

Metastatic Gastric Signet Ring Cell Carcinoma Mimicking Crohn's Disease

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ABSTRACT

Signet-ring cell carcinoma (SRCC) is an adenocarcinoma characterized by mucin-producing cells and most commonly arises in the stomach. Colonic SRCC can share features of colitis, including long segments of concentric bowel wall thickening and ulcerated mucosa with regions of sparing. We describe a rare case of metastatic gastric SRCC mimicking Crohn's disease. Our patient underwent 2 colonoscopies, and biopsies revealed chronic active inflammation with no evidence of malignancy. The diagnosis of SRCC was only made after colectomy was performed for recurrent bowel obstruction.

INTRODUCTION

Signet-ring cell carcinoma (SRCC) is an aggressive adenocarcinoma primarily characterized by mucin-producing cells. It most commonly arises in the stomach, but has also been reported in the colon, breast, prostate, and rectum.¹⁻³ Endoscopy reveals rigid and thickened gastric folds, termed *linitis plastica* (from the Greek term for "linen cloth"), which are characteristic of SRCC.⁴ Histologically, SRCC appears as signet-ring cells enclosing cytoplasmic mucin with peripherally displaced nuclei.⁵ Common metastatic sites are liver, lung, bone, and lymphatics; colonic metastasis is rare.⁶ In part due to the challenges involved in making the diagnosis and the low index of suspicion among clinicians, this disease can be confused with inflammatory bowel disease (IBD), resulting in delayed diagnosis.

CASE REPORT

A previously healthy 40-year-old Puerto-Rican man presented to another facility with 3 months of gradual onset of diffuse, cramping abdominal pain with nausea, loose brown stool, and a 9-kg unintentional weight loss. He denied anorexia, recent travel, new foods, or sick contacts. He had no prior surgeries, took no medications, and had no family history of gastrointestinal (GI) disease. His abdomen was soft, distended, and diffusely tender without peritonitis. Computed tomography (CT) revealed marked wall thickening of the transverse and proximal descending colon with ascending colonic dilation. Colonoscopy showed mucosal edema and inflammation with luminal stenosis 30 cm from the anal verge and extending to the distal transverse colon, which was traversed. Biopsies showed mild acute and chronic inflammation without evidence of malignancy or dysplasia. The patient was treated for suspected infectious colitis with ciprofloxacin and metronidazole; after mild improvement in symptoms, he was discharged.

One month later, he represented with continued symptoms. Work-up was notable for negative infectious stool studies and celiac panel, normal erythrocyte sedimentation rate, and magnetic resonance enterography (MRE)

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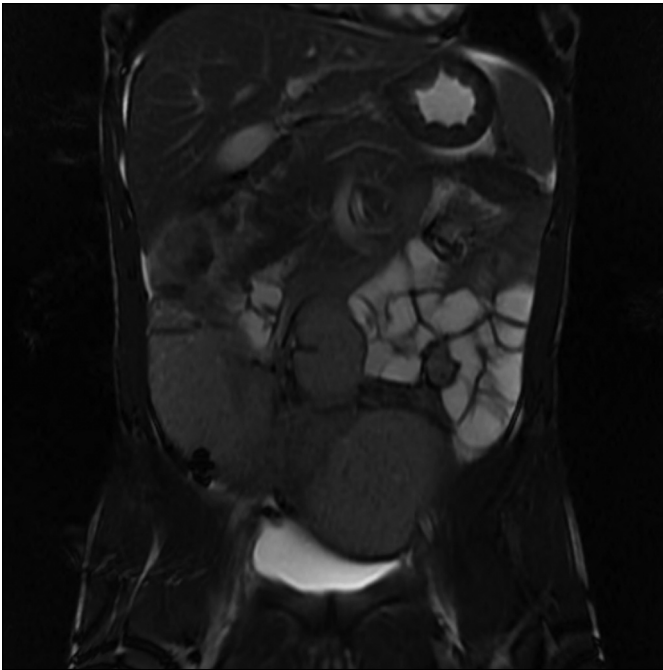


Figure 1. Magnetic resonance enterography demonstrating thickened transverse colon and proximal dilation of the right colon.

that demonstrated right colon dilation and transverse colon thickening with adjacent fat stranding. The patient initially improved with bowel rest, prednisone 60 mg daily by mouth, and mesalamine 800 mg 3 times daily by mouth for presumed IBD, but he reported intermittent symptoms at 1-month follow-up. Repeat CT scan showed severe transverse colitis with a dilated proximal colon, and he was started on infliximab with concern for refractory IBD. He was readmitted with pain and nausea 1 month later. Follow-up imaging was unchanged. Repeat colonoscopy showed segmental colitis with a stricture at the transverse colon, pseudopolyps, and a few small aphthous ulcers in the terminal ileum, concerning for Crohn's disease. Biopsies from the representative areas showed mild acute and chronic colonic and ileal inflammation without

granulomas, dysplasia, or malignancy, which was consistent with IBD. The patient was reluctant to restart anti-tissue necrosis factor and was discharged on azathioprine 100 mg daily by mouth in addition to prednisone and mesalamine.

The patient presented to our institution 1 month later with obstructive symptoms that did not improve with bowel rest and high-dose intravenous steroids. C-reactive protein was elevated at 32.7, and repeat MRE showed a thickened transverse colon without previously noted mesenteric stranding (Figure 1). The patient underwent a total colectomy with ileorectal anastomosis. The resected specimen included 9 cm of terminal ileum and 53 cm of colon. An area of transverse colon contained ulcerated mucosa with granulation tissue and wall thickening to 1 cm. Transmural invasion by a poorly differentiated carcinoma with signet-ring cell features was seen involving the hepatic flexure, transverse, and proximal descending colon. Angiolymphatic involvement was found in 1 of 9 lymph nodes. Immunohistochemical staining was positive for CK7 with CDX2 nuclear immunoreactivity and negative for CK20, TTF-1, and LCA staining, which suggested metastasis from the upper GI tract (Figure 2). The resected ileum was normal. Upper endoscopy revealed diffusely thickened gastric folds resembling poorly differentiated invasive SRCC, which were negative for *Helicobacter pylori* (Figure 3). The immunohistochemical profile was most suggestive of upper GI tract primary with distal metastasis. The postoperative course was complicated by anastomotic leak with abscess, which required exploratory laparotomy, anastomotic resection, and end ileostomy. The patient died with hospice services.

DISCUSSION

SRCC is a rare entity representing less than 14% of gastric cancers treated with gastrectomy and 1% of colon cancers treated with colectomy.^{7,8} Primary SRCC presents at younger ages than non-signet-ring cell cancer, often late in the disease course, and portends poor prognosis.⁹ Diffuse-type gastric cancers including SRCC are thought to involve the loss of cell cohesion, allowing malignant cells to infiltrate the visceral

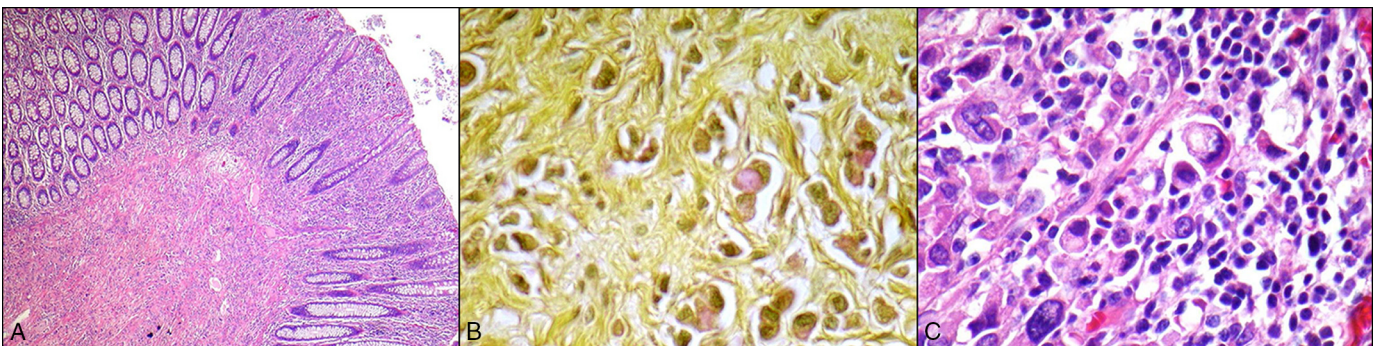


Figure 2. (A) Poorly differentiated carcinoma with signet-ring cell features involving the colonic wall, serosal surface, and subserosal adipose tissue, with no evidence of in situ carcinoma. (B) Mucicarmine immunohistochemical stain highlighting infiltrating tumor cells in the colon. (C) Periodic acid-Schiff stain of antral type gastric mucosa highlighting tumor cells of poorly differentiated adenocarcinoma, signet-ring cell type.

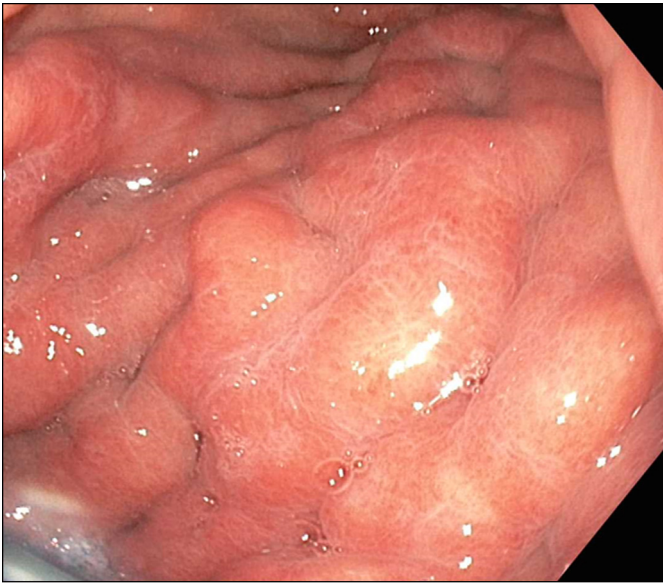


Figure 3. Gastric mucosa with linitus plastica appearance on upper endoscopy.

wall without forming a discrete mass.¹⁰ Primary gastric SRCC with colonic metastasis is thought to spread via the lymphatics or the gastrocolic ligament to the transverse colon.¹¹ Gastric SRCC with colon metastases mimicking Crohn's disease has been described in only one case report. Our case is unique in that the patient had several non-diagnostic studies prior to confirmatory diagnosis.¹²

Colonic SRCC commonly shares features of colitis, including long segments (>5 cm) of concentric bowel wall thickening, ulcerations, and the absence of an obstructing intraluminal mass.¹³ Colonoscopy can resemble IBD with luminal strictures and cobblestoned mucosal ulcerations.¹⁴ Patchy mucosal involvement and submucosal spread can compromise the yield of superficial biopsies, thus contributing to diagnostic delay.¹⁵ In addition, inflammatory ulcers are a shared feature of Crohn's disease and several GI malignancies. Diagnosing SRCC without objective histologic evidence of dysplasia or malignancy is challenging. In this case, ileal ulcers were not confluent with the neoplasm boundaries, suggestive of a secondary process. In retrospect, the CT demonstrated thickened gastric folds initially attributed to under-distension. Exploring this finding earlier may have expedited diagnosis, as SRCC was confirmed after colectomy.

This case provides a rare documentation of metastatic gastric SRCC mimicking Crohn's disease. This case highlights the importance of considering this malignancy on the differential diagnosis for recurrent bowel obstruction and strictures from

presumed IBD that do not respond to conventional treatment. SRCC is a rare malignancy, and this highlights an atypical presentation. Clinicians should maintain a high index of suspicion for malignancy in non-resolving strictures with indeterminate pathology to diagnose often aggressive malignancies as early as possible.

DISCLOSURES

Author contributions: MW Winter, A. Dokmak, and AN Levy wrote and edited the manuscript. Z. Marnoy wrote the manuscript. S. Sinagare wrote and edited the manuscript, and provided the pathology images. AN Levy is the article guarantor.

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