Endometrioid adenocarcinoma arising from colon endometriosis

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Abstract

Endometriosis-associated intestinal tumors represent the malignant transformation of gastrointestinal endometriosis. Approximately 50 cases have been reported in the literature. They are most commonly found among women aged 30–60 years, whereas exogenous hormone therapy and obesity are primary risk factors for the malignant transformation of endometriotic lesions. Clinical features simulate a primary colonic carcinoma. A high index of suspicion in conjunction with careful histological and immunohistochemical examination (CK7, CK20, CDX2, CD10, ER, and PR) is important for establishing a correct diagnosis. In this article, a rare case of a postmenopausal woman with no risk factors and conflicting clinical presentation, diagnosed with endometriosis-associated intestinal tumor, is described.

Keywords

Endometriosis, gastrointestinal, tumor, endometriosis-associated intestinal tumors

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Introduction

Endometriosis affects up to 10% of women. Epidemiologists forecast an increase in the diagnosed prevalent cases of endometriosis, from 5.66 million prevalent cases in 2012 to 5.86 million prevalent cases in 2022, at a growth rate of 3.4% over forecast period. Only 21.3% of the cases occur at extragonadal pelvic sites. The intestinal tract is involved in 3%–37% of all patients with pelvic endometriosis.1 The sigmoid colon and rectum are the most commonly involved areas in women with intestinal endometriosis.2 Malignant transformation of endometriosis may occur in up to 1% of women,3 whereas endometriosis-associated intestinal tumors (EAITs) are even rarer.4 In this article, a rare case of a postmenopausal woman with malignant transformation of an endometriotic lesion of the rectosigmoid colon without predisposing factors is described.

Case

A 75-year-old woman (virgo, gravida 0, para 0, body mass index (BMI) = 21) presented with diffuse abdominal pain and enterorrhagia. She entered menopause at the age of 55 and she had regular menstrual cycles with no dysmenorrhea. Her medical history includes hypertension treatment with angiotensin II receptor blocker. She had undergone knee arthroplasty bilaterally and had never complained of bowel or reproductive system symptoms before, while there is no family history of colorectal or endometrial neoplasms.

The patient underwent colonoscopy, which was not completed due to bowel intussusception, 28 cm from the anus. It was assumed that intussusception was the result of external pressure. Blind biopsies were performed and the relevant histopathological examination revealed intestinal mucosa with tubular adenoma of low-grade dysplasia. Computed tomography (CT) of the upper and lower abdomen demonstrated a midline pelvic lesion with a transverse

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diameter of 6.1 cm (Figure 1(a) and (b)). Additionally, two more nodal lesions with a transverse diameter of 2.8 cm each were found in a cephalad and caudal direction (Figure 1(c)). The caudal lesion was found to be in contact with the anterior surface of the fundus of the uterus. Thus, local expansion of the intestinal tumor to the uterus was hypothesized. Small (diameter <5 mm) local lymph nodes were also revealed. Small cystic lesions were found in both ovaries. The rest of the organs appeared normal (Figure 1). The lower abdomen ultrasound revealed an atrophic uterus (51 mm × 22 mm × 35 mm) with a thin endometrium (3 mm). The ovaries could not be visualized. No pathological findings were observed in the pouch of Douglas. A thorax CT scan was negative for pericardial or pleural effusion and for any other parenchymal diseases. The preoperative blood test results were normal.

The patient underwent sigmoidectomy, with excision of the intestinal mass found preoperatively in CT and colonoscopy, and end-to-end anastomosis with the use of a stapler. Intraoperatively, uterus and adnexa were normal, thus no hysterectomy and/or oophorectomy was carried out. The histological examination revealed a moderately differentiated adenocarcinoma of the colon. According to the morphological characteristics and the immunophenotypic analysis (CK7+ CK20–, Vimentin focally), an endometrioid adenocarcinoma arose from endometriosis while a lesion secondary to endometrioid adenocarcinoma of the endometrium or the ovaries is highly unlikely. The carcinoma caused the expansion of the whole intestinal wall and the serosa. The postoperative period was uneventful and the patient was discharged on the ninth postoperative day in a really good condition.

Discussion

Approximately 50 cases of malignant transformation of gastrointestinal endometriosis or EAITs have been reported in the literature. EAITs are most commonly found among women aged 30–60 years. The patients complain of abdominal and/or pelvic pain, dyschezia, deep dyspareunia, or bloody stools. Cases of irritable bowel syndrome, with chronic cyclic intestinal symptoms, have also been described. Small or large bowel obstruction due to a mass or acute abdomen due to intussusception or perforation have also been described as a first presentation of patients suffering from EAITs. Additionally, surgical exploration for other reasons may reveal serosal nodules and eventually lead to incidental discovery of EAITs.

During physical examination, a pelvic mass may be palpated. Exogenous hormone therapy and obesity are primary risk factors for the malignant transformation of endometriotic lesions. Therefore, these patients’ characteristics should alert the physicians for the possibility of EAITs. Dioxin and polychlorinated biphenyl pollution have also been reported as etiological factors for the development of deep infiltrating endometriosis in the gastrointestinal tract and for malignant transformation.

EAITs are most commonly found in areas where the peritoneum is irregularly folded, such as the antimesocolic border of the sigmoid colon. Parts of the bowel that lie in close proximity to the genital organs are also affected. The
sigmoid colon and rectum are involved in 15%–72% of the cases, followed in frequency by the small intestine, cecum, and appendix. Endometrioid adenocarcinoma is the most frequent. Endometrial stromal sarcoma is extremely rare, particularly in the rectosigmoid colon.

Endometrioid adenocarcinoma is the EAIT most likely to be confused with a colorectal carcinoma, as in the case of our patient. The following elements are essential for the differential diagnosis between EAIT and colorectal carcinoma. First, on gross examination, EAIT usually involves the serosa and subserosa (up to 70%) although involvement of the deeper bowel layers (muscularis propria, submucosa, or even mucosa) may be seen in symptomatic patients. Transmural tumors have a typical dumbbell shape consisting of a bulky serosal and polypoid mucosal tumor and a narrower neoplastic waist that extends through muscle bundles of the muscularis propria. This means that cancer types arising in endometriosis are developed in an extramural location and invade into the bowel wall from the outside. The mucosa is, therefore, frequently normal or only shows minimal changes endoscopically. On the contrary, primary colon carcinoma shows the opposite growth pattern in the bowel, always involving the mucosa and may be associated with adenomatous changes or a neoplastic polyp. Advanced colon carcinomas may be extended from the mucosa through the bowel wall to the serosal surface or the adjacent fat. Microscopically, squamous differentiation within a glandular neoplasm of the colon is a characteristic strongly suggesting the endometriotic origin of a tumor. Additionally, endometrioid adenocarcinomas typically form tubular glands with “clean” luminal contents, with the tumor cells lacking intracellular mucin and exhibiting an alcin blue–positive glycosyalx. On the other hand, primary colonic carcinomas are more likely to have intraluminal “dirty necrosis” and higher-grade nuclear features than those observed in most EAITs. Immunohistochemistry is a useful tool for the clinicians. The suggested minimal number of markers required is 2, corresponding to the cytokeratin subtypes 7 and 20. It is estimated that 80%–100% of endometrioid adenocarcinomas have a CK7-positive, CK20-negative phenotype, whereas 75%–95% of primary colonic adenocarcinomas have a CK7-negative, CK20-positive phenotype. In addition, CD10, ER, and PR are related to endometriosis, whereas CDX2 is a specific marker for adenocarcinoma of the gastrointestinal tract, particularly colorectal adenocarcinoma. The last mentioned markers are used as complementary tools in the diagnostic strategy.

Treatement of EAITs has been variably reported in the literature and is highly individualized. Primary surgical treatment with complete resection of all disease is the treatment of choice for non-metastatic disease presenting with pain, bleeding, altered bowel habits, and intestinal obstruction. This was also the treatment selected in the case of our patient, since no dissemination of the disease was revealed during laparotomy.

The prognosis of EAITs is associated with the stage of endometriosis. A 100% 5-year survival rate has been noted for malignant transformation in extragonadal endometriosis, confined to the site of origin. Disseminated intraperitoneal disease has a poor prognosis. Most patients with disseminated disease die within 2 years; the 5-year survival rate is only 12.5%.

**Conclusion**

In this article, we report a case of endometriosis-associated endometrioid adenocarcinoma with clinical features simulating a primary colonic carcinoma, including intussusception and enterorrhagia. In addition, this is a rare case of a postmenopausal woman with no history indicative of endometriosis, no hormonal treatment, or other risk factors. Six months postoperatively the patient lives a normal life, free of symptoms. A high index of suspicion in conjunction with careful histological and immunohistochemical examination (CK7, CK20, CDX2, CD10, ER, and PR) is important for establishing a correct diagnosis.

**Declaration of conflicting interests**

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**Ethical approval**

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**Informed consent**

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