Endometrial stromal sarcoma arising in extrauterine endometriosis: A case report

D. Kovač[1], *M.D., Ph.D., Prof.*; **I. Gašparović**[1], *student*; **M. Jašic**[1], *M.D.*; **D. Fučkar**[1], *M.D., assistant*
R. Dobi-Babić[2], *M.D., Ph.D., assistant prof.*; **H. Haller**[3], *M.D., Ph.D., Prof.*

[1]*Department of Pathology,* [2]*Department of Forensic Medicine, Medical School, University of Rijeka*
[3]*Department of Gynaecology and Obstetrics, Clinical Medical Center, Rijeka (Croatia)*

Summary

We report a rare case of a 46-year-old woman developing endometrial stromal sarcoma (ESS) on the grounds of extrauterine endometriosis. The patient presented with symptoms of stenosis of the rectosygmoid colon. The tissue samples were submitted to histological and immunohistochemical analyses using antibodies for indirect staining. The trial showed multiple foci of endometriosis and mesenchymal malignant tissue described as ESS in the bowel wall, mesentery and in the remnants of the left adnexae. According to our findings, we suspect that ESS might have arisen in colon endometriosis.

Key words: ESS; Endometriosis; Colon.

Introduction

Endometrioid adenocarcinoma is more likely to develop on the basis of endometriosis than endometrial stromal sarcoma (ESS). The etiology of endometrial stromal sarcoma is unknown, and also the pathogenesis. It accounts for approximately 1-2% of endometrial malignancies of which low-grade ESS occurs in 0.2% [1]. ESS occurs at an earlier age than most other uterine malignancies. The mean age is between 42 and 53 years. Mostly it occurs in postmenopausal patients, even though it has been documented in young women [2] and even children [3]. It is not associated with estrogen excess [4] although some studies have implicated differently. Persistence of functioning ovaries may not significantly affect the recurrence rate following surgery in Stage I patients [5].

Extrauterine ESS may develop from the ovary, fallopian tube, pelvis, colon, or retroperitoneum [4]. It is possible to consider the occurrence of metastatic tumor from the uterus years after the hysterectomy.

Most of endometrial stromal sarcomas are low-grade tumors. Women with Stage I low-grade ESS have a survival rate in excess of 80%. The outcome is less favorable for women with advanced-stage tumors (5-year survival rate is 40-50%) [2].

Case Report

A 46-year-old woman presented with symptoms of a stenosing process of the rectosygmoid colon in May, 2003. She had no history or symptoms of endometriosis. Laboratory analysis showed decreased MCH and high fibrinogen. At the time of presentation computed tomography showed a solid ovarian tumor measuring 9 cm in diameter, with spread to the adjacent peritoneum, mesentery and rectosygmoid colon. Laparotomy confirmed the CT findings. The surgical procedure consisted of oophorectomy, tumorectomy, omentectomy and resection of the colon with termino-terminal anastomosis with a 31 mm stapler.

Before that, the patient underwent surgical procedures twice, the first time in 1999 and the second time in 2001. In May 1999 the patient underwent total abdominal hysterectomy and right adnexectomy in the same hospital. The uterus was sent for pathohistological analysis. It measured 11x12x10. Three intramural well-defined nodules were found (measuring 0.5 cm, 4 cm and 8 cm in diameter). Histologically they were leiomyomas without atypia. The endometrium was in the proliferative phase, with no signs of adenomyosis. The fallopian tube and ovary had a normal histologic appearance. In September 2001 she underwent laparotomy to evacuate a pseudocystis of the left ovary in the same hospital. No specimens for pathohistology were sent. Cytologically, mesothelial cells, macrophages and red blood cells were found.

The patient has had high blood pressure for 30 years on medication. She had no history of taking hormonal or any other drugs.

Eleven months after the last surgical procedure the patient is well, without signs of disease.

Materials and Methods

Sections treated with hematoxylin-eosin were prepared from formalin-fixed, paraffin-embedded tumor tissue, underwent imunohistochemical studies performed by indirect staining methods and antibodies were used against cytokeratin (clone KL1, 1:50, Immunotech, Marseille, France), vimentin (3B4, 1:100, Dako, Glostrup, Denmark), smooth muscle actin (1A4, 1:50, Dako), neurofilaments (2F11, 1:75, Dako), CD117 (polyclonal, 1:100, Santa Cruz Biotechnology, Santa Cruz, CA), CD 10 (RTV-CD10-270, Novocast Newcastle, UK), estrogen receptor (1D5, 1:75, Dako), and progesterone receptor (PR88, 1:40, BioGenex, San Ramon, CA).

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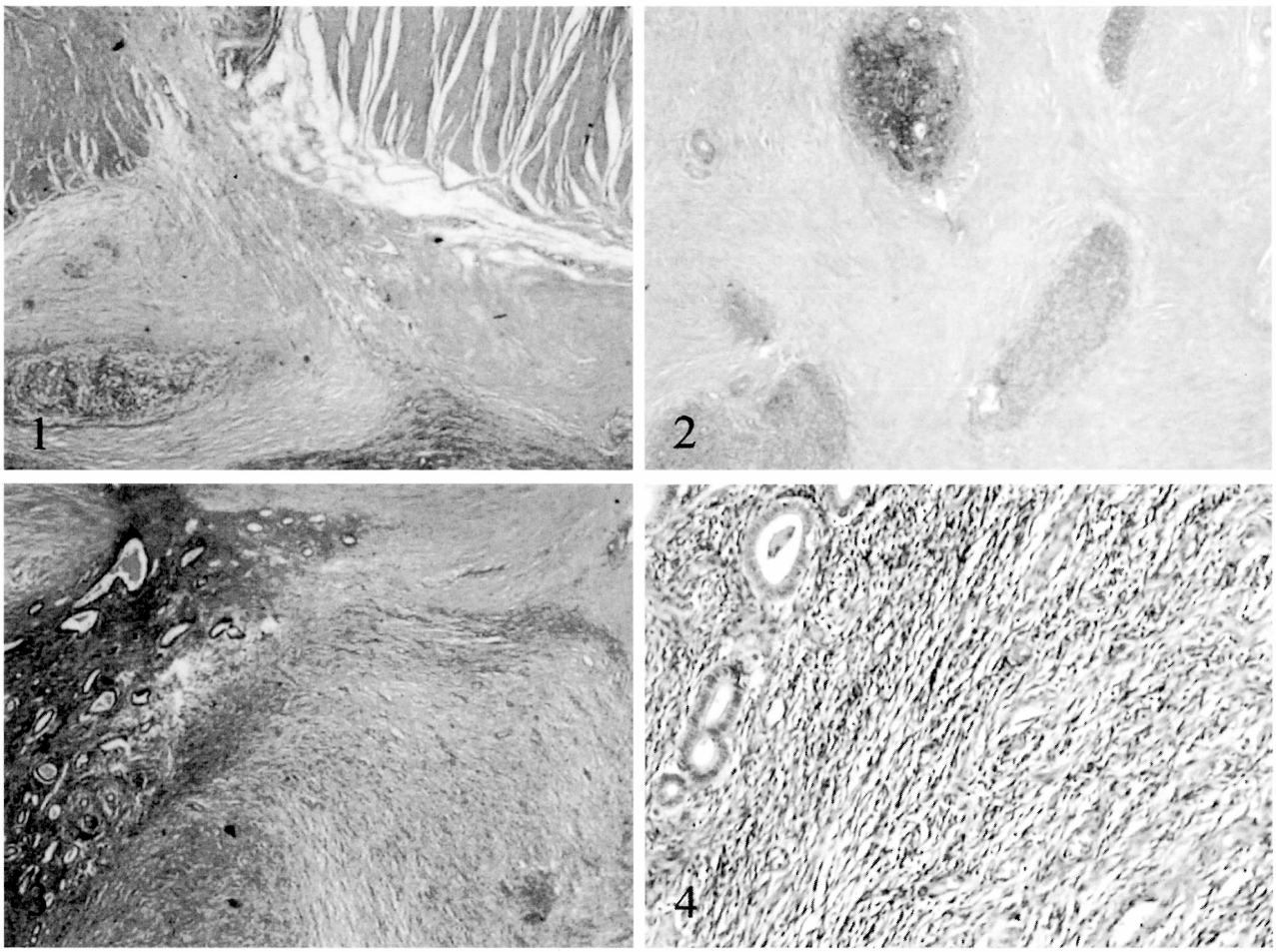

Figure 1. — Infiltrates of ESS in the bowel wall, H&E x 20.
Figure 2. — Infiltrates of ESS in the mesentery, H&E x 20.
Figure 3. — Infiltrate of ESS with the focus of benign endometriosis in the bowel wall, H&E x 20.
Figure 4. — Detail of Figure 3 in higher magnification, H&E x 100.

Pathologic findings:

Gross features:

1. Omentum of the size 17x12x1.5 cm with three ill-defined nodules measuring 0.5 cm, 2 cm and 3 cm in diameter.

2. A 12-cm long resection of the colon with a tumor 6 cm in diameter was found 3 cm from the margin. Two rings of the intestine 2 cm in diameter were also received (resection margins).

3. Tumor tissue 4 cm in diameter and part of the ovary 5 cm in diameter were received.

Microscopic features:

1. Tumor nodules consisted of fusiform cells with elipsoid, partly elongated nuclei with moderate polymorphism and rare mitotic activity (3 per 10 HPF) (Figure 1).

2. In the colon foci of benign endometriosis, nodules of regular endometriotic stroma and glands were found. As formerly described, tumor infiltrated all layers of the bowel wall (Figure 2). Ring-like resections were free of malignant tissue.

3. The tumor tissue was identical to the material in no. 1. Part of the fallopian tube and ovarian tissue were found. Whole material was analyzed and no signs of foci of benign endometriosis were found.

Immmunohistochemical features:

Estrogen receptors were positive only in the epithelial component, while the progesterone receptors were highly positive both in the stroma and the epithelium. Tumor tissue was positive for vimentin, SMA and CD 10, and negative for CK, NF and CD 117 (Figure 3 and 4).

Discussion

The development of stromal sarcomas in the foci of endometriosis is extremely rare and the differential diagnosis from other tumors of myogenic, vascular, hemopoietic or epithelial origin may present diagnostic difficulties [6].

Endometriosis should be suspected when there is dyspareunia, severe dysmenorrhoea, or unexplained abdominal, pelvic, bowel or bladder pain, a feeling of "heavy clothes" and ovulation pain, although the symptoms experienced are a poor indicator of the severity of the disease. Endometriosis of the gastrointestinal tract most frequently involves the rectosigmoid colon, the small intestine, cecum and appendix [7]. Patients may present

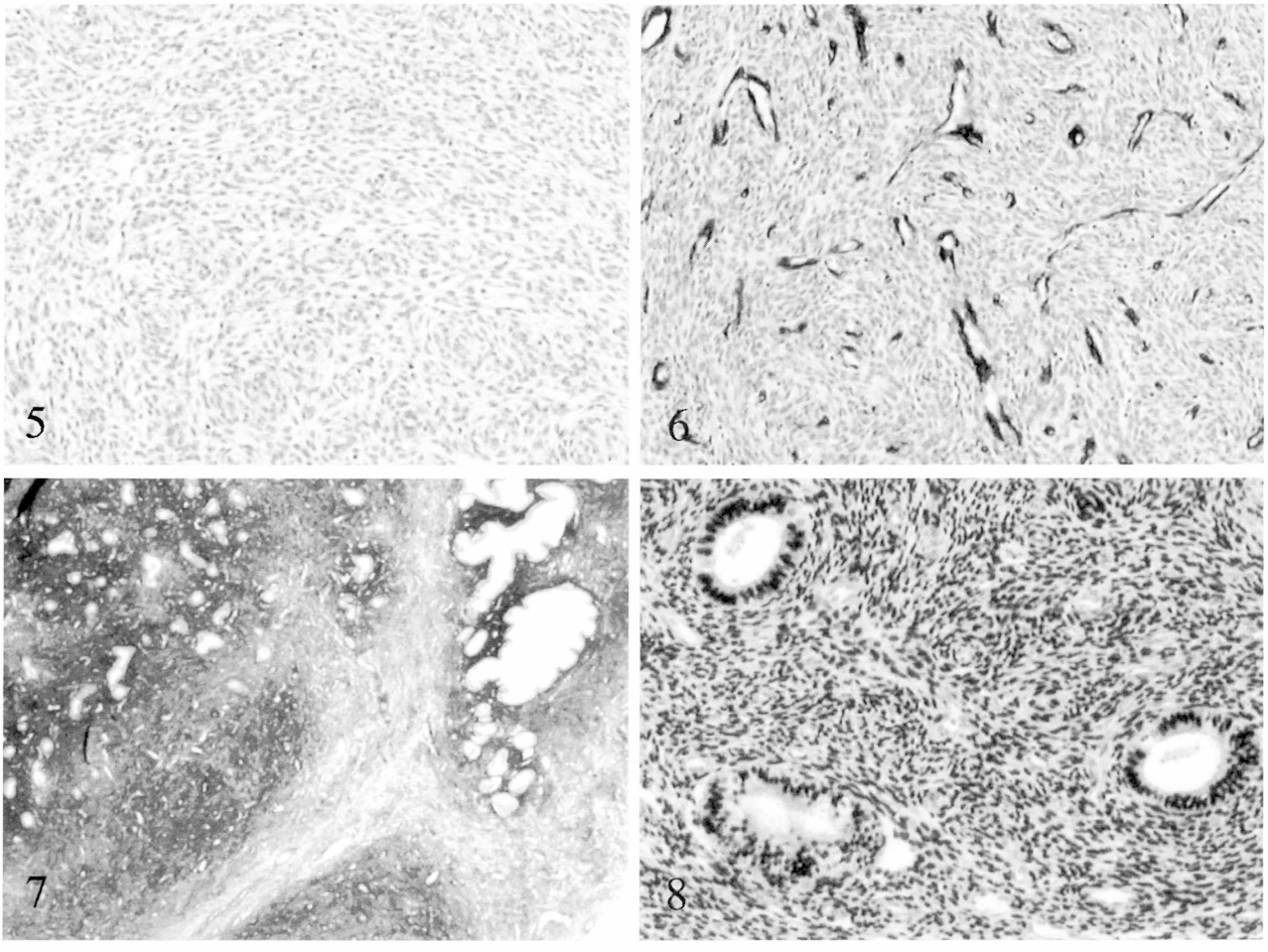

Figure 5. — Immunohistochemical staining for CD 117 x 100.
Figure 6. — Immunohistochemical staining for SMA x 100.
Figure 7. — Immunohistochemical staining for vimentin x 20.
Figure 8. — Immunohistochemical staining for progesterone receptors x 100.

with acute and chronic abdominal pain, bloody diarrhea, rectal bleeding, bloating, small or large bowel obstruction or an acute abdomen [7]. It can be mistaken for inflammatory bowel disease due to nonspecific changes retained by endoscopical biopsy or histological findings [7]. The diagnosis of endometriosis is generally confirmed by laparoscopy. Preoperative ultrasonography may be helpful [8]. The complications of intestinal endometriosis can be perforation (usually associated with pregnancy), volvulus, intussusception, acute appendicitis, appendiceal mucocoele, intramural hematoma, and the development of a malignant neoplasm [9-11].

Malignant transformation is an infrequent complication of endometriosis. The ovary is the primary site in 76% of cases, and extragonadal sites are identified in 24%. Endometrioid carcinoma is the most common histological type; sarcoma is very rare [12]. ESS is a tumor of the endometrial stromal cells that invades the myometrium. ESS has traditionally been divided into two categories, low-grade and high-grade stromal sarcoma [2]. Together with stromal nodule type, they form a group named endometrial stromal tumors, classified under non-epithelial neoplasia in the classification of malignant neoplasms of the uterine corpus by WHO [13]. In most studies ESS comprises less than 20% of uterine sarcomas and most are low-grade stromal sarcomas (LGSSs) [2].

LGSSs consist of relatively uniform cells giving the tumor a monotonous appearance. The tumor cells have round and ovoid nuclei with finely granular dispersed chromatin and small, inconspicuous nucleoli. Rare LGSSs consist predominantly of spindle-shaped cells with a fibroblastic appearance, with fusiform nuclei and elongated cell bodies. Mitotic activity is low, less than 10 MF/10 HPF. High-grade stromal sarcomas (HGSSs) on the other hand are tumors with 10 or more MF/10 HPF but some can also have less than 10 MF/10 HPF [2, 4]. The mitotic count cannot be used as the only criteria to differentiate HGSSs from LGSSs, but a high mitotic count is characteristic of HGSSs [12]. Proliferation of the small vessels and arterioles resembling the endometrial spiral arterioles is a characteristic finding in LGSSs. Limited smooth muscle differentiation is present. Epithe-

lial differentiation occurs in about 25% of LGSSs [2]. Characteristic imunohistochemical features are vimentin, SMA, positive CD 10, and negative CD 117, NF and CK. LGSSs is a slow progressive disease and the median time from diagnosis to death ranges up to 11 years [2]. On the other hand, high-grade ESS presents a poor prognosis, with a 5-year survival rate of 55% [4].

LGSSs usually grow slowly and tend to recur many years after the initial surgery; in some cases occurring up to 25 years later. The pelvic cavity followed by the vagina and lung are the main sites of metastases [4, 14]. The median time of recurrence is 34 months. The most common symptoms are menorrhagia, vaginal bleeding, pelvic or abdominal pain, metrorrhagia, and abdominal fullness and distention [4].

Extrauterine ESS may develop from the ovary, fallopian tube, pelvis, colon, or retroperitoneum [4]. Ovarian sex cord stromal tumors with a predominant spindle cell component, including cellular fibroma, thecoma, and Sertoli-Leydig cell tumors are also important differential diagnostic considerations [15, 16]. The main differential diagnosis of this unusual colonic neoplasm includes primary mesenchymal tumors, such as gastrointestinal stromal tumors (GISTs) [12]. In contrast to endometrioid stromal sarcoma, most GISTs are composed of spindle or epithelioid cells arranged in fascicles, sheets or clusters and the stroma in these lesions is frequently hyalinized or myxoid. Spindle cells are arranged like palisades; nuclear atypia and pleomorphism may be marked. They are well circumscribed [7]. GISTs show strong positivity for CD 117. ESS have, on the other hand, invasive "tongues" of tumor at the periphery of the neoplasm and have regular fascicles or sheets of monomorphous plump spindle cells and prominent arterioles with extensive vascular infiltration. Immunostaining for CD 117 is negative [7].

Ota *et al.* documented a rare case of spontaneous regression of ESS metastasis [14]. Recurrent low-grade sarcomas can be successfully treated with surgical excision, radiation or progestin therapy. Prognosis for this group is generally favorable with 90% of patients surviving ten years from diagnosis. In inoperable cases, about one-third of patients with metastatic gynecological sarcomas may derive some palliative benefit from chemotherapy. Radiotherapy may be added on an individualized basis to patients with metastatic sarcoma. Some low-grade uterine sarcomas are considered to be hormone responsive and hormonal therapy is recommended.

Conclusion

ESS may arise in the colon from endometriotic foci. The possible cause of endometriotic tissue appearing outside the uterus is presented by the metaplastic theory which points out the endometriotic differentiation of the coelomic epithelium [1]. In the present case, it seems possible that ESS arose in the foci of colon endometriosis. This hypothesis is supported by findings of benign stroma with glands and adjacent malignant tissue described as ESS in the bowel wall. Furthermore there was no evidence of benign endometriotic foci in the pathologic material (no. 3) [3]. A reverse way of ESS development is possible but one thing is certain - ESS in this case did not arise from endometriotic stroma of the uterus.

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Address reprint requests to:
D. KOVAČ, M.D.
Department of Pathology
Medical School
University of Rijeka
Braće Branchetta 20
51000 Rijela (Croatia)