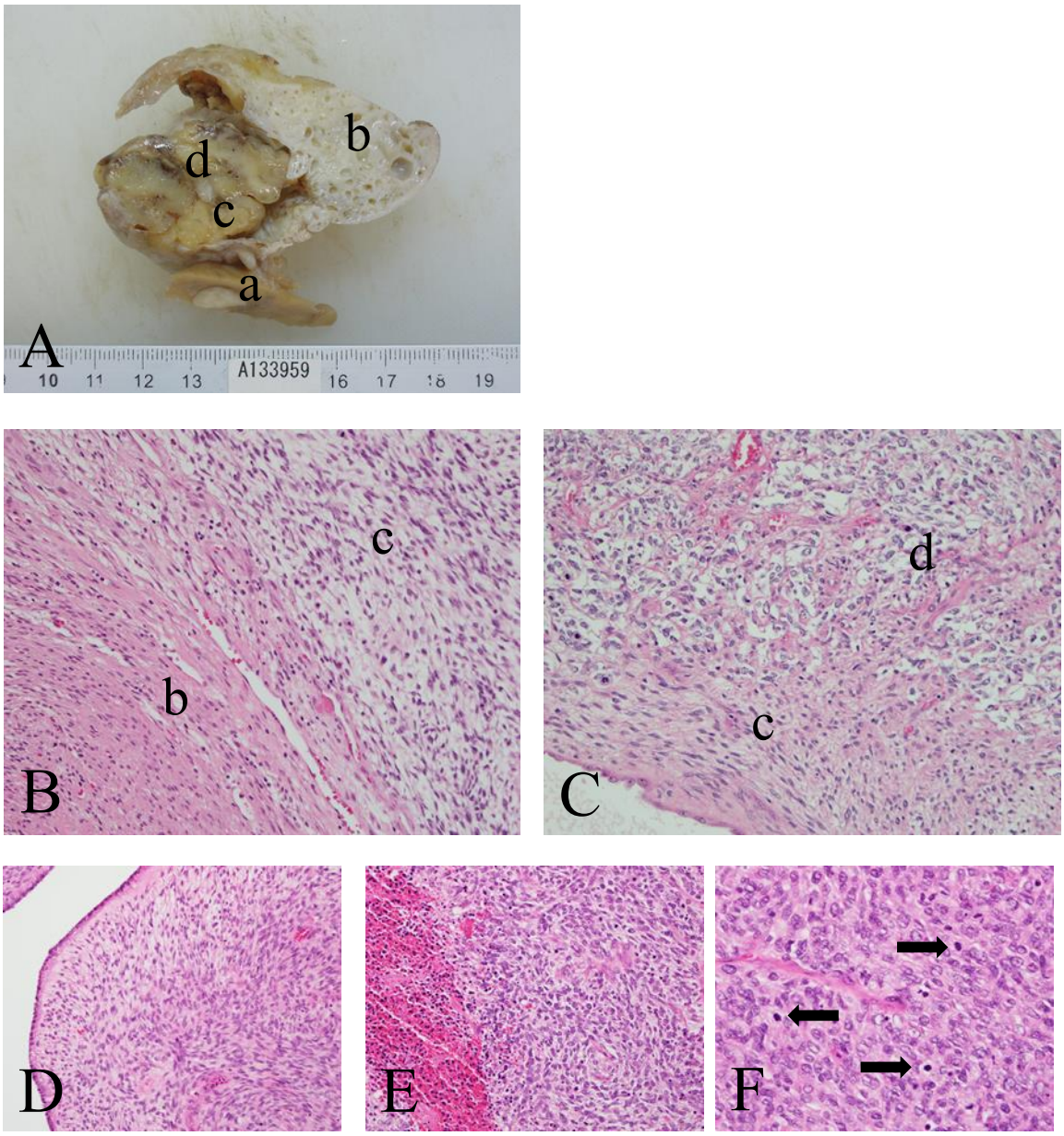

Figure 2. A) Macroscopic findings of a) endometrium, b) an endometrial polyp, c) low-grade ESS, and d) high-grade ESS, and microscopic findings showing B) a continuity between an endometrial polyp (b) and low-grade ESS (c), and C) a continuity between low-grade ESS (c) and high-grade ESS (d), HE stain, original magnification x200. Microscopic findings of D) low-grade ESS and E) high-grade ESS, HE stain, original magnification x200. F) Arrows indicate mitoses, HE stain, original magnification x400.

A focal or diffuse positivity for α-smooth muscle actin (α-SMA) and desmin was noted in both low-grade and high-grade ESS, but not in an endometrial polyp. The positive rate of Ki-67 of an endometrial polyp was less than 5% and it was almost negative for p53. The positive rates of Ki-67 and p53 of low-grade ESS were 10% to 20% and less than 5%, respectively, but both rates of high-grade ESS were elevated up to over 90%. (Figure 5)

She was diagnosed as having ESS in a stage IA. After surgery, she received no further treatment. She has been without recurrence for 4 years since an initial surgery.

Table I. Histological and immunohistochemical analyses.

	Endometrial polyp	Low-grade ESS	High-grade ESS
Glands	+	+	−
Neoplasm cell	−	spindle cell	polygonal cell
CD10	++ diffuse	+ not diffuse	± focal
Estrogen receptor (ER)	++ diffuse	++ diffuse	−
Progesterone receptor (PR)	++	++	−〜±
α-SMA	−	+ diffuse	± focal
Desmin	−	± focal	+ not diffuse
H-caldesmon	−	−	−
Ki-67	± ≦5%	+ 10-20%	++ ≧90%
p53	− almost negative	− ≦5%	++ ≧90%

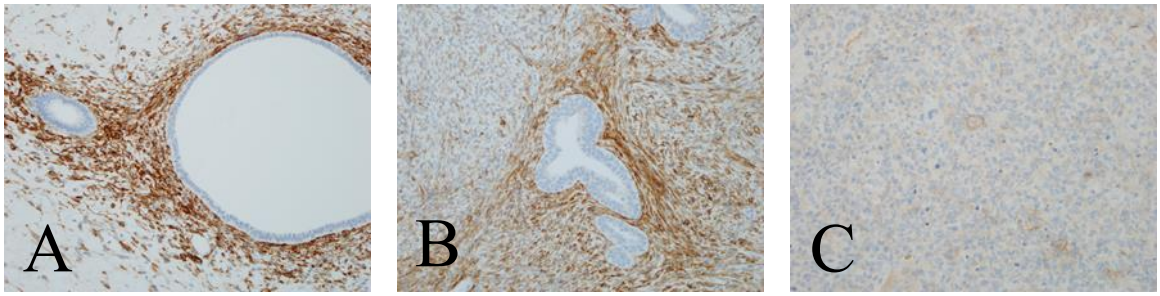

Figure 3. Immunohistochemistry of CD10 in A) an endometrial polyp, B) low-grade ESS, and C) high-grade ESS, original magnification x200

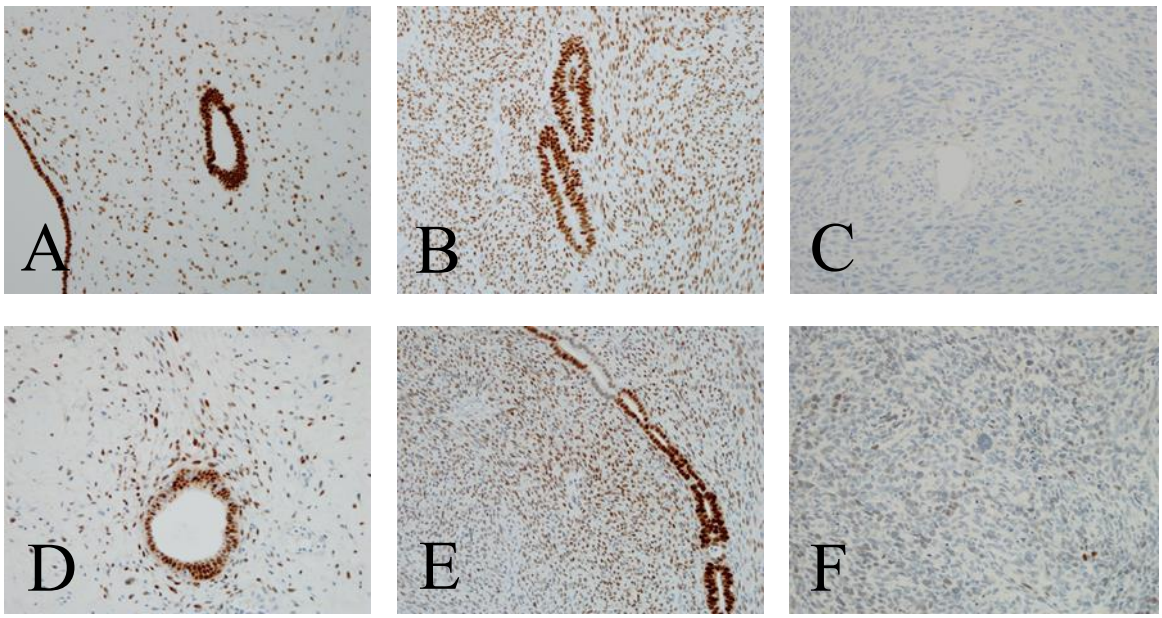

Figure 4. Immunohistochemistry of ER in A) an endometrial polyp, B) low-grade ESS, and C) high-grade ESS, and immunohistochemistry of PR in D) an endometrial polyp, E) low-grade ESS and F) high-grade ESS, original magnification x200.

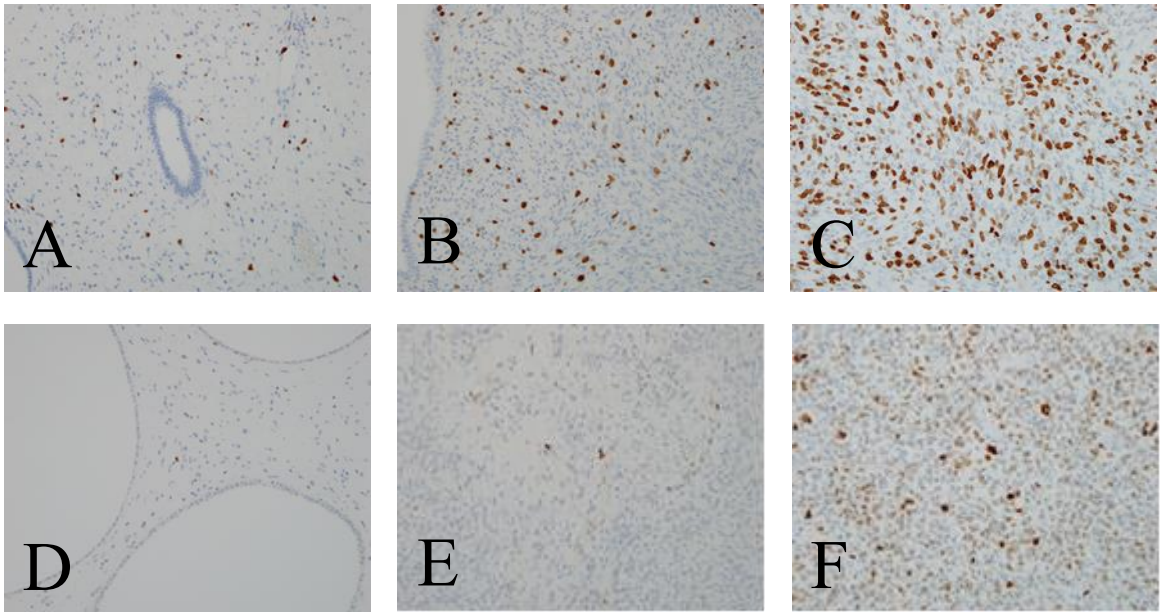

Figure 5. Ki-67 index in A) an endometrial polyp, B) low-grade ESS, and C) high-grade ESS, and immunohistochemistry of p53 in D) an endometrial polyp, E) low-grade ESS and F) high-grade ESS, original magnification x200.

DISCUSSION

We presented an uncommon morphology of ESS arising from an endometrial polyp with a transition from low-grade ESS to high-grade ESS. To our best knowledge, there has been no information regarding malignant transformation of an endometrial polyp to ESS. Furthermore, a transition from low-grade ESS to high-grade ESS is rarely reported except for a few cases (1,5,6,12,17,22).

To identify the sequential spectrum of malignant transformation from an endometrial polyp, through low-grade ESS, to high-grade ESS, we examined the differences in histological and immunehistochemical findings among an endometrial polyp, low-grade ESS, and high-grade ESS.

In our case, the tumor was present on the endometrium as a polypoid lesion. Histologically, the stem of the tumor was constituted with an endometrial polyp, and low-grade ESS developed in a direct continuity with an endometrial polyp. Histological examination confirmed a direct continuity between an endometrial polyp and low-grade ESS and between low-grade ESS and high-grade ESS. No apparent fibrous components that separated these tumors were noted.

Immunohistologically, ESS is shown to be usually positive for CD10, ER, and PR, and it may also be positive for smooth muscle markers, including H-cardesmon and desmin (9,14,21). CD10 is shown to be specifically expressed in the endometrial stroma (7,14), and CD10 is reported to be present diffusely or focally in low-grade ESS and focally in high-grade ESS (11). In this case, a diffuse immunostaining for CD10 was identified in an endometrial polyp, but not diffuse in low-grade ESS, and focally observed in high-grade ESS.

Balleine et al. (2) reported that the expression of PR in low-grade ESS closely resembles the pattern of expression of these proteins in normal endometrial stroma. In the present case, immunostaining for ER and PR were diffusely positive in an endometrial polyp and low-grade ESS, but negative for them in high-grade ESS.

To distinguish the tumor from sarcomas of smooth muscle origin, we examined immunopositivity for α-SMA, desmin, and H-caldesmon. In our case, immunoreactive α-SMA was diffusely present in low-grade ESS, but focally present in high-grade ESS. However, immunostaining for desmin was focally noted in low-grade ESS, but diffusely observed in high-grade ESS. Immunoreacive H-caldesmon was negative in low-grade ESS and high-grade ESS. H-caldesmon is a more specific marker in recognizing smooth muscle differentiation than desmin (16,19). Our results showing the positive staining for α-SMA and desmin and the negative staining for H-caldesmon indicates that this tumor is not of smooth muscle origin.

The distinctive differences between low-grade ESS and high-grade ESS were detected in Ki-67 index and p53 immunoreactivity. The both in high-grade ESS was higher than those in low-grade ESS. These findings indicate the highly malignant potential of high-grade ESS.

Although optimal therapy of ESS has not been established, surgical therapy remains the primary treatment for ESS (10). A total abdominal hysterectomy and salpingo-oophorectomy are basic surgical procedures. Seagle et al. (20) have reported that women with high-grade ESS had markedly decreased survival compared to those with low-grade ESS (five-year survival (95%CI): 32.6% versus 90.5%) and that median survival (95% CI) of

high-grade ESS was only 19.9 months (20). The authors described that the best treatment of high-grade ESS was early and complete surgical resection including lymphadenectomy and that the use of adjuvant chemotherapy and radiotherapy was associated with an increased survival for women with high-grade ESS. Because our patient was diagnosed as having stage IA disease, she was not given adjuvant treatment. She has been free from recurrence for 4 years since an initial surgery.

In conclusion, we presented an uncommon ESS arising from an endometrial polyp, characterized by a sequential malignant transformation from an endometrial polyp, through low-grade ESS, to high-grade ESS. Immunohistochemical analyses are useful for make an accurate diagnosis of a transition from low-grade ESS to high-grade ESS in addition to the conventional method.

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