Title

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Sigmoid endometriosis diagnosed preoperatively using endoscopic ultrasound guided fine needle aspiration – case report

Short title: Sigmoid endometriosis diagnosed by EUS-FNA

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None of the authors have personal or financial conflicts to declare.

Authors' contributions:

Kenichi Kishimoto, Kousaku Kawashima, and Shunji Ishihara designed the case report and wrote the manuscript.

Ichiro Moriyama, Mayumi Okada, Shohei Sumi, and Hiroki Sonoyama contributed to the endoscopic procedure and data collection.

Ryoji Hyakudomi and Yoshitsugu Tajima contributed to preparation of the surgical findings.

Makiko Nagase, Noriyoshi Ishikawa, and Riruke Maruyama contributed to preparation of the pathological findings.

Yoshikazu Kinoshita was the supervisor of this case report and added important opinions regarding the findings.

All authors have read and approved the final version of the manuscript.

Abstract

We report a case of sigmoid endometriosis diagnosed preoperatively based on endoscopic ultrasound guided fine needle aspiration (EUS-FNA) findings. A 42-year-old female came to us with left lower abdominal pain and bloating that had started 3 months prior. CT and MRI results showed wall thickening of the sigmoid colon. A colonoscopy procedure could not be completed because passage through the sigmoid colon was blocked due to severe stenosis, while mucosal biopsy samples obtained during that procedure could not confirm a diagnosis. EUS-FNA was then performed and specimens were obtained from the muscular layer with stenosis, which revealed a thickened hypoechoic lesion. Histological findings obtained by use of EUS-FNA demonstrated a large amount of fibrosis in endometrial glands and a diagnosis of sigmoid endometriosis was confirmed by additional immunostaining. Thus, a laparoscopic sigmoidectomy was performed, with sigmoid endometriosis finally diagnosed. Confirmation of a diagnosis of intestinal endometriosis based on histological findings of mucosal biopsy specimens obtained by colonoscopy is difficult, because endometrial implants are primarily located in the serosal and/or muscular layer. When safe aspiration is possible, we consider that EUS-FNA can be an effective method for preoperative diagnosis of intestinal endometriosis, which may contribute to avoidance of unnecessary or excessive surgery.

Key words: sigmoid endometriosis, EUS-FNA, preoperative diagnosis

Introduction

Intestinal involvement in endometriosis, a gynecologic disorder defined by the presence of endometrial glands and stroma outside the uterine cavity [1], has been estimated to occur in approximately 10% of affected women [2, 3]. However, it is difficult to confirm a diagnosis of intestinal endometriosis using mucosal biopsy samples obtained by colonoscopy, because endometrial tissue is primarily located in the serosal and/or muscular layer. Several reports of diagnosis of rectal endometriosis by endoscopic ultrasound guided fine needle aspiration (EUS-FNA) findings have been presented [4, 5], while there are few regarding sigmoid endometriosis. Here, we present a rare case of sigmoid endometriosis with severe stenosis diagnosed using findings from EUS-FNA performed prior to surgical resection.

Case report

A 42-year-old female had suffered from left lower abdominal pain for approximately 1 year. With pain gradually increasing in intensity, she made visits to a local hospital because of abdominal bloating for 3 months. No hematochezia was noticed throughout period. Colonoscopy findings revealed stenosis of the sigmoid colon, though the cause could not be determined because biopsy samples obtained from mucosa in the area of stenosis demonstrated only non-specific inflammation. The patient was referred to our hospital for additional examinations.

A complete blood count showed mild anemia with hemoglobin at 11.3 g/dL. Examined tumor markers showed positivity for CA125 at 47.5 U/mL, while CA 19-9 and CEA were negative. Other laboratory test results were within normal ranges. A computed tomography (CT) examination revealed segmental wall thickening and narrowing of the lumen of the sigmoid colon (Fig. 1a). Furthermore, T2-weighted magnetic resonance imaging (MRI) revealed scattered high intensity signals in an area of the thickened sigmoid colon with low intensity (Fig. 1b), while T1-weighted MRI showed signals with slightly high intensity. Those findings suggested minute hemorrhaging in the thickened sigmoid colon. Next, the patient underwent a colonoscopy and the findings revealed normal mucosa in the narrowed area of the sigmoid colon. However, the scope could not pass through that stenosis area (Fig. 2a), which had a length of approximately 2 cm, as shown by contrast findings (Fig. 2b). Thus, we pushed forward a guidewire into the deeper part of the stenosis and then inserted an endoscope for EUS over the guidewire around the stenosis using a ropeway method (Fig. 2c). EUS findings showed that the thickened muscular layer contained a hypoechoic lesion. We then performed EUS-guided fine needle aspiration (EUS-FNA)

using a 22-gauge needle 3 times (Fig. 2d). Histological findings demonstrated that part of the glandular tissue consisted of ciliated epithelium with a large amount of fibrosis resembling endometrial glands (Fig. 3a, b). In immunostaining results, those were positive for estrogen and the progesterone receptor (Fig. 3c, d), findings compatible with sigmoid endometriosis.

The patient suffered from severe symptoms induced by the stenosis, thus a laparoscopic sigmoidectomy was performed based on a preoperative diagnosis of sigmoid endometriosis. Laparotomic views showed that the sigmoid colon was affected by severe stenosis, while the ileocecal areas and rectum also had endometrial lesions. In addition, disseminated lesions of endometriosis, such as blueberry spots and petechial hemorrhaging, were scattered throughout the abdominal cavity, for which we performed cauterization as much as possible. The diagnosis of intestinal endometriosis was confirmed based on pathological findings of a resected specimen (Fig. 4). Thereafter, the patient began treatment with a progesterone product for prevention of recurrence.

Discussion

Endometriosis is a chronic gynecological disorder frequently occurring in women of child-bearing age that can be found throughout the whole body, including the gastrointestinal tract, urinary tract, lungs, central nervous system, and skin, though ectopic endometriosis is most commonly found in the pelvis. Involvement of the gastrointestinal tract has been estimated to occur in approximately 10% of patients with endometriosis [2-3]. As for gastrointestinal lesions, the rectum and sigmoid colon are the most common sites, accounting for 70-93% of reported cases [6]. In many, symptoms such as periodic hematochezia, dysmenorrhea, and dyspareunia emerge synchronously with the menstrual cycle. However, that relationship can be disrupted by an intestinal obstructive change induced by a large amount of fibrosis in the intestinal wall as a result of repeated bleeding over an extended period. In the present patient, continuous abdominal pain and bloating had emerged because of severe stenosis, unrelated to the menstrual cycle. In such cases, a diagnosis of intestinal endometriosis may be difficult, because a relationship with the menstrual cycle is an important clue.

To confirm a diagnosis of intestinal endometriosis, histological identification of endometrial tissue is necessary. Regarding endoscopic diagnosis, it is difficult to collect endometrial tissue in mucosal biopsy samples obtained by colonoscopy, as that is mainly located in the serosal to muscular layer of the intestinal wall. A previous report presented colonoscopy findings of intestinal endometriosis, such as mucosal erythema, polyps or masses, eccentric wall thickening, and surface granularity and nodularity [7]. However, there is a low possibility of detection of these in endoscopic findings. A systematic review of colorectal endometriosis cases that underwent bowel resection found that only 6.4% of those had lesions that penetrated into the mucosa [8]. Thus, an

exploratory laparoscopy procedure is generally considered to be the gold standard for diagnosis confirmation [9].

Recently, EUS and EUS-FNA have become increasingly utilized for evaluations of subepithelial masses in the gastrointestinal tract, as they are minimally invasive and provide accurate characterization of tissue morphology [10]. Several investigations have evaluated the usability of EUS-FNA for diagnosis of recto-sigmoid endometriosis [4-5, 11]. Among those, 9 cases of rectal endometriosis that underwent EUS-FNA were reported, of which 7 were definitively diagnosed. As for sigmoid endometriosis, only a single case diagnosed using EUS-FNA findings has been presented [5], possibly because of difficulty with guiding the endoscope to the sigmoid colon for EUS. To avoid intestinal perforation during EUS scope insertion, the endoscopist must pay close attention to delivering the scope to the sigmoid colon along the guidewire by carefully confirming its position using X-ray fluoroscopy visualization.

Furthermore, even when the endoscope can be guided to the sigmoid colon, accurate aspiration in the target area may be difficult, as the sigmoid colon is not fixed on the retroperitoneum. Although seeding of endometrial cells in the peritoneal cavity during EUS-FNA has not been reported, a report of several cases of tract seeding of cancer cells during EUS-FNA has been presented [12]. Likewise, it is possible that seeding of endometrial cells can occur in the peritoneal cavity during EUS-FNA, if the puncture for endometriosis was deeper than expected. Close attention must be given by the endoscopist to the depth of the puncture by confirming the position of the needle tip. At present, it is unclear how much thickness of the muscular layer is safe for puncture when using EUS-FNA. For patients with a gastrointestinal stromal tumor (GIST), it is difficult to perform an accurate puncture when the tumor is small, because that may not

be fixed during EUS-FNA and needle movement inside the tumor is limited. Therefore, it is considered difficult to obtain sufficient material by EUS-FNA with a small GIST. Hoda et al. reported diagnostic rates ranging from 40-50% for GISTs under 10 mm in size in cases diagnosed using EUS-FNA findings [13]. Based on these results, it might be safer to have a thickness of at least 10 mm before attempting to puncture. Should safe aspiration be possible, it is considered that EUS-FNA is an effective method for diagnosis of intestinal endometriosis.

The first choice of treatment for gastrointestinal endometriosis is generally hormonal therapy, such as estrogen-progestin agents, gonadotropin-releasing hormone agonists, danazol, or aromatase inhibitors, though a surgical option is preferred for cases with severe fibrosis and stenosis. In a cohort study of deeply infiltrating endometriosis, approximately one-third of those patients showed an inadequate response to medical therapy and required surgical management [1]. In the present case, we selected resection of the narrowed part of the sigmoid colon, because the symptoms induced by stenosis were severe and the massive fibrosis was considered to be irreversible. It is important to note that deep infiltrating endometriosis may require intestinal resection. Furthermore, occasionally, intestinal endometriosis cannot be distinguished from malignant neoplasms. Should preoperative diagnosis of intestinal endometriosis be obtained with EUS-FNA, an excessive surgical procedure such as lymph node dissection may be avoided.

In conclusion, we report a rare case of sigmoid endometriosis diagnosed preoperatively using EUS-FNA. Based on our findings, we consider that EUS-FNA can serve as a method for preoperative diagnosis of intestinal endometriosis as long as safe aspiration is possible, which can contribute to avoidance of an unnecessary or excessive

193 surgical procedure.

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233 **Figure Legends**

234 **Fig. 1. A.** Enhanced CT findings. White arrows indicate segmental wall thickening and
235 narrowed lumen of the sigmoid colon. **B.** T2-weighted MRI findings. White arrow
236 indicates scattered high intensity in low signal area of thickened sigmoid colon.
237
238 **Fig. 2. A.** Colonoscopy findings showing normal mucosa with narrowed sigmoid colon.
239 **B.** Contrast examination results showing sigmoid colon stenosis approximately 2 cm in
240 length. **C.** An endoscope for EUS was inserted over a guidewire around the area of
241 stenosis using a ropeway method. **D.** EUS-FNA using a 22-gauge needle was performed
242 from the muscular layer, which detected a thickened hypoechoic lesion.
243
244 **Fig. 3.** Histological findings of samples obtained by EUS-FNA. **A.** Hematoxylin and
245 eosin (H&E) staining. **B.** H&E staining, high powered view of area enclosed by red
246 square in A. **C.** Immunostaining for estrogen receptor. **D.** Immunostaining for
247 progesterone receptor.
248
249 **Fig. 4.** Resected specimen from sigmoid colon. **A.** Macroscopic view. A stenotic
250 segment 2 cm in length with the thickened muscular layer can be seen. The mucosa of
251 the stenotic segment was normal. **B.** Microscopic view. Endometrial tissue in the
252 thickened muscular layer with fibrosis is shown. **C.** Microscopic view (high-power
253 field). Endometrial glands with multiple hemorrhaging are seen.
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