

# Radiographic and endoscopic regression of metastatic gastric cancer to the colon in the setting of 5-aminosalicylic acid use

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**Abstract:** Colonic metastases from gastric cancer are a rare phenomenon and sparsely reported in the literature. We report a case of a 59-year-old woman who presented with vague abdominal symptoms and initial computer tomography (CT) imaging suggestive of a colonic apple-core lesion with serial colonoscopic biopsies diagnostic of metastatic signet ring cell gastric adenocarcinoma. This case is unique given the evolving CT and endoscopic findings that suggested a regression in colonic wall thickening in the setting of 5-aminosalicylic acid (5-ASA) use prior to histologic diagnosis.

**Keywords:** Stomach neoplasms; signet ring cell carcinoma; neoplasm metastasis

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## Introduction

Gastric cancer is the third leading cause of cancer-related death worldwide and presents a major public health issue (1). Signet ring cell gastric cancer comprises around 35–45% of all gastric cancer, and is increasing in incidence (2,3). Advanced stages of this disease may result in multiple organ involvement, though metastasis to the colon is very rare and sparsely reported. We present a case report of metastatic signet ring cell gastric adenocarcinoma to the colon diagnosed by serial colonoscopic biopsies with regressing computer tomography (CT) imaging and endoscopic findings in the setting of 5-aminosalicylic acid (5-ASA) use.

## Case presentation

A 59-year-old Caucasian female presented to the outpatient GI clinic for consultation given recurrent complaints of nausea, vomiting, vague abdominal cramping, loose stools, and subjective fevers lasting up to 5 days at a time over the past 3–4 months. She provided a report from a recent CT abdomen/pelvis with IV/PO contrast suggestive of an apple-core lesion of the ascending colon, with a second area of focal wall thickening involving the hepatic flexure.

She had a past medical history of cholecystectomy, cesarean section, and a previous 7-pack year smoking history. She denied any family history of GI-related cancer or disease. Medications included calcium/vitamin D and multivitamin, and recent additions of omeprazole and ondansetron by her primary care provider. Review of systems were negative for GI bleeding though notable for a 15–20 lbs unintentional weight loss over the past few years. She had never undergone an upper endoscopy and reported a normal colonoscopy 3 years prior.

Colonoscopy was performed and was notable for sigmoid diverticulosis and a severe stenosis 40 cm proximal to the anus that was unable to be traversed with an adult gastroscope or pediatric colonoscope (*Figure 1*). Mucosa at the site appeared thickened and nodular; no ulcerated tissue was seen and mucosal integrity appeared preserved. The area was tattooed and biopsies were taken which revealed mild acute and chronic inflammation without evidence of dysplasia or carcinoma. CT abdomen/pelvis with IV contrast was subsequently performed within the next month and showed diffuse wall thickening and mucosal hyperenhancement involving the ascending, transverse, and descending colon with minimal mesenteric



**Figure 1** First colonoscopy—severe stenosis with nodular and intact thickened mucosa.

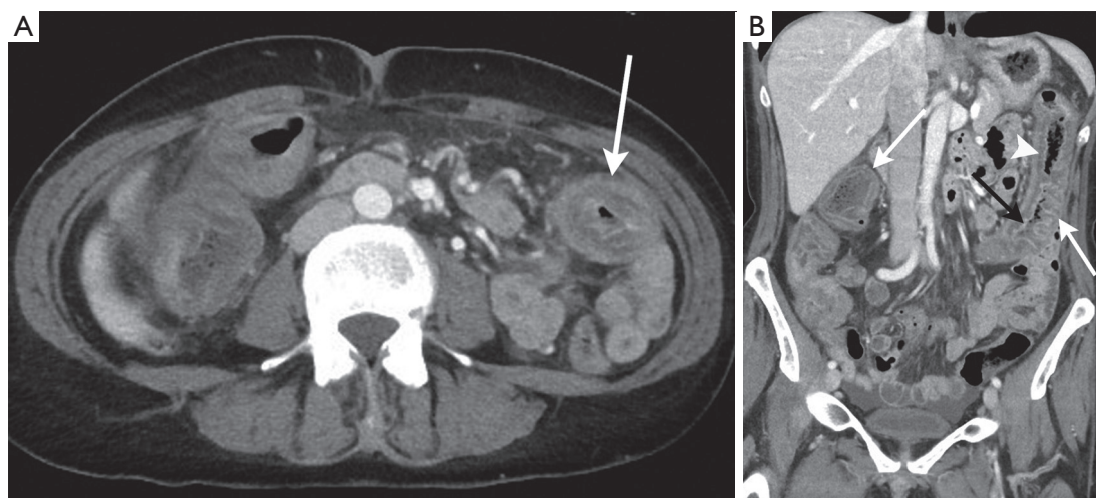
or retroperitoneal lymphadenopathy and patent mesenteric vasculature consistent with colitis, though no apple-core lesion (*Figure 2*). Stool cultures, examination for ova & parasites, clostridium difficile toxin assay, and fecal leukocyte assay were ordered and resulted negative. The clinical decision was made to start her on mesalamine, which she tolerated with mild improvement of symptoms and stabilization of her weight after 2 months. Repeat CT abdomen/pelvis with IV contrast was performed and redemonstrated mucosal thickening involving the ascending colon and transverse colon, though substantially less marked.

Because of continued clinical concern, ambiguity in diagnosis, and persistent dyspepsia, repeat colonoscopy and upper endoscopy was performed which showed benign-appearing intrinsic mild stenoses in the sigmoid, transverse, and ascending colon with normal appearing mucosa (*Figure 3*). Colonoscopy was completed to the terminal ileum. Endoscopic examination of the upper GI tract showed erythematous and cobblestoned appearance in the gastric fundus and body, and normal appearing duodenum and esophagus. Biopsies revealed primary signet ring cell adenocarcinoma of the stomach and metastatic signet ring cell adenocarcinoma of the ascending colon (*Figure 4A,B*). She was seen by Oncology and Surgery and underwent a PET-CT that showed no further metastases. A diagnostic abdominal laparoscopy with peritoneal washings was negative. She was initiated on FOLFOX chemotherapy followed by successful total gastrectomy and right hemicolectomy. The stomach contained signet ring cell carcinoma with full-thickness gastric wall involvement (from mucosa to serosa) and metastatic carcinoma in one gastric

lymph node. The colectomy specimen revealed metastatic signet ring cell carcinoma involving the colon (*Figure 4C,D*), mesentery and mesoappendix. The metastatic carcinoma also involved the full-thickness of colonic wall, and presented in six colonic lymph nodes. She is continuing FOLFOX chemotherapy at the time of this report with most recent CT scan 1 month after surgery showing no evidence of recurrent or metastatic disease.

## Discussion

Colonic metastases are generally a rare occurrence, though post-mortem studies suggest a higher incidence than expected (4). The most common route of metastatic occurrence to the bowel is from peritoneal seeding typical of ovarian carcinoma, though hematogenous dissemination to the colon has also been described in breast carcinoma, lung carcinoma, and melanoma (5-8). Colonic metastases from gastric cancer have been rarely reported (4,9-11). This unusual phenomenon has typically been associated with Lauren's diffuse type histology and linitis plastica with a hematogenous dissemination route of metastasis, though a peritoneal route has also been described (4,11). A retrospective study of intestinal metastasis from gastric adenocarcinoma noted 21 patients with metastasis to the colon, rectum, or appendix. Of these, six cases (29%) showed poorly differentiated adenocarcinoma with signet ring cell features and five (24%) showed signet ring cell gastric adenocarcinoma (4). The majority of these patients (82%) had linitis plastica, which was also found in our case upon surgical removal. Linitis plastica of the stomach can be identified on CT scan by diffuse thickening and a narrowed lumen, though these features were interestingly not observed on serial CT scans in our patient. The majority of the rare cases of colonic metastases from gastric cancer show long circumferential involvement, multiplicity, and an inner layer with distinct enhancement and thickening reminiscent of a "target" pattern (4). Though bowel wall thickening itself is nonspecific and may represent an inflammatory, infectious, or ischemic process, the distinct pattern of inner layer enhancement is peculiar and may represent a hallmark of metastatic signet ring cell adenocarcinoma (4). Interestingly, in our patient CT findings of the colon appeared regressive, with initial findings of an apple-core lesion to later scans demonstrating diminishing degrees of pancolonic wall thickening with mucosal hyperenhancement. This correlated with experience on serial colonoscopy, with the first colonoscopy



**Figure 2** Computer tomography (CT) abdomen/pelvis with IV contrast. Axial (A) and coronal (B) images of the abdomen and pelvis shows a colitis involving the right and left colon (white arrows) with colonic wall thickening, hyperenhancement of the colonic mucosa (black arrow) and edema within the colonic wall (white arrow head).



**Figure 3** Second colonoscopy—mild benign-appearing stenoses with intact mucosa.

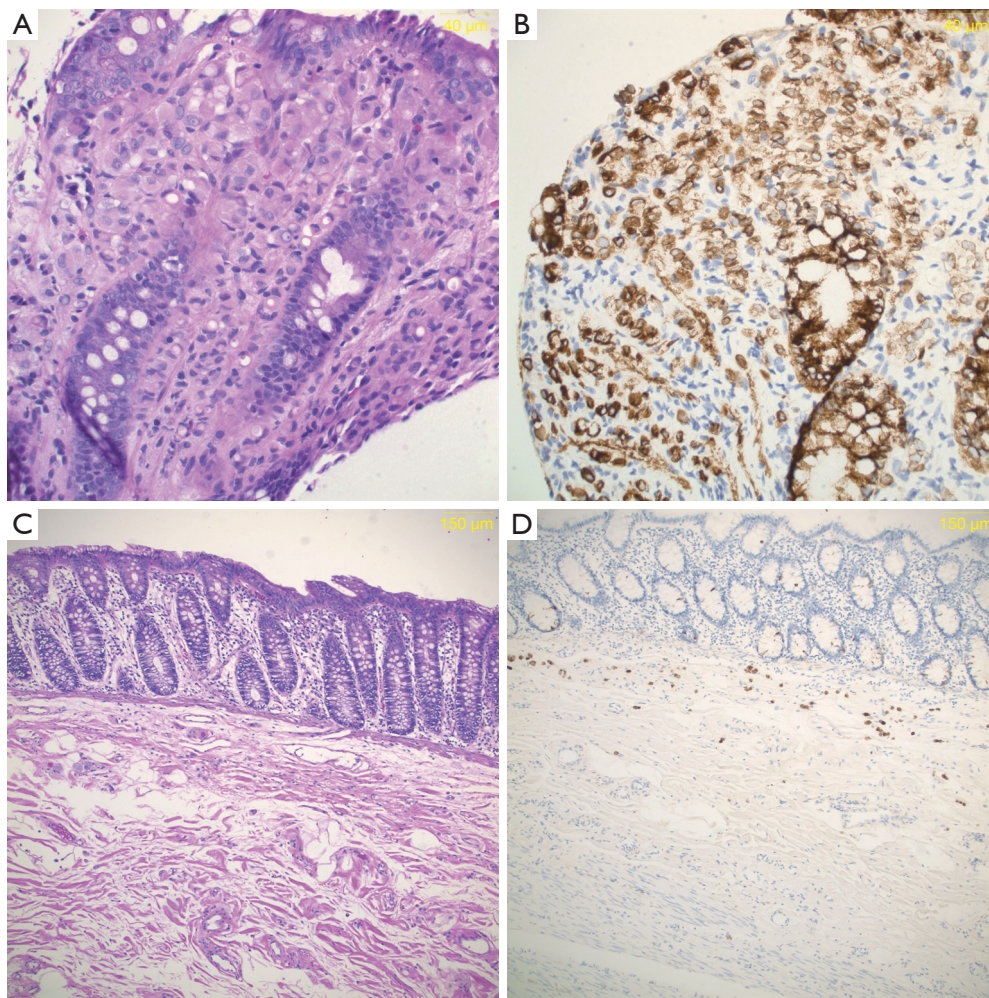
attempt noting a tight nodular non-traversable stricture and the second noting mild benign-appearing stenoses throughout the colon that were easily traversable. This is unusual, as sparse evidence regarding the radiological evolution of colon metastases show progression as would be expected clinically with the evolution of this cancer over time. We hypothesize that this pattern of regression may be due in some degree to waxing and waning edema in the setting of lymphatic involvement, and perhaps also because of mesalamine use, a 5-ASA compound. 5-ASA medications are a common drug class used for maintenance of remission in inflammatory bowel disease (IBD), mainly ulcerative colitis, and epidemiological studies suggest that

long-term consumption decreases the colon cancer risk for these patients (12,13). Furthermore, 5-ASA compounds have been demonstrated to have pro-apoptotic and anti-proliferative effects on several cancer-derived cell lines through a multitude of mechanisms including EGFR activation, COX-2 expression, and inhibition of Wnt/ $\beta$ -catenin pathway (14-18). Though no studies in the literature exist on the impact of 5-ASA compounds on gastric adenocarcinoma cell lines, it may be possible that similar anti-tumor and anti-inflammatory effects played a role in the evolution of findings in our patient.

Our case also illustrates the difficulty in colonoscopic mucosal biopsies in relaying a positive result as metastatic carcinoma is often deep in the wall, leading to a false negative result in up to 54% of cases (4). Even with a deeper tunneled biopsy specimen, the scarcity and deceptively bland morphology of tumor cells may hinder detection (4). The colectomy specimen in our case revealed very limited mucosal involvement, with carcinoma cells predominantly present in submucosa and deeper portion of the colonic wall, consistent with the metastatic/implantation nature of the disease (*Figure 4C,D*). As our case demonstrated, the clinician should be hyper-vigilant in pursuing a diagnosis and consider repeat endoscopic evaluation as a case evolves.

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**Figure 4** Colonic histopathology. (A) Colonic biopsy (H&E stain). Signet ring cell carcinoma invades the superficial portion of the lamina propria of colonic mucosa, which makes endoscopic biopsy diagnosis possible; (B) colonic biopsy (immunohistochemical stain for pancytokeratin). Immunohistochemical stain for pancytokeratin highlights the normal colonic crypts as well as individual infiltrative signet ring cell carcinoma cells in the lamina propria; (C) colectomy specimen (H&E stain). The colonic architecture is preserved, with very inconspicuous signet ring cell carcinoma cells in the superficial submucosa; (D) colectomy specimen (immunohistochemical stain for cytokeratin 7). Immunohistochemical stain for cytokeratin 7 highlights individual infiltrative signet ring cell carcinoma cells in the submucosa.

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### Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

*Informed Consent:* Written informed consent was obtained from the patient for publication of this manuscript and any accompanying images.

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