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CASE REPORT | COLON

Colorectal Signet Ring Cell Carcinoma Presenting as Ulcerating Rectosigmoid Stricture

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ABSTRACT

Colorectal signet ring cell carcinoma is a rare type of colon cancer. Early diagnosis remains challenging because of nonspecific colonoscopy findings, such as diffuse circumferential thickening, stricture, and ulcerations, and the potential absence of typical pathological features in the initial biopsy sample. In this article, we report a 41-year-old man with ulcerating rectosigmoid stricture in the rectosigmoid colon with inconclusive histology. Subsequently, the patient developed small bowel obstruction and was diagnosed with stage 4 colorectal signet ring cell carcinoma with peritoneal carcinomatosis.

KEYWORDS: colorectal signet ring cell carcinoma; ulcerating rectosigmoid stricture; peritoneal carcinomatosis

INTRODUCTION

Signet ring cell carcinoma constitutes 1% of all colorectal cancers, and early diagnosis is challenging due to nonspecific colonoscopy findings or superficial ulcerations. We present a case of colorectal signet ring cell carcinoma in a patient who presented with ulcerating rectosigmoid stricture on colonoscopy.

CASE REPORT

A 41-year-old man with no significant medical history was referred to a gastroenterology clinic because of bright red blood per rectum. During colonoscopy, an intrinsic, ulcerating, inflammatory, circumferential, fibrosing stenosis was identified in the rectosigmoid colon, measuring 20 cm in length with an inner diameter of 9 mm (Figure 1). There were no observed inflammatory mucosal changes in other parts of the colon. Biopsies were obtained from the stricture, and the pathology revealed architecturally distorted colonic mucosa with superficial ulceration, granulation tissue, and abundant fibrinopurulent exudate (Figure 2). Rare atypical glands were identified in the inflamed background, staining positive for caudal-type homeobox 2 (CDX-2) immunostain (Figure 3). Although these cells can be reactive in the background of inflammatory change, the possibility of malignancy cannot be entirely excluded. Unfortunately, the patient was lost to follow-up after the colonoscopy, which limited further investigation of this potential malignancy.

The patient was hospitalized 3 months later for abdominal pain and distention. A CT scan showed ascites, dilated small bowel loop, and a markedly enlarged heterogeneous and edematous rectum. An abnormal mass was detected within the posterior pelvis. Retroperitoneal and pelvic lymphadenopathies were also present, along with thickening and nodularity of the peritoneum. A biopsy

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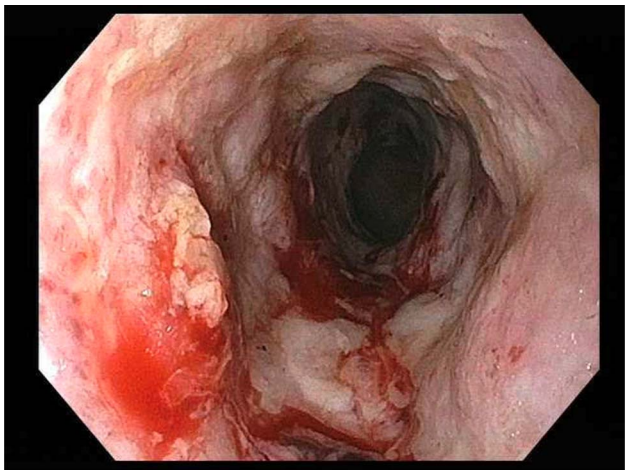

Figure 1. An intrinsic, ulcerating, inflammatory, circumferential, fibrosing friable severe stenosis was found in the rectosigmoid colon, measuring 20 cm (length) and 9 mm (inner diameter).

was obtained from an inguinal lymph node by interventional radiology. Histological examination showed metastatic poorly cohesive signet ring cells (Figure 4). Immunostains revealed that the neoplastic cells were strongly and diffusely positive for CDX2 and cytokeratin 20 while negative for cytokeratin 7, confirming the colorectal origin of the cancer. Immunostains for neuroendocrine markers (synaptophysin and chromogranin) were negative. Consequently, the diagnosis of colorectal signet ring cell carcinoma (SRCC) was established. Additional immunohistochemistry testing for DNA mismatch repair was also performed, which yielded no mismatch repair deficiency within the tumor. After the small bowel obstruction improved with conservative management, the patient was discharged with outpatient oncology follow-up for palliative chemotherapy.

DISCUSSION

SRCC constitutes approximately 1% of all colorectal cancers.[1] This aggressive subtype of adenocarcinoma has a propensity for intramural spread and peritoneal carcinomatosis, compared with conventional colorectal adenocarcinoma.[2] SRCC originates from undifferentiated stem cells of the mucosa lamina propria. The classic pathological finding is that more than 50% of the lesion is composed of mucin-prominent cells. SRCC has a younger onset, higher aggressiveness, and poorer prognosis.[3] The median age at diagnosis for colon and rectal SRCC is 65.2 and 57.8 years, respectively, which is generally younger than for colon and rectal conventional adenocarcinoma (68.7 and 64.4 years, respectively).[1] More than 80% of the patients were diagnosed at an advanced stage (stage III/IV) based on a national cancer database report.[4] An analysis from the Surveillance, Epidemiology, and End Result database indicated the 5-year cause-specific survival was 33.2% and 28.1% for colon and rectum SRCCs, respectively.[5] Notably, early-stage SRCC shared a similar survival rate as conventional adenocarcinoma, emphasizing the importance of early detection of SRCC.[6] Unlike conventional adenocarcinoma, SRCC displays a low frequency of mutations in adenomatous polyposis coli, Kirsten rat sarcoma, and phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha signaling pathways, but a high incidence of BRAF and high degree of microsatellite instability.[3,7]

Diagnostic colonoscopy with biopsy has been the most commonly used initial diagnostic approach for detection of SRCC. However, diagnosis remains challenging because of several reasons. First, colonoscopy findings could be nonspecific, such as thick bowel wall with fibrosis, diffuse circumferential thickening, or stricture. Superficial ulceration can sometimes be found, as in this case, and is often confused with inflammatory bowel disease.[8] Second, typical pathological features may not be present on the initial biopsy sample. A few cases have reported that initial biopsies on SRCC yielded inflammatory changes similar to our case, which showed granulation tissue and abundant fibrinopurulent exudate.[9–11] This could further lower the sensitivity of a diagnostic colonoscopy with biopsy. In a single-centered case series of SRCC in China, 25% lesions were misdiagnosed as inflammatory changes and 31% of the cases had false-negative results based on endoscopic biopsy.[12] Immunohistochemical testing could potentially help increase the diagnostic yield and in the early identification of cancer cells. SRCC is known to exhibit positivity for estrogen receptors, CDX2, mucin2, Her Par 1, and mucin 5AC. Her Par 1 is more commonly of gastric origin while SATB homeobox 2 and CDX2 are more suggestive of colorectal origin.[13,14] However, the specificity of these markers remains low.

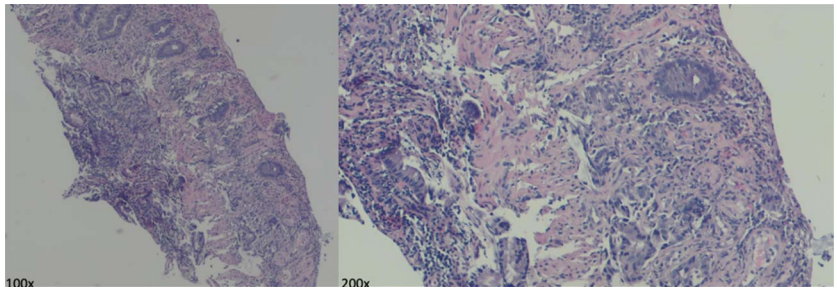

Figure 2. Hematoxylin and eosin stain showed architecturally distorted colonic mucosa with superficial ulceration, granulation tissue, and abundant fibrinopurulent exudate (100× and 200× magnification).

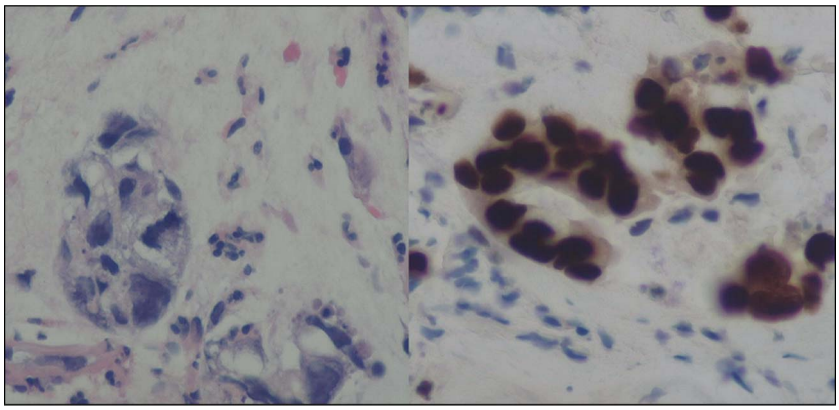

Figure 3. Rare atypical glands were identified in the inflamed background, staining positive for CDX-2 immunostain (400× magnification).

Owing to its low incidence rate, there was no large randomized controlled trial designed for the treatment strategy of colorectal SRCC. Treatment generally follows the conventional adenocarcinoma approach, including surgical treatment and systemic chemotherapy. Perioperative radiotherapy was shown to improve survival outcome in patients with stage III rectal SRCC.[15] Adjuvant chemotherapy showed comparable benefits between SRCC and conventional adenocarcinoma.[6]

In our case, the patient presented with ulcerating rectosigmoid stricture on colonoscopy. The biopsy showed CDX2-positive atypical cells within granulation tissue with fibrinopurulent exudate. This was very likely a false-negative result given the patient's later presentation of metastatic disease. Our case highlights the importance of close follow-up for abnormal diffuse strictures and ulcerations in the colorectal area. These lesions may require rebiopsy, coscreening with abdominal imaging, or exploratory laparotomy to further characterize pathology. More immunohistochemical investigation and studies are needed to accurately diagnose colorectal SRCC.

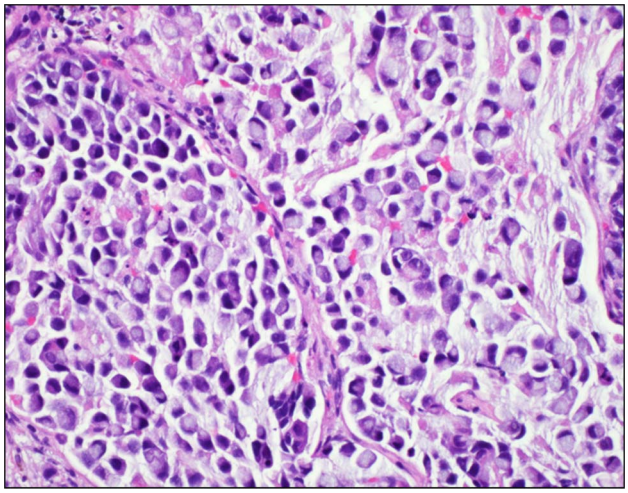

Figure 4. Histological examination of a biopsied inguinal lymph node. Hematoxylin and eosin stain showed metastatic poorly cohesive signet ring cells (200× magnification).

DISCLOSURES

Author contributions: B. Chen, B. Liu, Z. Yuan, and K. Sun wrote the article. B. Chen, B. Liu, and B. Zheng reviewed the literature and revised the article for intellectual content. A. Shapsis, H. Chung, C. Cordeiro, and C. Virmani participated in clinical assessment and treatment. K. Sun and Z. Yuan evaluated the biopsies. All authors approved the article. B. Chen is the article guarantor.

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