

CASE REPORT

Endometrial Adenocarcinoma Metastatic to the Colon Masquerading as a Primary Colon Cancer

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ABSTRACT

While the majority of colonic malignancies represent primary tumors, secondary tumors are not uncommon. We present a case of endometrial cancer metastatic to the colon masquerading as a primary colonic adenocarcinoma. The clinical and pathologic characteristics of each disease are discussed. To our knowledge, this is the first reported case of endometrial cancer metastasis to the colon in the absence of endometriosis. It demonstrates the importance of using immunohistochemistry to distinguish morphologically similar tumors in a patient who seemingly presents with more than one primary malignancy.

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Key words: Metastatic endometrial cancer; Secondary colon cancer; Immunohistochemistry

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INTRODUCTION

The majority of colon cancers are primary tumors, but secondary

tumors are not uncommon. Secondary tumors are typically of lung, breast, and ovarian origin^[1]. There are only a small number of case reports of secondary colon cancers of endometrial origin, most of which are due to endometriosis rather than metastatic disease. We present a case of endometrial cancer metastatic to the colon masquerading as primary colonic adenocarcinoma.

CASE

The 70 year-old female in this case had a history of total abdominal hysterectomy with bilateral salpingo-oophorectomy for endometrial cancer at an outside hospital in May 2008. Sections from the uterus showed endometrial adenocarcinoma, endometrioid type, FIGO grade II (Figures 1 and 2), with garland-like glandular architecture and intraluminal necrosis. She was determined to have stage IB disease (T1b N0 M0) that invaded slightly more than half of the myometrial thickness. This was not followed by any chemotherapy or radiation. In October 2009, she experienced rectal bleeding and colonoscopy revealed an obstructing intraluminal recto-sigmoid mass. She underwent low anterior resection of her colon at our institution. At time of operation, the mass was noted to be invading the abdominal sidewall, ureter, and obturator nerve, from which the tumor was excised. Sections showed a moderately differentiated adenocarcinoma, with a necrotic background, involving the mucosal surface of the colon (Figures 3 and 4). Thirteen negative lymph nodes were obtained. The pathologic diagnosis was moderately differentiated adenocarcinoma extending into the serosa, consistent with T4 N0 M0 colonic adenocarcinoma. She subsequently had 12 cycles of fluorouracil, leucovorin, and oxaliplatin followed by radiation therapy to the abdominal sidewall.

In August 2010, 10 months after surgery, this patient presented with a mass at her abdominal wall incision site. Fine needle aspiration and subsequent mass excision revealed metastatic moderately differentiated adenocarcinoma. This specimen was morphologically consistent with metastasis from a primary colonic source (Figure 5). However, immunohistochemical staining showed the tumor cells to be positive for cytokeratin 7 (CK7) and estrogen receptor (ER), and negative for cytokeratin 20 (CK20) and CDX2, which is atypical for a colonic primary. Retrospectively, the endometrial and colon specimens also underwent immunoperoxidase staining. All three specimens were morphologically similar with the same immunophenotype, making the diagnosis primary uterine cancer with metastasis to the colon and invasion of the abdominal wall.

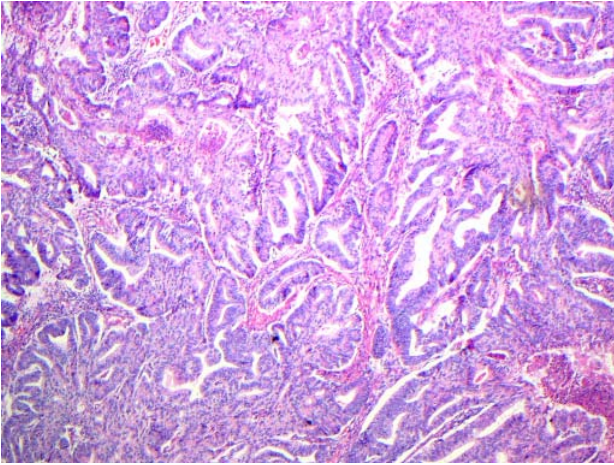


Figure 1 Sections from the uterus specimen show a moderately differentiated, FIGO grade II adenocarcinoma with complex, garland-like architecture (H&E, 100 \times).

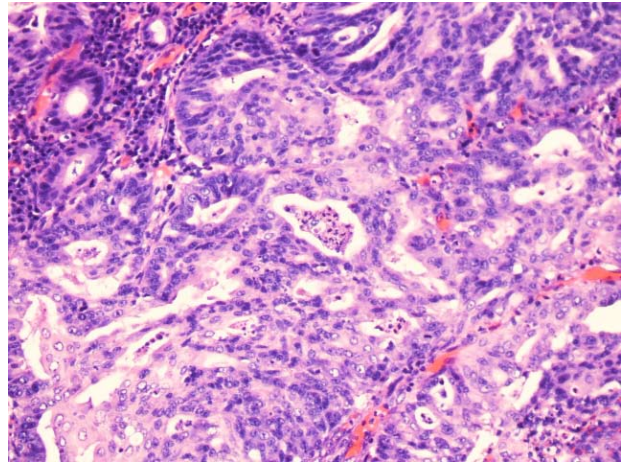


Figure 4 Higher power of colon showing cribriform architecture with intraluminal necrotic debris, mimicking a primary colonic adenocarcinoma (H&E, 200 \times).

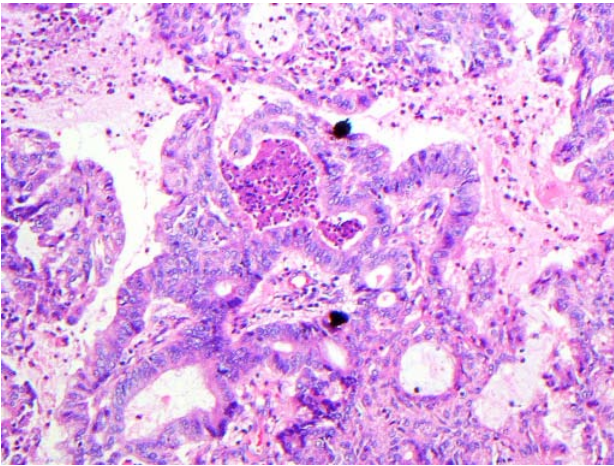


Figure 2 Higher power of uterus showing intraluminal necrosis and cellular pleomorphism (H&E, 200 \times).

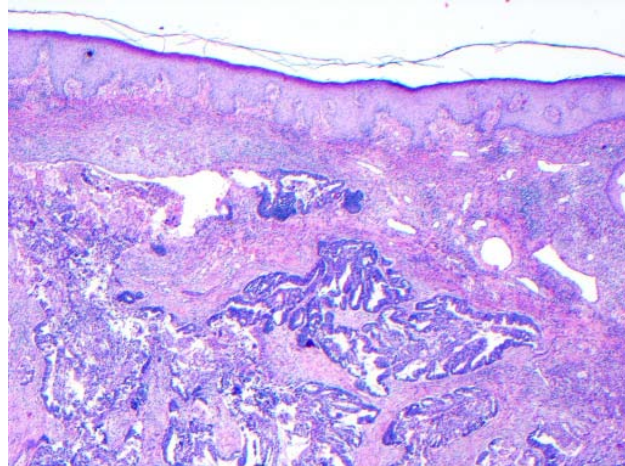


Figure 5 Sections from the skin show moderately differentiated adenocarcinoma. The tumor cells stained positive for CK7 and ER, and negative for CK20 and CDX2 (H&E, 40 \times).

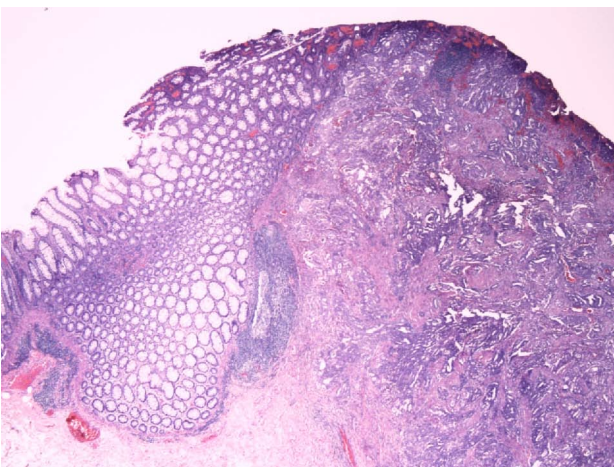


Figure 3 Sections from the colon specimen show a moderately differentiated adenocarcinoma with cribriform architecture. Note the involvement of the mucosal surface (H&E, 20 \times).

DISCUSSION

Secondary tumors of the colon can result either from direct spread or peritoneal seeding. They usually present as serosal implants to the colon, rather than as an intraluminal mass as seen in our patient.

Endometrial cancer is staged surgically, with higher stages relating to propensity for direct invasion of surrounding organs and lymphatic spread. Stage I endometrial cancer, as seen in this patient, is regularly controlled during surgical staging with pelvic lymphadenectomy. It has been reported that 2.8% of stage I endometrial cancers can recur in distant anatomical locations years after resection of the initial cancer. This is due to hematologic spread. Mariani *et al*^[2] demonstrated that in stage I endometrial cancers, the only independent risk factor for distant recurrence was greater than 66% myometrial invasion. Our patient had only 56% myometrial invasion. Others report that of those tumors that recur, most (64%) are noted within two years of surgery, while nearly all (97%) recur by five years^[3].

Recurrence patterns of endometrial cancer have also been studied in recent literature. In a retrospective review of 86 patients with recurrent endometrial cancer at a single institution, the most

common sites were lymph nodes (48%), vagina (42%), peritoneum (27%), and lung (24%). Only 3 patients (near 3%) developed recurrence in the rectum, and no patients developed recurrence in the colon^[3]. This study and other case reports have demonstrated rarer recurrences of endometrial cancer, including the pancreas^[3, 4] and the small intestine^[5]. There are very few previously reported cases of endometrial cancer of the colon that mimic primary colon cancer^[6, 7]. One report is of a patient with a history of total abdominal hysterectomy and bilateral salpingo-oophorectomy for presumed uterine leiomyomas who presented with a sigmoid colon mass 34 years later. Similar to our case, this patient was originally diagnosed with primary colon adenocarcinoma, until follow-up revealed the metastatic nature of the lesion^[6]. There are other reports of endometriosis-associated intestinal neoplasms, including one series with 14 cases^[7]. However, these cancers are usually differentiated from other primary cancers because of background endometriosis and lack of mucosal involvement^[6]. Our patient had no history of endometriosis, and, of even greater significance, showed near-obstructing colonic mucosal involvement by the metastasis, mimicking a primary malignancy.

Incisional site recurrence, as seen in this patient, is rare in both colorectal and endometrial carcinomas. The rate for colon cancer recurrence at the incisional site after open colectomy has been reported to be just under 1%, most likely due to disseminated cancer rather than isolated implantation^[8]. More recently, studies have looked at incisional site recurrence after laparoscopic resection of colorectal cancer, with varying results. Some studies report a 0% port-site recurrence^[9, 10] while others report rates consistent with open surgery^[11]. Shukla's limited series reported an incisional recurrence rate of 21.4%^[12]. Proposed mechanisms for port-site recurrence include direct contamination during tumor extraction or by contact with instruments, indirect contamination by dispersement in the insufflation gas, metabolic and immunological factors, or hematogenous spread. It is thought that the most common reason for isolated surgical site metastasis is poor technique^[12].

Recurrence of endometrial carcinoma in incisional scars is even less common with only a handful of case reports in the literature^[13, 14]. The proposed mechanisms for incisional recurrence of low-stage endometrial cancer are isolated implantation during surgery^[13-15] and positive peritoneal cytology with subsequent wound seeding^[16]. As our patient had negative peritoneal cytology, the most likely mechanism for recurrence is through isolated implantation of cancer cells during surgery.

Colon and endometrial adenocarcinoma share some morphologic features but have different immunohistochemical profiles. Moderately differentiated colonic adenocarcinoma classically demonstrates a low cuboidal epithelium arranged in complex architectural patterns, including a cribriform pattern as seen in the colon specimen in our patient. Intraluminal necrotic debris and moderate pleomorphism are common, and these features were present in our case^[17]. Colon adenocarcinoma cells frequently contain high nuclear grade and frequent mitoses. In contrast, endometrial adenocarcinoma (endometrioid type) can show a range of nuclear atypia and pleomorphism, reflected in the FIGO grade. Well differentiated endometrioid adenocarcinoma (FIGO grade I) shows back-to-back or cribriforming glandular architecture, with mild nuclear atypia and varying mitotic activity. More complex glandular architecture and/or increased nuclear atypia is seen in moderately differentiated (FIGO grade II) carcinoma^[18]. Focal squamous differentiation of endometrial cancer is present in up to 20% of all pathological specimens, although its presence does not

confer increased relapse rate^[19]. Focal squamous differentiation is also seen in colorectal carcinoma, although much less commonly, and is reported around 1% in a large series. In contrast to endometrial carcinoma, squamous differentiation in colorectal carcinoma is thought to represent an inherently neoplastic phenomenon, and also serves as a marker for high risk malignant transformation of colorectal polyps^[20].

The common immunohistochemical profile of endometrial adenocarcinoma, as seen in our patient, is CK7 positive, ER positive, CK20 negative, and CDX-2 negative^[21]. Colon adenocarcinoma is almost always positive for CDX-2^[22] and usually positive for CK20, while negative for CK7 and ER^[23]. CDX-2 expression is primarily associated with gastrointestinal carcinomas; however, occasional extra-intestinal adenocarcinomas (especially those with intestinal or mucinous differentiation) may express this marker^[22, 24].

In summary, we present an unusual case of primary endometrioid type endometrial adenocarcinoma, with metastasis to the colon involving the mucosal surface, mimicking a primary colonic malignancy. To our knowledge, this is the first reported case of endometrial cancer metastasis to the colon in the absence of endometriosis. It demonstrates the importance of using immunohistochemistry to distinguish morphologically similar tumors in a patient who seemingly presents more than one primary malignancy.

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