

Multifocal endometriosis

Ludmila Lozneanu^{1,2}, Delia Gabriela Ciobanu-Apostol^{1,2}, Raluca Anca Balan¹, Ioana Păvăleanu¹, Simona Eliza Giușcă¹, Irina-Draga Căruntu¹, Cornelia Amalinei^{*,1,3}

¹Department of Morfofunctional Sciences I, "Grigore T. Popa" University of Medicine and Pharmacy, Iasi, Romania, ²Department of Pathology, "Sf. Spiridon" Clinical Emergency Hospital, Iasi, Romania, ³Department of Pathology, Institute of Forensic Medicine, Iasi, Romania

Abstract

Endometriosis represents a complex entity, characterized by tissue located in ectopic sites, outside uterus, with the highest incidence in ovaries and peritoneum. We report a rare case, with multiple endometriotic foci, in a 34 year old woman. The patient presented with intestinal subocclusion syndrome, associated with pelvic and abdominal pain. The imagistic exploration identified two peritoneal and one left ovarian masses and the clinical exam detected a 48/22 mm Douglas pouch mass. The surgical treatment, by exploratory laparotomy, resulted in segmental resection of the rectosigmoid junction and left adnexectomy. The intraoperative frozen section consultation, followed by paraffin-embedded, routine and immunohistochemical staining, led to a rare diagnosis of multiple foci of endometriosis, involving left adnexa, colorectum, and pericolic lymph nodes, without any atypia or malignancy. The postoperative evolution had been favorable. According to the identification of multiple endometriotic foci in our case, the hypothesis of different etiopathogenic mechanisms involvement may be supported by our findings.

Keywords: *endometriosis, multiple foci, immunohistochemistry*

Introduction

Endometriosis concept is reflecting a pathologic process characterized by the presence of endometrial glands and stroma in an extra-uterine location, most frequently associated with chronic inflammatory reaction. Endometriosis involves 10-15% of women of reproductive age, being stimulated by ovarian hormones [1]. The high association of endometriosis with infertility triggered numerous related studies. Despite scientists' interest, the origin and the mechanism of endometriosis development are still incompletely deciphered. There are several

theories which interconnect several mechanisms as attempts to elucidate the initiation pathways and the treatment approach in endometriosis. Although the most frequent location is pelvis (ovary, peritoneum), we present a multiple location (adnexa, colon, and lymph nodes), as a rare diagnostic entity. Within this context, the characteristics of our case may support several associated etiopathogenic mechanisms and developmental pathways in endometriosis.

Case report

We are reporting the case of a 34 year old patient, admitted in Department of Surgery, First Surgery Clinic, "Sf. Spiridon" Emergency Hospital, Iasi, Romania, in January 2016, with subocclusive syndrome, colicative pelvic and abdominal pain, and rectorrhagia. The patient declared a history of decreased bowel movements, with onset one year prior to

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*Corresponding author: Prof. Cornelia Amalinei, MD, PhD, "Grigore T. Popa" University of Medicine and Pharmacy Iasi; Institute of Forensic Medicine, 16 Universitatii Street, Iasi-700115, Romania
E-mail: cornelia.amalinei@umfiasi.ro

hospitalization, without any family gynecological or endometriosis history. The preoperative assessment by imagistic studies (ultrasound, abdominal and pelvic CT scans) revealed three tumor masses, two of them located in the peritoneum and another one in the left ovary, highly suspicious of malignancy. Clinical examination also found a 48/22 mm mass in Douglas pouch, between the uterus and the sigmoid colon. Following these observations, exploratory laparotomy has been performed, with left adnexectomy and segmental resection of rectosigmoid junction, considered as necessary due to deep, profound infiltration and severe symptomatology. Intra-operative frozen section consultation has been requested for the adnexal mass.

Pathologic examination has been performed in the Department of Pathology, "Sf. Spiridon" Emergency Hospital, Iasi, Romania. The intra-operative frozen section consultation of the left adnexa showed endometrial glands and stroma distributed within a vascular connective tissue, features highly suggestive of endometriosis. The gross inspection of the rectosigmoid junction showed the presence of an ulcerovegetant mass, measuring 5/3.5/1.6cm, with heterogeneous features, white-tan color, with focal hemorrhage, and increased consistency. Grossly, five pericolic lymph nodes have been identified. A hemorrhagic cystic lesion of approximately 32mm has been noticed in the ovary, with brown-violet color, smooth inner wall, and evident vascularization. The surgical

specimens have been paraffin-embedded, followed by 4 µm microtome sections and routine Hematoxylin-eosin staining.

Microscopy showed the presence of multiple foci of endometriosis, composed of endometrial glands and stroma, with left paratubal and cortical ovarian location (Figures 1a and 1b), transmural rectosigmoidian involvement, with submucosal, muscularis propria (Figures 2a and 2b), and serosal invasion (Figure 3), and two subcapsular lymph nodes implants (Figure 4). The glands have been lined by simple columnar epithelium of endometrial type, without evidence of significant proliferative activity or atypia, associated with local inflammatory reaction. The lesion has been typically associated with hemosiderin laden macrophages and perilesional fibrosis. In order to confirm the presence of endometriosis areas, immunohistochemistry has been performed in the Department of Pathology, using several markers, as following: CD10 and Vimentin have been mainly used for the stromal component (Figures 5a and 5b) and hormonal receptors, ER (estrogen receptor) and PR (progesterone receptor), (Figures 6a and 6b) have been mainly used for the glandular component. The morphological features identified corroborated with the immunohistochemical findings have set the diagnosis of multifocal endometriosis.

The postoperative evolution had been favorable, without any complications and routine follow up had been decided.

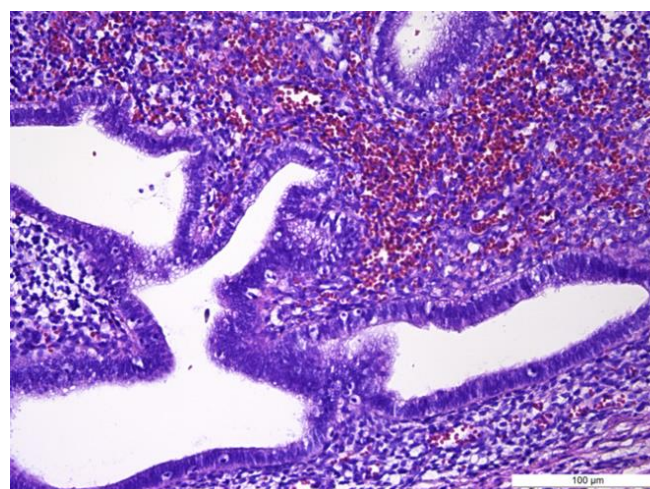


Fig. 1a. Left mesosalpinx endometriotic focus (HE, x200)

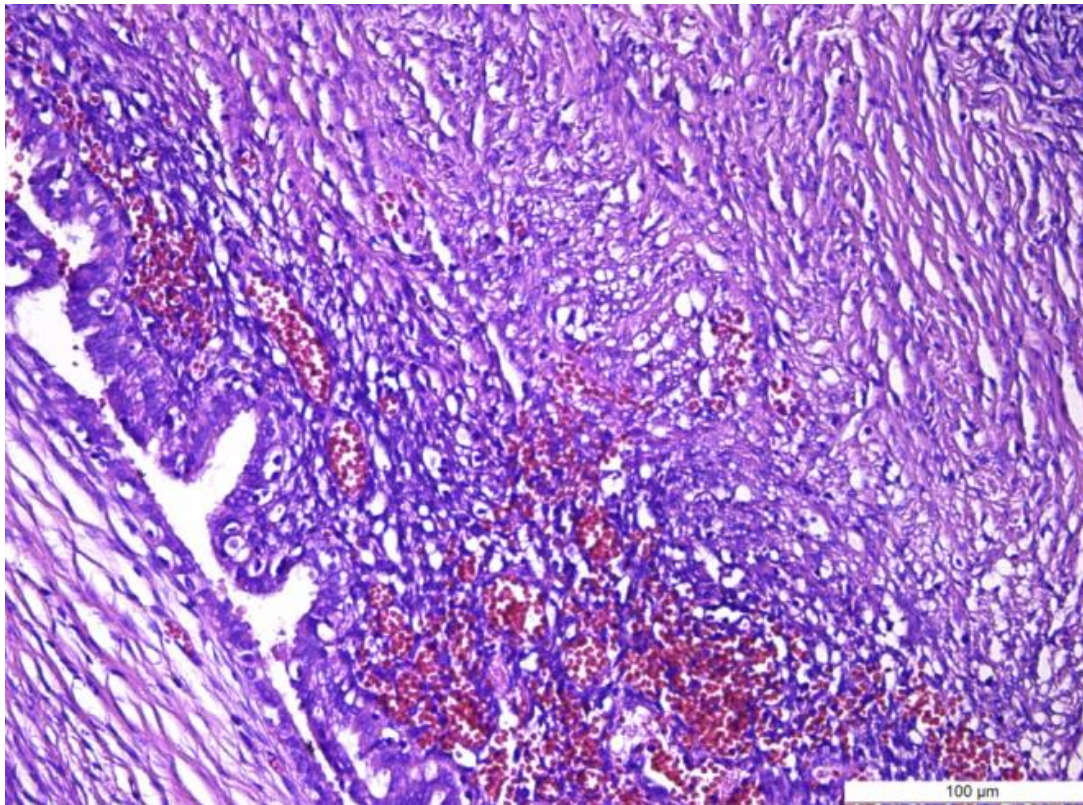


Fig. 1b. Left ovary endometriotic focus (HE, x200)

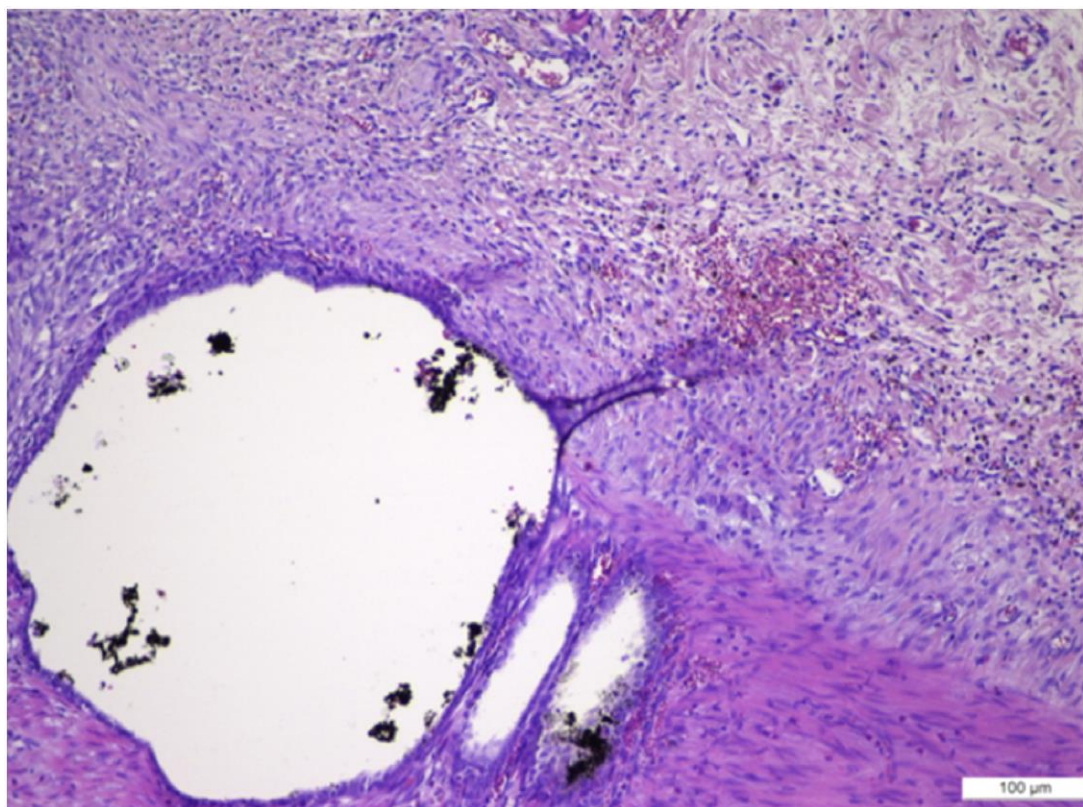


Fig. 2a. Colonic submucosal endometriotic focus (HE, x100)

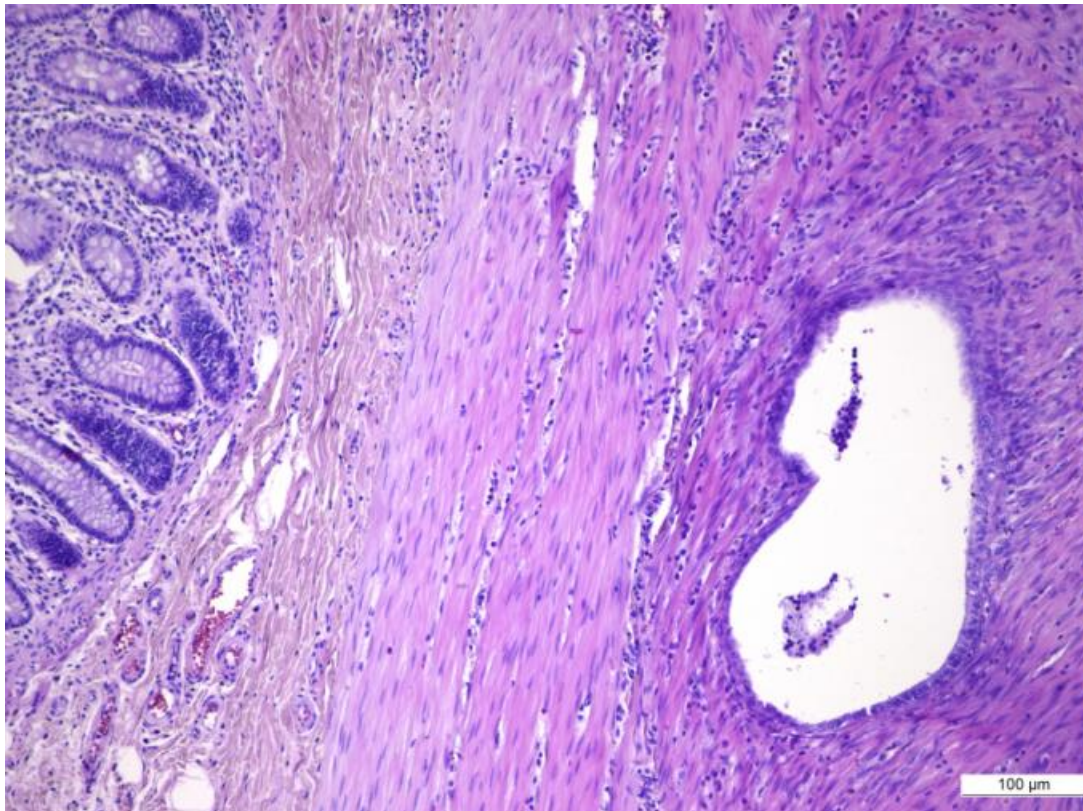


Fig. 2b. Colonic muscularis propria endometriotic focus (HE, x100)

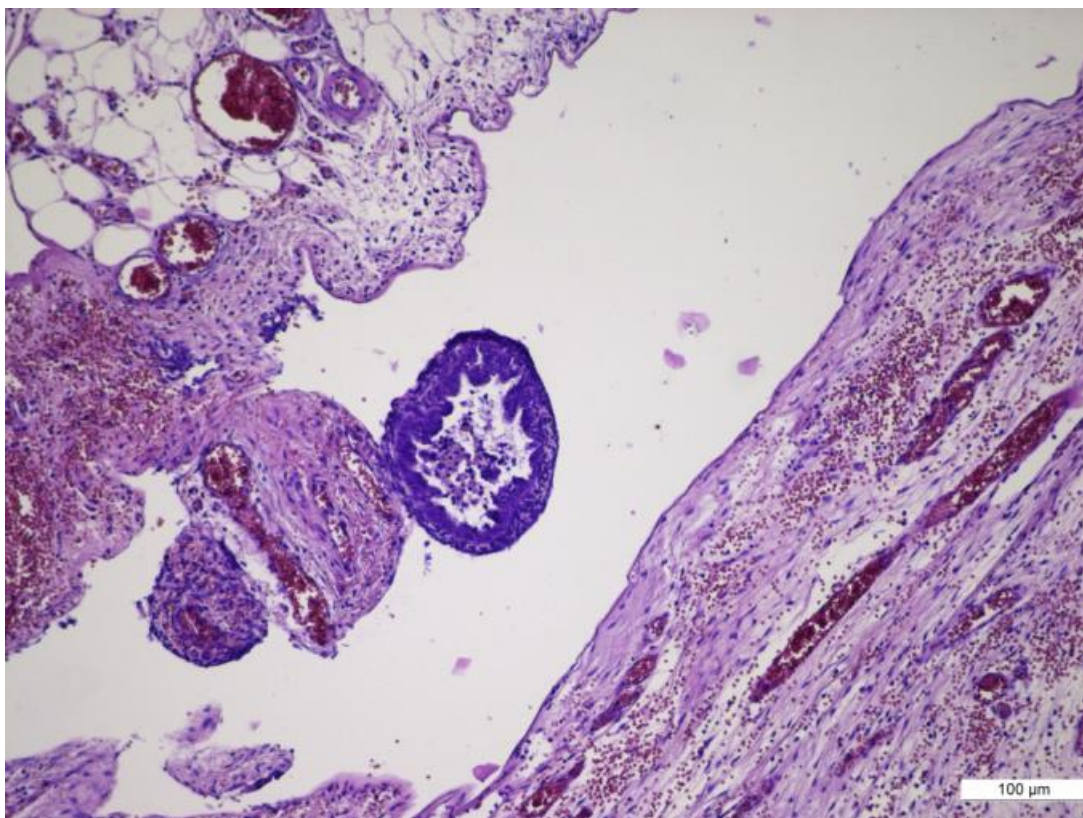


Fig. 3. Endometriotic focus exhibiting a single gland adherent to the peritoneal serosa (HE, x100)

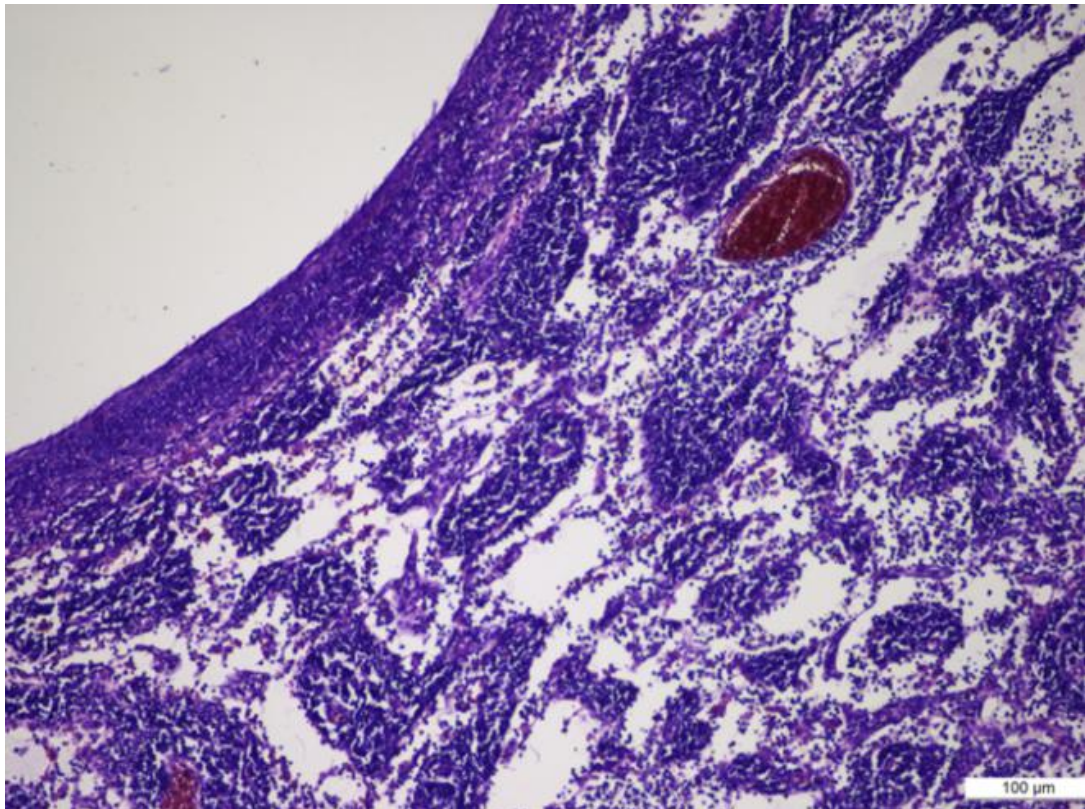


Fig. 4. Lymph node endometriosis (HE, x100)

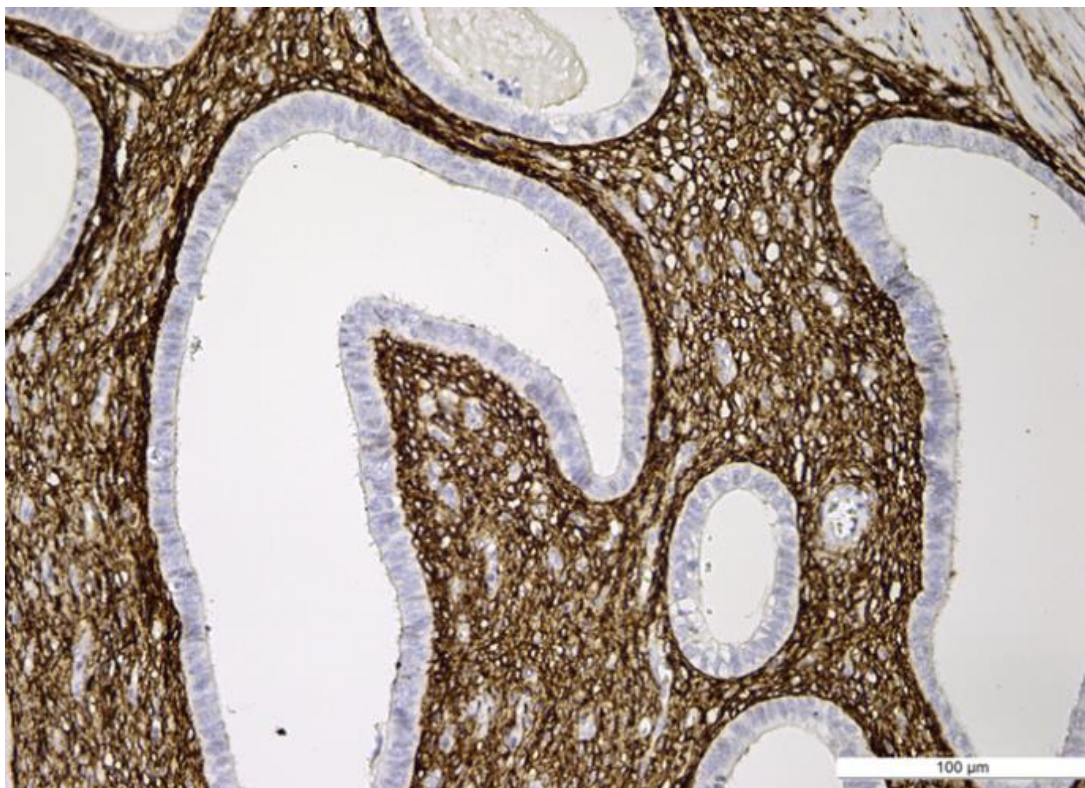


Fig. 5a. CD10 positive in stromal cells of a colonic endometriotic focus (IHC, Ab anti-CD10, x400)



Fig. 5b. Stroma and glandular components of a colonic endometriotic focus (IHC, Ab anti-Vimentin, x100)

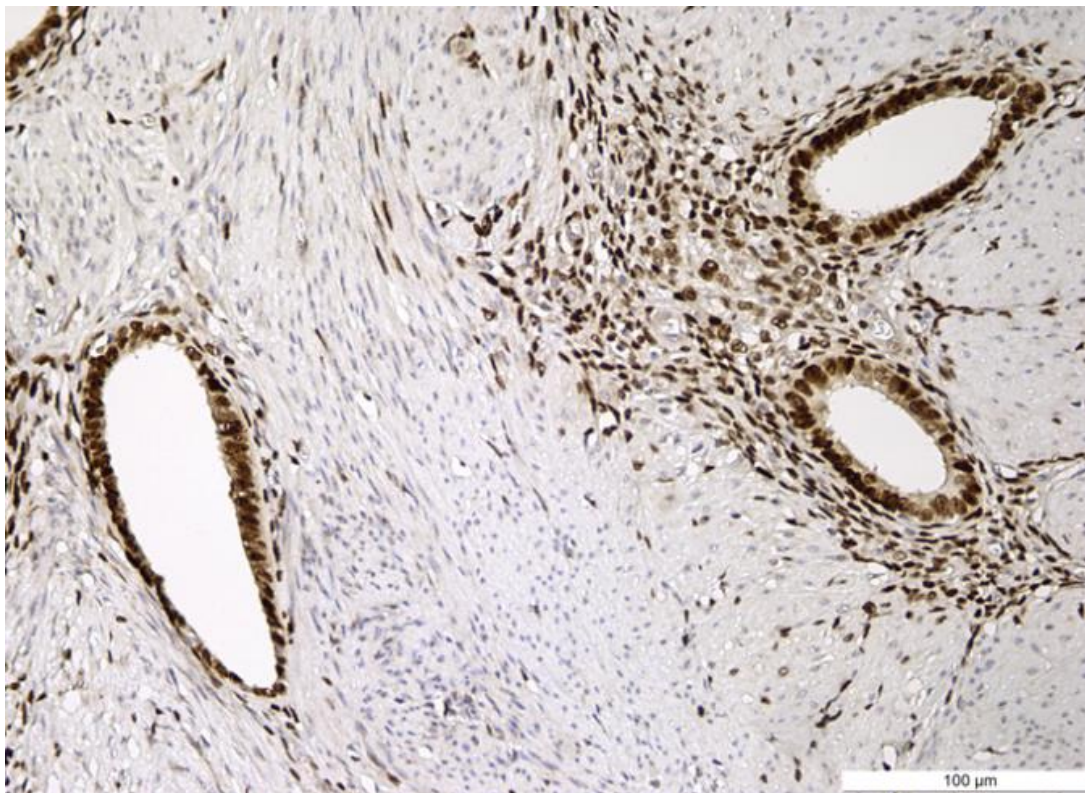


Fig. 6a. Glandular and stromal components of a colonic endometriotic focus (IHC, Ab anti-ER, x200)

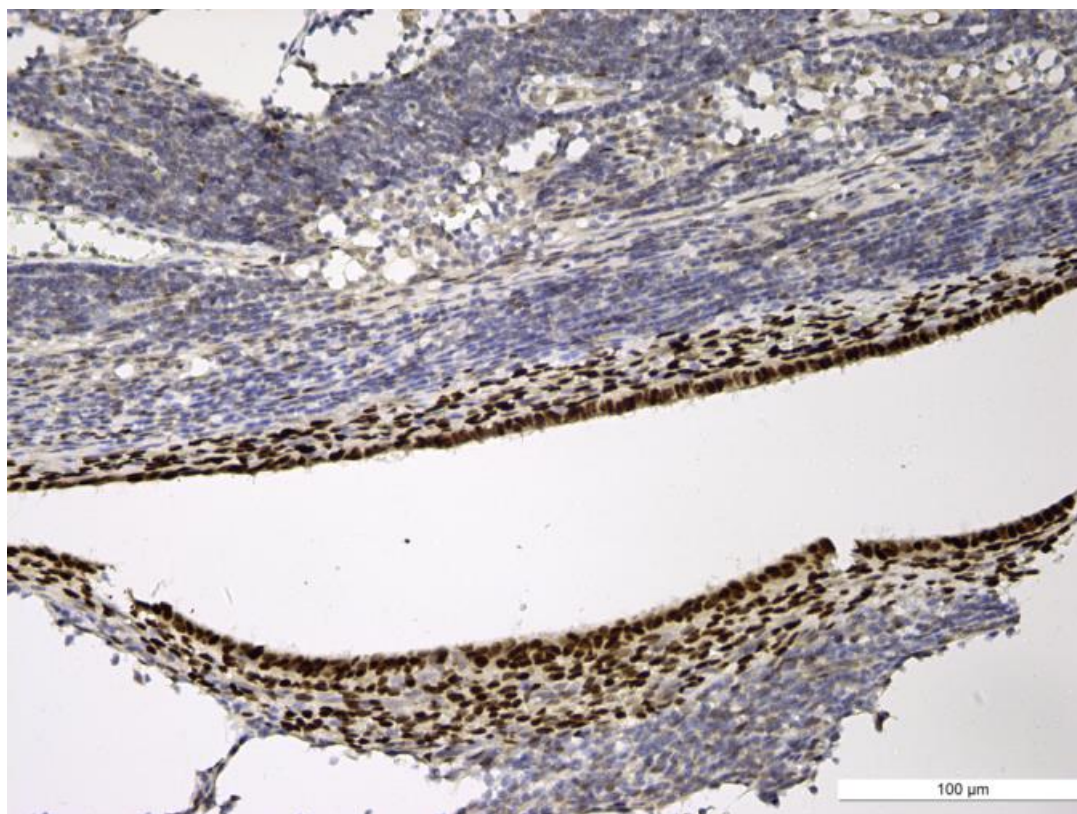


Fig. 6b. Glandular and stromal components of lymph node endometriosis (IHC, Ab anti-PR, x200)

Discussions

Endometriosis involves approximately 2% of the general female population [2] and approximately 70% of these cases have associated pelvic inflammatory diseases [3]. The exact prevalence is still unknown due to asymptomatic cases and incidental identification of the disease. Endometriosis is associated with infertility in 25-30% cases [4]. Endometriosis consists of a complex lesion, with chronic evolution, mainly diagnosed during reproductive life, as had been also the patients' age (34 years old), in the presented case, although in our last year files we registered a broad age distribution (25-74 years old). Endometriosis is rare after menopause, a characteristic that certifies the estrogenic dependence [4], being diagnosed in only 12.50% of cases in post-menopause, in our last year files. Deep endometriosis is frequently the reason for patients' presentation for a gynecological consultation due to infertility, dyspareunia, dysmenorrhea, and chronic pelvic pain [5], the latter symptom being the clinical manifestation in our patient.

Endometriosis can be abdominal and extra-abdominal [3]. The abdominal type may be intraperitoneal (ovarian, broad ligament, tubal, pelvic peritoneum, Douglas space, appendix, and small intestine) or extraperitoneal (cervix, vagina, recto-vaginal septum, round ligament, and post-surgery abdominal scars, mainly post C-section) [3, 6]. The locations from our last year files had been, in descending order of frequency: ovary (40%), uterine cervix (20%), post-C section (13.33%), appendix (13.33%), colon (6.66%), fallopian tube (6.66%), the symptoms being variable, from intestinal occlusion, acute appendicitis, cicatricial external endometriosis, pelvic pain accentuated during menstruation, and colonic motility disorders. The presented case is the only case from our files with multiple locations: left adnexa, rectosigmoid, and pericolic lymph nodes.

Extra-abdominal endometriosis is rare, such as hepatic [7], pulmonary [8], urinary tract [9], cutaneous, and nasal cavity [3]. Other rare locations reported in literature are: iliac vein wall [10] and hernial sac wall [11].

Gastro-intestinal endometriosis is frequently reported in colorectum (70%), as had also been in two cases from our files, including the presented patient, and ileum (1-7%) [12, 13]. Rectosigmoid and lymph node endometriosis is reported in 26.3% to 50% of cases [14, 15], being confirmed in several studies [6, 13-20]. Considering the literature data, the possibility of ectopic implants to be independently produced by retrograde menstruation to three different sites, or the participation of a metaplastic process involved in colonic location, associated with the possibility of dissemination, by lymphatics, from ovary and, furthermore, from colon to lymph nodes, are probable mechanisms. The degree of contribution of each mechanism to the complex picture of this case remains speculative.

The risk of lymph node endometriosis is increased when intestinal endometriosis is circumferential, as has been also noticed in the presented case (transmural involvement), and over 1.75cm length [14], as has been also measured in our patient (5/3.5/1.6cm). According to our review, this is the only involvement of two lymph nodes in our files.

Numerous theories and etiopathogenic mechanisms are debated in literature. Although the most plausible hypothesis is that of retrograde menstruation, especially in cases with adnexal location, according to Sampson's theory [21], other hypotheses seem to be more likely involved in other locations. In colon endometriosis, caelomic epithelium metaplasia is the most plausible phenomena, according to Meyer's theory [22], and lymphatic dissemination seems to be more likely involved in lymph nodes endometriosis, as stated by Halban's theory [23]. According to literature data, the mechanism of lymph node involvement is still unclear. In order to explain the significance of lymph node involvement, several theories have been launched. According to the some opinions, lymph node involvement may signify a chronic intestinal endometriosis [24]. Some authors support the low incidence of lymph node involvement in ovarian and/or peritoneal disease [25]. The identification of endometrial elements in lymph nodes may be highly correlated to the co-existence of possible foci of endometriosis

encompassing the evident lesions, as a strong predictor of local or distance recurrence [13]. Another hypothesis is that endometriosis histogenesis may be different according to the location and lesion type [26]. Thus, ovarian and deep endometriosis may probably originate from a metaplastic process, while peritoneal lesions may probably be the result of peritoneal implantation [26]. A relatively recent theory is that of Müllerian remnants or stem cells activation in this location [27]. Considering the multiple foci of endometriosis in the presented case, the mechanism of retrograde menstruation (for the ovarian location) could be associated with a metaplastic process of the caelomic epithelium (for the colonic location) and a lymphatic dissemination (for the pericolic lymph node location).

Endometriosis is a highly heterogeneous entity, considering its hormonal, immunological, genetic, metabolic influences, and characteristics of a systemic disease, with typical and atypical features manifested during the disease and evolution toward adhesions, invasion, and metastasizing [28]. Normal endometrium is different from that of a patient with endometriosis due to proliferative, apoptotic, invasive, (lymph)angiogenic, hormonal, and immunological characteristics similar to a malignant process [14, 29], with high risk of recurrences, either as consequences or of intrinsic pathogenic characteristics. There are numerous literature data to support endometriosis association with endometrioid and clear cell ovarian carcinoma [30]. No evidence of cytological atypia and no significant mitotic activity have been identified, thus the malignant transformation has been excluded in the presented case.

The differential diagnosis included other clinical instances that could result in pelvic and abdominal pain, such as rectorrhagia, constipation, peritoneal proliferation, and pelvic disorders, or neuromuscular and musculo-skeletal chronic lesions [31].

The morphological differential diagnosis had to be done with ovarian endosalpingiosis [32], a lesion frequently overdiagnosed as endometriosis, due to histological resemblance, and ovarian serous cystic lesions, while colon location has been

differentiated from colon carcinoma and lymph nodes from cystic lesions, all these being excluded by characteristic histology. Supplementary, immunohistochemical profile performed in the presented case has confirmed the presence of areas of endometriosis by ER and PR dominant epithelial, CD10 stromal, and Vimentin stromal and epithelial immunopositivity

Conclusions

The presented case illustrates a typical endometriosis, diagnosed during the reproductive age, asymptotically developed until the onset of a subocclusive syndrome. Considering the particularities of this case, although relatively rare, the possibility of endometriosis occurrence and its differential diagnosis should be considered in young women with abdominal pathology. Due to multiple foci identified in the presented case,

the hypothesis of combined etiopathogenic mechanisms may be supported.

Numerous research data have demonstrated that endometriosis has the characteristics of a benign proliferative process with the possibility of malignant transformation. Although the stage of “atypical” endometriosis is rarely seen in practice, the malignancy risk should be considered as an intrinsic characteristic and should be dismissed only after a thoughtful, systematical analysis of the involved tissue.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Conflict of interest

The authors declare no competing interest.

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