Chirurgia (2015) 110: 482-485
No. 5, September - October

Accurate Diagnosis of Sigmoid Colon Endometriosis by Immunohistochemistry and Transmission Electron Microscopy - A Case Report

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Rezumat

Diagnosticul pozitiv al endometriozei colonului sigmoid prin imunohistochimie și microscopie electronică - prezentare de caz

Endometrioza este descrisă ca fiind dată de prezența de țesut endometrial funcțional în zone anatomice din afara cavității uterine. Până la 15% din femeile aflate în perioada fertilă pot fi afectate de această problemă. Endometrioza este cel mai frecvent localizată la nivelul ligamentelor uterosacrate, intravaginal sau în septul rectovaginal, regiunea rectosigmoidiană, fosa ovariană, peritoneul pelvin, uretere și vezica urinară - determinând modificări ale anatomiei pelvine. Afectarea colică este rară, obișnuit situată la nivelul rectului sau colonului sigmoid; prezentarea acută cu ocluzie sau perforație intestinală este de asemenea rară. Malignizarea leziunilor endometriale, rareori prezența, atrage probleme de management când sunt evidențiate displaziile la examenul histopatologic. Imunohistochimia și electronomicroscopia sunt esențiale în realizarea acestor decizii terapeutice. Prezentăm cazul unei femei de 38 ani cu ocluzie intestinală determinată de endometrioza colonului sigmoid, cu displazie moderată, și la care electronomicroscopia a fost utilizată pentru diagnosticul postoperator. Analiza detailată în această situație, deși dificilă, poate fi extrem de utilă pentru înțelegerea etiologiei și fiziopatologiei bolii.

Cuvinte cheie: endometrioza colon sigmoid, imunohistochimie, electronomicroscopie

Abstract

Endometriosis is described as the presence of functioning endometrial tissue at sites outside the uterus. Up to 15% ofwomen in their reproductive period are affected by this condition. Endometriosis is mostly foundon the uterosacral ligaments, inside the rectovaginalseptum or vagina, in the rectosigmoid area, ovarianfossa, pelvic peritoneum, ureters, and bladder, causinga distortion of the pelvic anatomy. Colonic involvement is rare but is usually found at the level of the rectum or the sigmoid colon. Acute presentation with intestinal obstruction or perforation is rare. While malignant transformation of endometrial lesions is rare, findings of dysplasia on pathology sections can give rise to questions of management. Immunohistochemistry and electron microscopy can help decision making. We present the case of a 38 year old woman with intestinal obstruction caused by sigmoid colon endometriosis with moderate dysplasia in which transmission electron microscopy was used for postoperative diagnosis. Detailed analysis of these cases, while logistically difficult, can prove useful in understanding the etiology and pathophysiology of the disease.

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Key words: sigmoid colon endometriosis, immunohistochemistry transmission electron microscopy

Introduction

Endometriosis is described as the presence of functioning endometrial tissue at sites outside the uterus. Endometriosis represents a clinical entity (benign, estrogen-dependent, tumorlike disease characterized by chronic pelvic pain, dysmenorrhea, dyspareunia, infertility or subfertility - due to the uncontrolled ectopic growth of proliferative endometrial tissue) affecting 3-10 % of women of reproductive age, and occurs when functioning endometrial cells are implanted outside the uterus, commonly in the pelvis: in peritoneum, ovaries, and rectovaginal septum (1). The symptoms of endometriosis may markedly reduce a woman's quality of life. The prevalence of endometriosis in women varies: 0.7-11 % in populations presenting for general health care, 2-22 % when undergoing surgical sterilization, 17-47 % among infertile women, and 2-74 % in women with chronic pelvic pain (2). Development of the disease is still unclear. From earlier theories like the retrograde menstruation (3), recent studies have revealed several other factors like dysregulation of apoptosis, fibrosis, and epigenetic factors to play important roles in the pathophysiology. Epidemiological studies found that shorter menstrual cycles, longer and heavier menstrual flow, low parity are risk factors for the disease (4). The classic theory on the pathogenesis of endometriosis includes implantation theory, coelomic metaplasia theory, and embryonic Mullerian remnants. A recent study found that extrauterine stem cells originating from bone marrow may differentiate into endometrial tissues (5). Endometriosis affects the bowel in 3-37% of cases and usually involves the rectum or sigmoid colon (6). Clinical data showed that malignant transformation of endometriosis occurs in less than 1% of patients with endometriosis (7).

Case report

We present the case of a 38 year old woman who was admitted into our department with acute abdominal pain of recent onset and lack of bowel movement for the previous 48 hours. Prior medical history reveals a cesarean section 7 years before presentation, pelvic menstrual pain and menstrual irregularity in the previous year. She has been self administering oral contraceptives for the past 4 years. On presentation she has a symmetrical, distended abdomen, painful in all quadrants, especially in the left-lower quadrant. Percussion of the abdomen shows tympanism. Digital rectal examination found a normal rectum but with no feces. Physical examination is otherwise normal. Abdominal ultrasound finds grossly distended bowel loops that make the examination difficult, with no other information being provided. Plain abdominal x-ray shows distended small and large bowel loops and air-fluid levels in the entire abdomen. Exploratory laparotomy was decided and the following was founded: a small amount of free fluid, distended small and large bowel loops, a circumferential tumor of the sigmoid colon completely obstructing the bowel lumen. The rest of the abdominal organs were normal on inspection including the reproductive organs and liver. Left hemicolectomy was performed with a mechanical colo-rectal anastomosis, abdominal lavage and drainage. Postoperative course was uneventful with bowel function restoration on the 4th postoperative day and discharge on the 7th day.

Histological findings revealed endometrial-like glands and stroma infiltrating the bowel wall and moderate dysplasia. Immunohistochemistry revealed a rather high proliferative index as revealed by ki67 staining (Fig. 1). Transmission electron microscopy was performed on the specimen with a

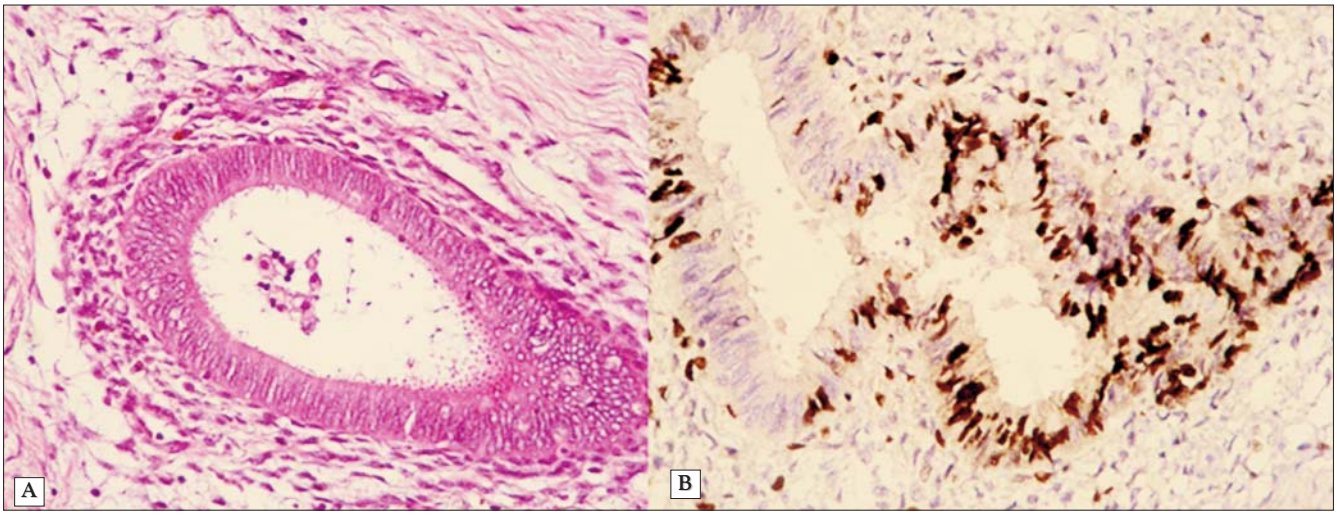

Figure 1. *Colonic endometriosis with moderate dysplasia (**A**); IHC staining for ki67 (**B**)*

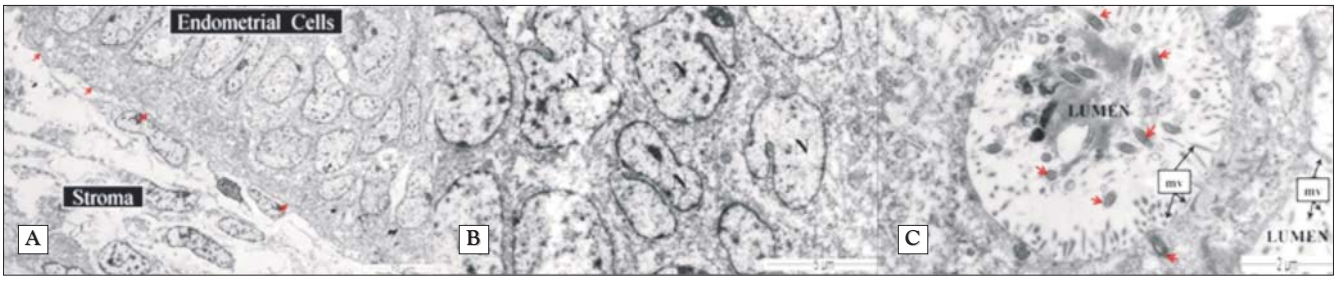

Figure 2. *Transmission electron microscopy. (**A**) The periphery of an endometrial lesion at the stroma interface. Polymorphic and large nuclei are visible. A basement membrane (red arrows) separates endometrial structure from the adjacent stroma. (**B**) Detail from inside of the endometriotic lesion. Nuclei are large and euchromatic; some of them are indented (N). Intercellular junctions of desmosome type are almost missing. (**C**) Detail for a lumen inside of an endometrial lesion. Microvilli (mv) and cilia (arrow) sectioned in different incidental planes are visible*

JEOL JEM-1400 microscope operated at an accelerated voltage of 80kV. Electron microscopy revealed that the endometrial lesions are hyperplastic and include ciliated cells. Nuclei are polymorphic and euchromatic, many lining cells have prominent cilia and microvili projecting into the luminal space and desmosome type intercellular junctions are almost missing(Fig. 2). Detection of cilia and their detailed ultrastructural aspects concerning the 9+2 doublets pattern similar to the ciliated uterine cells tell us about the real origin of ectopic endometriosis developed in sigmoid colon (Fig. 3). Apart from the associated stroma to the endometriotic epithelium, a fibrotic stroma accommodates the whole endometriotic lesion inside of the colon wall (Fig. 4).

The patient was started on oral hormone therapy and closely monitored both clinically and by imagery. One year after surgery the patient showed no signs of recurrence or disease progression.

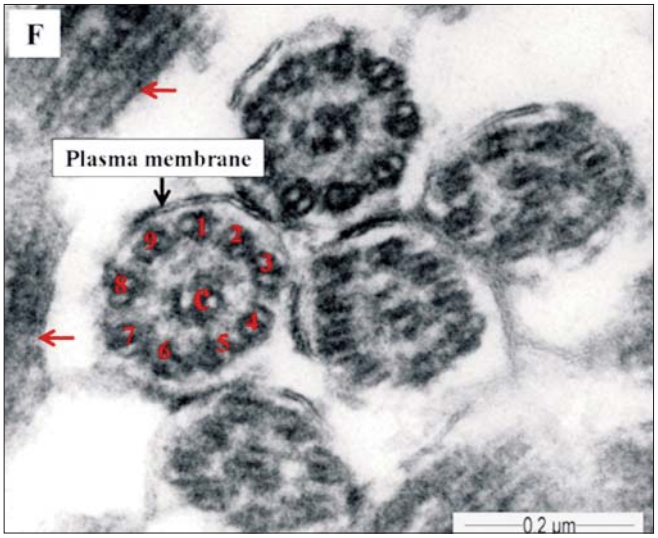

Figure 3. *Few cross or longitudinal (arrow) sectioned cilia. In cross section, cilia exhibit a 9+2 doublets organization. Plasma membrane envelops/enrolled each 9 peripheral (1-9) + 2 central (c) doublets*

Discussion

Endometriosis is a common health disorder in women, defined by the presence of endometrial-like tissue outside the uterus. Bowel involvement is relatively rare, with a difficult diagnostic and therapeutic management. Whether the clinical picture develops over several months or the patient presents with an acute disease, as the situation of the case presented with intestinal obstruction, the general surgeon is involved in the management. While intraoperative differential diagnosis can be difficult, there are circumstances where pathology results can be unclear in differentiating colonic endometriosis from adenocarcinoma. Moreover the ambiguous nature of the disease rises questions about its benign or malignant nature. In our case a result of dysplasia found by conventional pathology and a relatively high proliferation index, as evidenced by ki67 staining, was resolved by transmission electron microscopy that showed a hyperplastic lesion. While electron microscopy is not yet available for large scale use in the diagnosis of common conditions, its use in selected cases can help management and further the understanding of this enigmatic pathology.

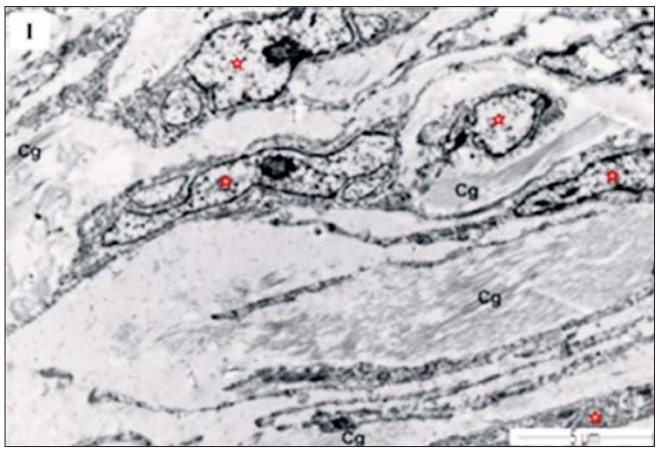

Figure 4. *Fibrotic wall of the colon where the endometrial lesion was developed. Connective cells (stars) embedded in strong bundles of collagen fibers (Cg) can be seen*

Acknowledgements

The co-authors (M.N. and M. A.-M.) acknowledge, for financing, support coming from project No. RO1567-IBB07/2014 - the Institute of Biology Bucharest of the Romanian Academy.

Conflict of interest

Vlad Constantin, Alexandru Carâp, Simona Bobic, Ion Păun, Elvira Brătilă, Bogdan Socea, Ana-Maria Moroșanu, and Nicolae Mirancea declare no conflict of interest.

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