

Case Report

Rectal mucosal endometriosis primarily misinterpreted as adenocarcinoma: a case report and review of literature

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Abstract: Endometriosis involving intestinal mucosa is relatively uncommon. It poses a diagnostic challenge for clinicians and pathologists. We herein report a case of colonoscopic specimen revealing rectal mucosal endometriosis. A 39-year-old woman complained of red rectal bleeding and intermittent abdominal pain. Colonoscopic examination showed a rectal mass with ulceration and circum wall involvement. Biopsy was processed in the suspicious of carcinoma. Morphologically, irregular glands replaced residual colorectal ones, displayed mucin depletion, nuclear stratification and subtle subnuclear vacuoles. The stroma was full of spindle cells with abundant pink cytoplasm and unclear boundary. Due to subjectively interpreting as dysplastic glands in desmoplastic setting, primary rectal adenocarcinoma was firstly raised. Immunohistochemically, CK7, ER and CD10 identified the essence of ectopic endometrium. CK20 and CDX2 highlighted residual glands. In case of misdiagnosis, any pathologists should be aware of intestinal endometriosis for each female's colorectal biopsy, especially for that morphology not typical for primary adenocarcinoma or endometriosis. Reading slides carefully combined with a panel of immunomarkers would solve the pitfall.

Keywords: Rectal mucosal endometriosis, misinterpret, adenocarcinoma

Introduction

Endometriosis, firstly described by Rokitansky in 1860, is characterized by presence of endometrial glands and/or stroma outside the uterine cavity, predominantly in the pelvic cavity [1]. Most victims are in their reproductive age and often associated with pelvic pain and infertility [2].

Endometriosis affecting gastrointestinal tract has been well described in the literature. However, it's still posing a diagnostic challenge for both clinicians and pathologists [3]. To our knowledge, the clinicopathologic features of intestinal mucosal endometriosis have not been well-documented, much less in the endoscopic specimens' setting. Herein, we report a case of rectal endoscopic biopsy revealing endometriosis involving the mucosa, which was primarily misinterpreted as adenocarcinoma.

Materials and methods

The endoscopic specimens were fixed in 10% neutral buffered formalin solution and embed-

ded in paraffin. Four micrometer-thick sections were stained with hematoxylin-eosin. Immunohistochemical stains were carried out using the ChemMate EnVision/HRP Kit (Dako, Glostrup, Denmark). Commercially available antibodies performed were CK7, CK20, ER, CD10, and CDX2. These antibodies were obtained from Dako Cytomation (Carpinteria, CA) and Santa Cruz Biotechnology (Santa Cruz, CA), and all stained according to the manufacturer's instructions.

Case report

Clinical findings

The 39-year-old woman came to our hospital in the complaining of bright red rectal bleeding and intermittent abdominal pain, which was not in accordance with menstrual cycle. Endoscopic examination was performed. As the endoscopy was pushed forward around 10 centimeters, a rectal mucosal mass with ulceration and touched bleeding was in sight. The mass appeared swelling, surrounded the enteric cav-

Endometriosis misinterpreted as adenocarcinoma

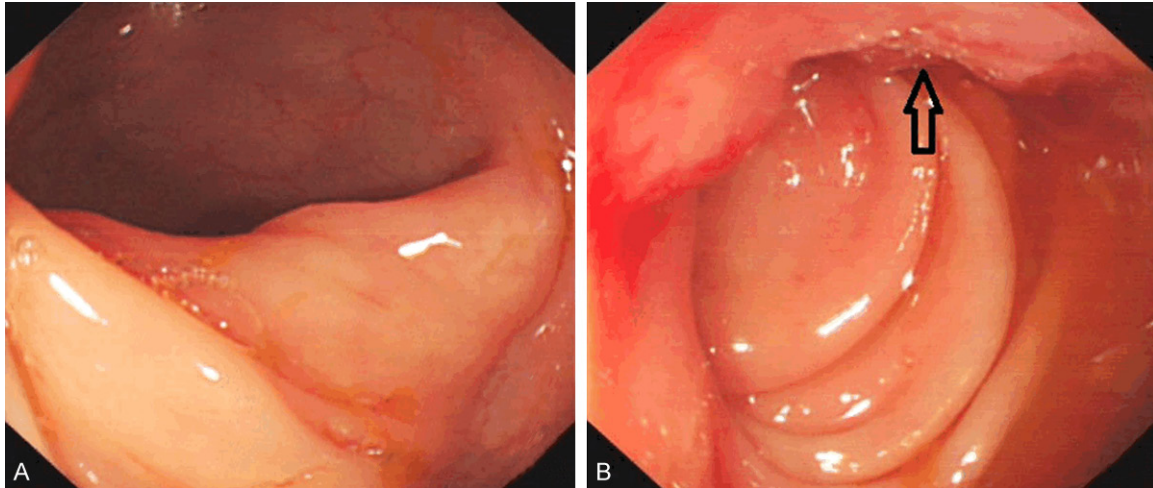


Figure 1. Endoscopic examination. A. The rectal mucosal mass surrounding enteric cavity and causing luminal stenosis but not obstruction. B. The mass showing ulceration (black arrow) and touched bleeding.

ity and caused luminal stenosis but not obstruction (**Figure 1**). The rest of colonic wall was visibly normal.

Pathological findings and diagnostic process

Three grains of colonic mucosa were submitted for pathological evaluation. Two of them displayed non-specific inflammatory infiltration in lamina propria. The last one was remarkably abnormal (**Figure 2**). The glands were irregular in shape and scattered in stroma. The cells displayed mucin depletion with nuclear stratification. The nuclei were oval in shape with mild enlargement. The stroma around glands was full of spindle cells with abundant pink cytoplasm and unclear boundary. Nucleoli were readily identified. Superficial epithelium was in erosion. At peripheral, residual glands displayed architectural distortion, cell enlargement, hyperchromasia and partial lack of polarity. Combined all these histological features above, which were subjectively interpreted as dysplastic glands in desmoplasia-like setting with atypical residual glands around, one of our residents interpreted as adenocarcinoma cannot be excluded. Fortunately, one of us double-checked the slide and raised the suspicion of endometriosis. Subsequently, we applied immunohistochemical stains (**Figure 3**). As expected, all of the abnormal glands expressed CK7 and ER strongly and diffusely, and the surrounding stroma was positive for CD10 and ER. On the contrary, all the residual colonic glands

were positive for CK20 and CDX2. And the residual lamina propria was negative for ER.

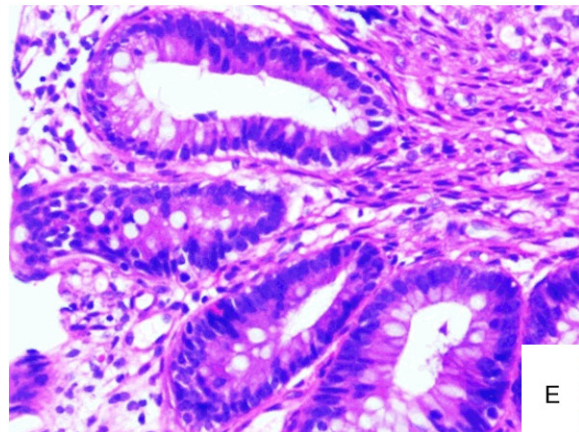
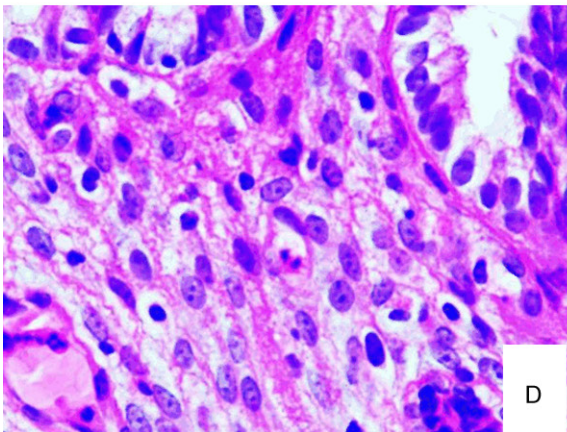
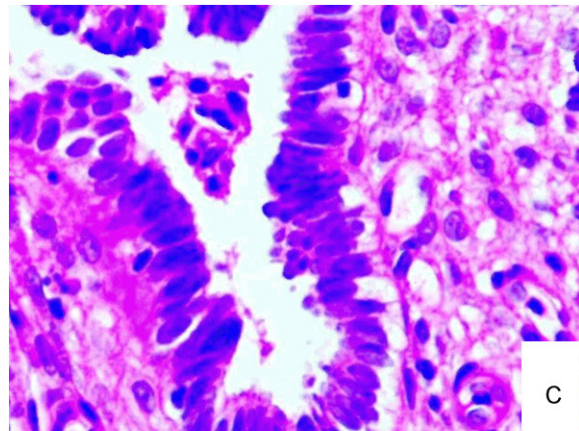
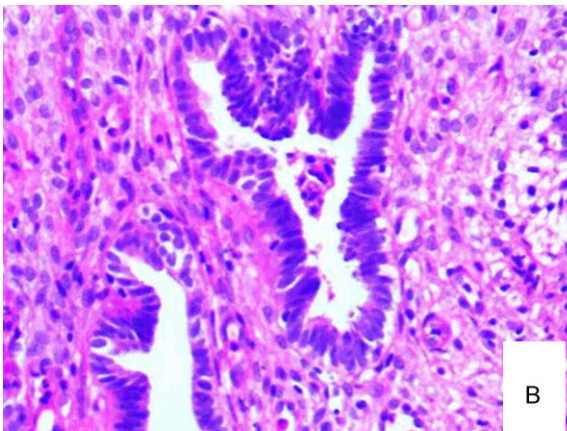
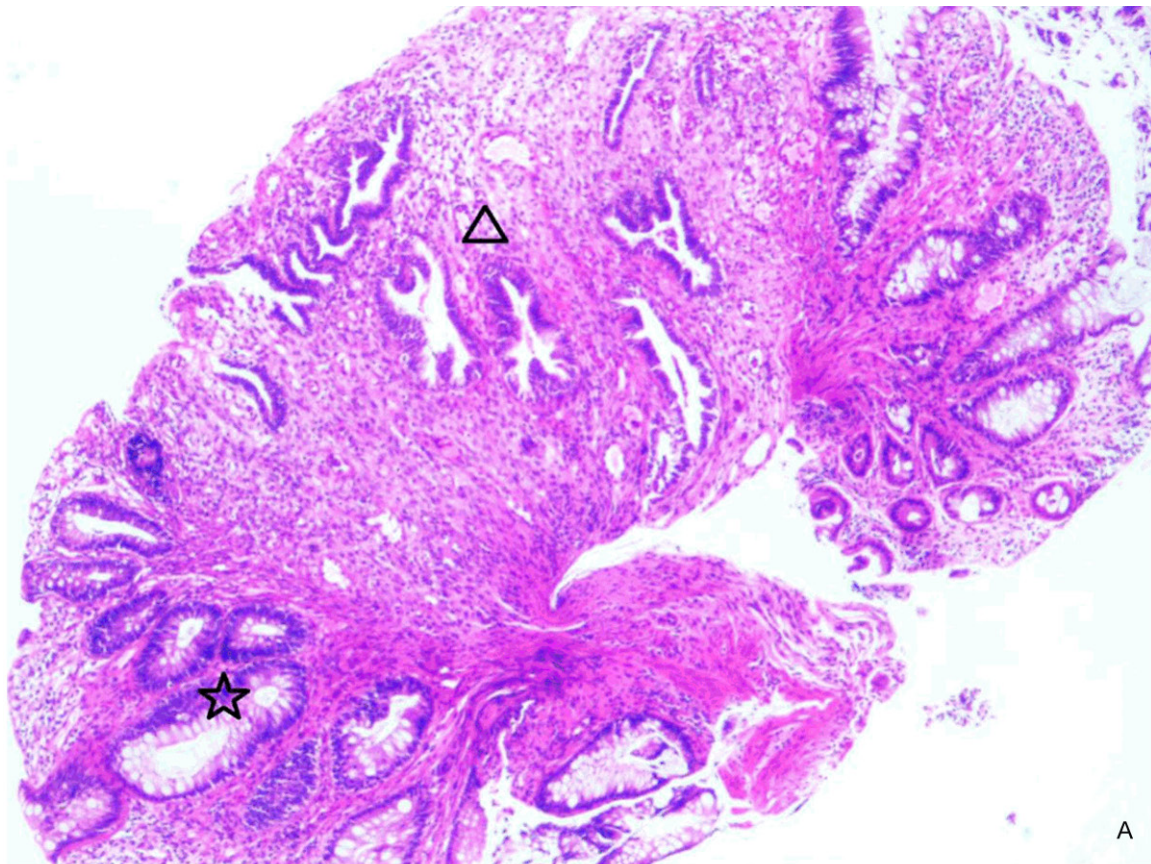
Therefore, the rectal mucosal endometriosis was confirmed.

Discussion

Except for myometrium or uterine appendages, endometriosis can affect any anatomical locations even central nervous system [4]. Some theories were proposed to explain the pathogenesis for endometriosis. Retrograde menstruation favors abdominal serosal implantation and progressively invading into parenchymal organs [2, 5]. This might also explain the reason for most intestinal endometriosis locating in serosa and muscularis propria [6, 7]. Müllerian remnant differentiation or migration and coelomic epithelium metaplastic into endometrium were also suggested. Moreover, other molecular mechanisms could be involved [2].

Endometriosis affecting gastrointestinal tract has been found in 3% to 37% of female patients in such an order: rectum, sigmoid colon, appendix, ileum and cecum [4, 8]. Patients might be asymptomatic or present with abdominal pain, gastrointestinal tract bleeding, constipation, diarrhea, stool form changing, and even intestinal obstruction [9-11]. However, none of these symptoms is specific to intestinal endometriosis. Symptoms might be cyclical and clinically indicative of endometriosis. When the lesion develops, symptoms might not be related to

Endometriosis misinterpreted as adenocarcinoma



Endometriosis misinterpreted as adenocarcinoma

Figure 2. Histological examination. A. Low power view of rectal mucosal endometriosis with superficial erosion. Ectopic endometrium in the middle (black triangle) showing irregular glands and pink stroma. Residual glands displaying architectural distortion at peripheral (black Pentagram). B, C. High power view of ectopic glands displaying mucin depletion, stratified nuclei with fine chromatin, and focal subnuclear vacuoles. D. High power view of ectopic stroma showing spindle cells with abundant pink cytoplasm and small nucleoli. E. High power view of residual glands showing nuclear enlargement with hyperchromasia and losing polarity.

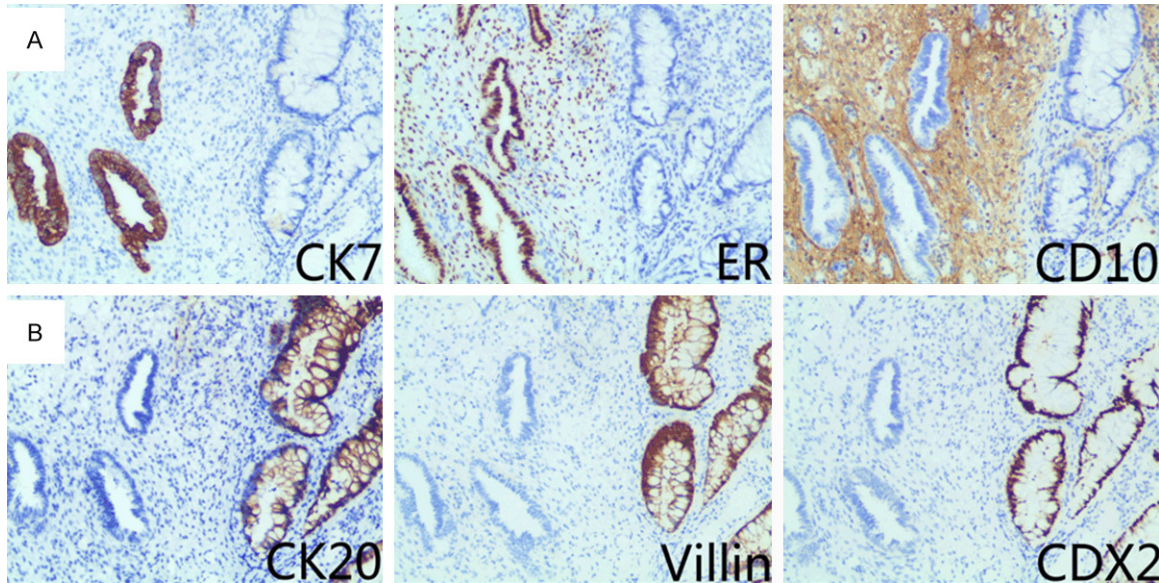


Figure 3. Immunohistochemical examination. A. Ectopic endometrial glands expressing CK7 and ER, while the stroma expressing ER and CD10. Residual rectal mucosa negative for all in glands or lamina propria. B. Residual rectal glands expressing CK20, Villin and CDX2, while ectopic endometrium negative for all.

menstruation, even become permanent [8]. Just as present case, bleeding and abdominal pain were not in accord with menses. Physical and imaging examinations show overlapping features with other intestinal entities, leaving the diagnosis confused clinically [12].

As for pathology, the accurate diagnosis of intestinal endometriosis is often straightforward in resection specimens [13]. But when it goes to biopsy, endoscopic specimen in particular, that will be another story. Since endometriosis most commonly affects serosa or muscularis propria, mucosa often exhibits non-specific inflammatory infiltration, ulceration, cryptitis or architectural changes, which are all mimicking inflammatory bowel disease, ischemic colitis, solitary rectal ulcer syndrome or mucosal prolapse [14-16]. In present case, residual glands displayed architectural distortion, cell enlargement, hyperchromasia and partially lack of polarity, which are all features of severe chronic mucosal injury but not characteristics of intraepithelial neoplasia. The latter shows

architectural and cellular dysplasia. Actually, intestinal mucosa can be involved by endometrium and was reported in 10% and 30% of case series in two different articles [6, 17]. Recently, Wei described 15 cases of intestinal mucosal endometriosis, contributing the largest case series to date on this subject [18]. Ectopic endometrial glands can replace or merge with residual ones, display various metaplasia, dysplasia, and even develop endometrioid adenocarcinoma [19]. Clear cell carcinoma arising in ectopic endometriosis does exist [20, 21]. Ciliated metaplasia was the most common type of metaplasia, others like squamous, eosinophilic, hobnail, mucinous and Paneth cells metaplasia [22] were also documented. Any of these when present strongly suggests ectopic endometriosis. Ectopic endometrial stroma might exhibit decidua, pseudodecidua, edematous change, smooth-muscle metaplasia, fibroblastic metaplasia, even develop sarcoma [23]. In the present case, superficial epithelium was in erosion which might explain clinical bleeding. Ectopic endometrium

Endometriosis misinterpreted as adenocarcinoma

replaced residual mucosa, displayed abnormal architecture without any kind of epithelial metaplasia and misled us to the response of adenocarcinoma. But at high power, the nuclei of glands were relatively uniform with fine chromatin and lack of nucleoli or mitosis, which were not diagnostic of adenocarcinoma. Furthermore, subtle glandular cells harbored tiny subnuclear vacuoles. The surrounding stroma, other than desmoplasia which would be more eosinophilic staining, did not exhibit typical endometriosis as blue spindle stroma in proliferative phase or birck-like decidual one in secretory phase, which primarily misdirected us to desoplastic response and further raised the possibility of adenocarcinoma. Actually, predecidual change was the correct answer. Neither of the glands or stroma in this case showed dysplasia.

To identify the essence of present case, immunostain played the decisive role. As eutopic endometrium, ectopic glands express CK7, ER, and stroma expresses CD10 and ER. Rectal glands are well known to express CK20 and CDX2, but negative for CK7, ER, or CD10. CDX2 was regarded as a highly sensitive and specific marker of intestinal epithelium [24]. However, some literatures reported CDX2-positivity was seen both in eutopic and ectopic endometrial glands [3, 25]. Therefore, CDX-2 applied alone might cause diagnostic pitfall. A panel of antibodies (CK7, CK20, ER, CD10, and CDX2) was proposed to assist the diagnosis.

The treatment of intestinal endometriosis is depended on clinical severity. Bowel resection is recommended when endometriosis involves more than 50% of the intestinal circumference or in cases of multiple nodules or for nodules greater than 3 cm [26]. In Kavallaris's study consisting of 50 cases of rectal involvement, 62% of which were multifocal disease and 38% were multicentric [17]. The author suggested bowel resection margin with a distance of >2 cm to the main lesion.

In summary, endometriosis involving intestinal mucosa is relatively uncommon, and diagnosis is challenging both in clinical aspect and pathology, especially for endoscopic specimen. Clinicians and pathologists should always bear the awareness of colorectal endometriosis for any female patients presenting symptoms in accord with menstrual cycle or not. If the pos-

sibility is raised when assessing tissue slides, a panel of immunomarkers will confirm the diagnosis.

Disclosure of conflict of interest

None.

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Endometriosis misinterpreted as adenocarcinoma

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