Müllerian Endometrioid Adenocarcinoma Arising from Colonic Endometriosis: Report of a case that presented with bowel obstruction

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Citation

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Abstract

Gastrointestinal endometriosis-associated malignancies are rare and diagnostically challenging. Mullerian endometrioid adenocarcinoma is the most common and likely to be confused with a primary colonic adenocarcinoma due to their overlapping histological features. We present a case of mullerian endometrioid adenocarcinoma arising from colonic endometriosis in a 61-year-old woman who presented with bowel obstruction. The tumor had histological features remarkably simulating a primary colonic adenocarcinoma because of its transmural involvement of the sigmoid colon, colonization of the colonic surface epithelium and mesenteric lymph node metastasis. A high index of suspicion in conjunction with careful histological and immunohistochemical examination (CK7, CK20, CDX2, CD10, ER and PR immunostains) is important for establishing a correct diagnosis.

CASE HISTORY

The patient, a 61-year-old woman, presented with vaginal bleeding, worsening nausea, vomiting and constipation over 10 days before admission. At the outside hospital, she was found to have bowel obstruction involving descending to sigmoid colon, confirmed by Barium enema imaging and flexible sigmoidoscopy, and a pelvic mass greater than 25 cm with MRI features consistent with uterine smooth muscle tumor. The patient had a past medical history of hypertension and chronic venous insufficiency of lower extremities. An elevated serum CA-125 level was also noted (110 U/ml, normal: <35 U/ml). She was transferred to the Gynecological Oncology Service at Yale-New Haven Hospital for total abdominal hysterectomy, bilateral salpingo-oophorectomy and rectosigmoid resection.

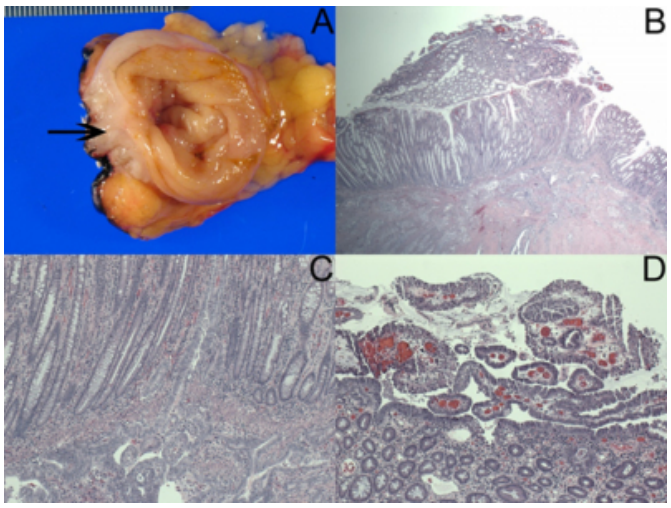
At surgery, the uterus was found markedly enlarged with multiple leiomyomas. Extensive adhesions were noted between posterior aspect of the cervix and rectum. The large bowel was severely dilated from the ileocecal valve to the junction of the descending and sigmoid colon, where a 3.0 cm mass was noted with collapsed large bowel beyond this point. Small bowel, appendix, liver, pancreas, and bladder appeared unremarkable. Frozen sections demonstrated an “infiltrating adenocarcinoma, favor mullerian primary in the colon”. Subsequent pelvic lymph node dissection, omentectomy and peritoneal sampling were performed.

PATHOLOGICAL FINDINGS

The uterus weighed 2800 grams and measured 17.0 x 17.0 x 15.0 cm. The endometrium was atrophic and its cavity was markedly distorted. There were multiple leiomyomas ranging from 0.6 to 11.0 cm involving submucosa and myometrium. The attached ovaries measured 4.0 x 2.5 x 0.7 cm on the right and 3.0 x 2.0 x 0.7 cm on the left. The surgically removed sigmoid colon demonstrated an obstruction site, 3 cm from the proximal resection margin, where a white tan retraction area (2.0 x 2.0 cm) on the serosa and a 2.5 x 1.5 x 1.5 cm white tan infiltrative mass lesion involving the colonic wall were found (figure 1A). The remaining colonic mucosa showed no evidence of ulceration or polyps.

Figure 1

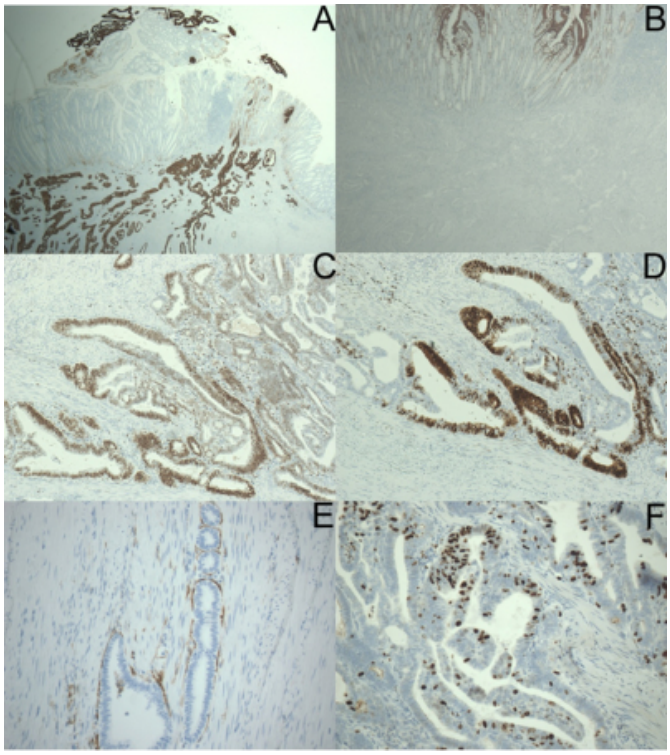
Figure 1: Gross and Microscopic Findings. An ill-defined infiltrative lesion involved the colonic wall (Panel A, arrow points to the lesion). Low power view showed an endometrioid adenocarcinoma infiltrating the submucosa and mucosa (Panel B, Hematoxylin-eosin, original magnification x 100). The adenocarcinoma involved the submucosa (Panel C, Hematoxylin-eosin, original magnification x 200) and colonized the mucosal epithelium (Panel D, Hematoxylin-eosin, original magnification x 200).



Microscopically, the colonic mass showed an infiltrative, well to moderately differentiated adenocarcinoma involving colonic muscularis propria and submucosa (Figure 1, B and C) with focal replacement of surface colonic epithelium (Figures1, D), simulating colonic adenomatous polyp. At the periphery of the carcinoma, there were scattered foci of endometriosis with cystic glandular structures, lined by müllerian endometrial or tubal epithelium. Immunohistochemistry showed that the carcinoma cells were positive for CK7 (Fig. 2 A), ER (Fig. 2C), and PR (Fig. 2D), but negative for CK20 (Fig. 2B), CDX2, WT-1 and TTF-1 (data not shown). Stromal cells surrounding the endometriotic glands were positive for CD10 immunostain (Fig. 2E). The proliferative index was estimated at 20-40% in the tumor cells based on Ki-67 staining (Fig. 2F). The overall histological and immunohistochemical findings were diagnostic of a mullerian endometrioid adenocarcinoma arising from colonic endometriosis. Six of thirty-one mesenteric lymph nodes had metastatic adenocarcinoma. Metastasis was not found elsewhere including bilateral pelvic lymph nodes. The uterus had multiple leiomyomas and an atrophic endometrium. Both ovaries had endometriosis and epithelial inclusion cysts. The fallopian tubes were microscopically unremarkable.

Figure 2

Figure 2: Immunohistochemical Findings. The carcinoma cells were positive for CK7 (Panel A, original magnification x 20), ER (Panel C, original magnification x 200), and PR (Panel D, original magnification x 200); but were negative for CK20 (Panel B, original magnification x 40). Stromal cells of the colonic endometriosis were positive for CD10 (Panel E, original magnification x 200). Ki-67 Immunostaining demonstrated a high proliferative index associated with tumor cells (Panel F, original magnification x 200).



DISCUSSION

Approximately 50 cases of malignant transformation of gastrointestinal endometriosis or endometriosis-associated intestinal tumors (EAIT) have been reported in the literature. These malignancies include endometrioid adenocarcinoma, clear cell carcinoma, squamous cell carcinoma, carcinosarcoma, mullerian adenosarcoma, endometrial stromal sarcoma, mixed müllerian tumors, and endometrioid adenofibroma of borderline malignancy [$_{123456}$]. Endometrioid adenocarcinoma is the most common malignancy arising from gastrointestinal endometriosis and is the most likely to be confused with a colonic adenocarcinoma since both have a similar morphology [$_{5}$]. The mean age of patients with the condition is 54 years (range 36–76 years) [$_{56}$]. Forty percent of the reported endometriosis-associated intestinal tumors involved relatively young women in their late 30s to early 50s, which is one to two decades earlier than primary

colonic adenocarcinoma. The rectosigmoid colon is the most frequent site for EAIT. The most common presenting symptoms are abdominal/pelvic pain, pelvic mass, bowel obstruction and GI bleeding [$_{567}$]. Our patient had a clinical presentation with bowel obstruction secondary to the sigmoid EAIT compounded by large uterine leiomyomas. The carcinoma had a transmural involvement of the colon with mucosal surface colonization and extensive mesenteric lymph node metastases, simulating a primary colonic adenocarcinoma.

Distinguishing an endometrioid adenocarcinoma associated with endometriosis from a primary colonic adenocarcinoma has important clinical implications since the treatments for the two entities are different. Generally, EAIT frequently involves the muscularis propria and/or serosa with endometriosis or endosalpingiosis in the neighborhood. However, when the tumor involving the mucosa and particularly colonizing the surface epithelium, it may become difficult to differentiate it from a colonic primary adenocarcinoma. Immunohistochemistry is generally helpful when there is doubt. Overall, 75% to 95% of primary colonic adenocarcinomas have a CK20 - positive and CK7- negative immunophenotype, whereas 80% to 100% of endometrioid adenocarcinomas have a CK20-negative and CK7-positive profile [[[[8.9]]]]. CDX2 is expressed in the colonic adenocarcinoma and negative in the endometrioid adenocarcinoma. In our case, the tumor cells were positive for CK7, but negative for CK20 and CDX2. With additional positivity for progesterone receptor (PR) and estrogen receptor (ER) and the presence adjacent endometriosis with surrounding CD10-positive stromal cells, the diagnosis of endometriosis-associated mullerian endometrioid adenocarcinoma can be established [$_{10}$].

The etiology of malignant transformation arising in endometriosis / endosalpingiosis is unknown, although unopposed exogenous estrogen status has been hypothesized [$_{111213}$]. Currently, there are no guidelines for staging EAIT. Clinically, it may be reasonable to approach such a malignancy as a primary peritoneal adenocarcinoma. Indeed, the post surgical management of our patient has been tailored as a Stage IIIC (American Joint Committee on Cancer 2006) peritoneal mullerian adenocarcinoma by our gynecological oncologists.

In summary, we present a case of endometriosis associated endometrioid adenocarcinoma with clinical and pathological features simulating a primary colonic carcinoma, including bowel obstruction, colonization of colonic surface epithelium and mesenteric lymph node metastases. Endometriosis – associated intestinal tumor should be included in the differential diagnosis of unusual colorectal tumors in female patients. 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.

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