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Rare Presentation of Gastroesophageal Carcinoma with Rectal Metastasis: A Case Report

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Data Collection B
Statistical Analysis C
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Manuscript Preparation E
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Patient: Female, 60
Final Diagnosis: Gastroesophageal carcinoma with rectal metastasis
Symptoms: Bloating • constipation • weight loss
Medication: —
Clinical Procedure: Endoscopy • flexible sigmoidoscopy • lower endoscopic ultrasound
Specialty: Gastroenterology and Hepatology

Objective: Unusual clinical course

Background: Gastroesophageal cancers, previously considered rare, are rapidly increasing worldwide. We present here a unique case of gastroesophageal carcinoma with metastasis to the rectum.

Case Report: A 60-year-old female patient presented with constipation, bloating, and weight loss of 4-month duration. She had undergone sleeve gastrectomy 6 years before. Endoscopies performed revealed a friable-looking mucosa in the lower esophagus and a polypoid rectal mass. Histopathological examination from both the esophageal and rectal lesions revealed poorly differentiated adenocarcinoma cells. Immunohistochemistry stain from both specimens was positive for CK7 supporting the gastric site primary with metastasis to the rectum. Further evaluation also revealed metastasis to bone and malignant pleural effusion. Chemotherapy with palliative intent was initiated.

Conclusions: Colorectal metastasis is commonly seen from cancers of the breast, stomach, melanoma, kidney, prostate, and ovaries. However, colorectal metastasis from gastroesophageal cancer has never been reported in the medical literature. Diagnosis relies on histopathologic examination and immunohistochemical staining of the tumor. Treatment depends on the tumor stage. Tumors with widespread metastatic disease are candidates for palliative chemotherapy.

MeSH Keywords: Colorectal Neoplasms • Esophagogastric Junction • Neoplasm Metastasis

Full-text PDF: http://www.amjcaserep.com/abstract/index/idArt/898534

Background

Gastroesophageal junction cancer has been classified by some researchers under as both gastric and esophageal carcinomas. However, gastroesophageal carcinoma is different from gastric and esophageal cancers [1]. Incidence of gastroesophageal carcinomas in the United States is increasing more rapidly than any other malignancy [2]. Colorectal metastasis from gastroesophageal cancer has never been reported. We report a case of rectal metastasis from gastroesophageal junction adenocarcinoma confirmed histologically in a 60-year-old woman presenting with constipation.

Case Report

A 60-year-old female patient presented to our hospital with complaints of worsening constipation, abdominal bloating, and about 20-pound-weight loss of 4-month duration. She denied dysphagia, abdominal pain, nausea, vomiting, heartburn, hematemesis, or melena. She did not have any significant medical problems in the past. She had undergone bariatric surgery (sleeve gastrectomy) 6 years ago in the Dominican Republic; the endoscopy findings prior to the surgery are not known. She had also undergone cesarean section and tubal ligation 17 years ago. Her grandmother had uterine cancer. She denied tobacco, alcohol, or illicit drug use. On examination, the blood pressure was 120/70 mm Hg, the pulse was 96 beats per minute, the temperature 37.1°C, and the respiratory rate 14 breaths per minute. There was dullness on percussion posteriorly at the right lung base with absent breath sounds on auscultation of the same area. The other results of the general and systemic examination were unremarkable.

The serum level of alkaline phosphatase was elevated to 226 U per liter (normal reference range, 43–160), and the serum albumin was 2.8 gm per deciliter (normal reference range, 3.2–4.6). Her carcinoembryonic antigen level (CEA) was 68.4 ng/ml (normal reference range <5 ng/ml). The rest of the liver function test results were normal, as were the complete blood count, levels of electrolytes, glucose, calcium, and results of renal function tests and coagulation panel. X-ray chest revealed bilateral patchy opacities with right-sided pleural effusion.

Upper gastrointestinal endoscopy was performed, which showed a single diverticulum in the distal esophagus, abnormal-looking friable and granular mucosa at the lower esophageal end, and evidence of prior sleeve gastrectomy (Figure 1). Histopathological examination of the lower esophageal abnormal-looking mucosa and proximal gastric mucosal biopsies showed foci of atypical cell infiltrate in the lamina propria (Figure 2). Flexible sigmoidoscopy revealed a polypoid rectal mass (Figure 3). Lower endoscopic ultrasound confirmed

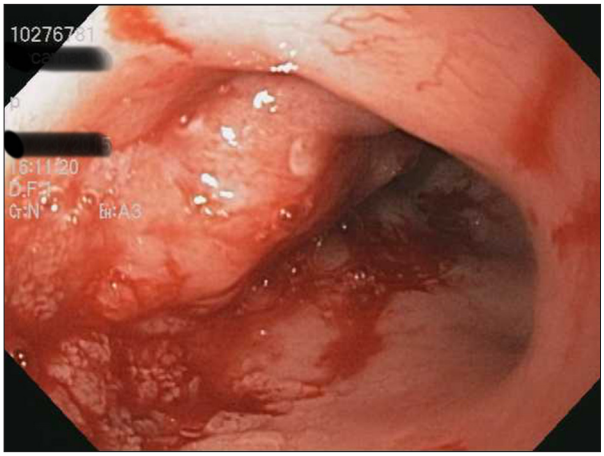

Figure 1. Friable mass at the lower end of esophagus as seen on esophagogastroduodenoscopy.

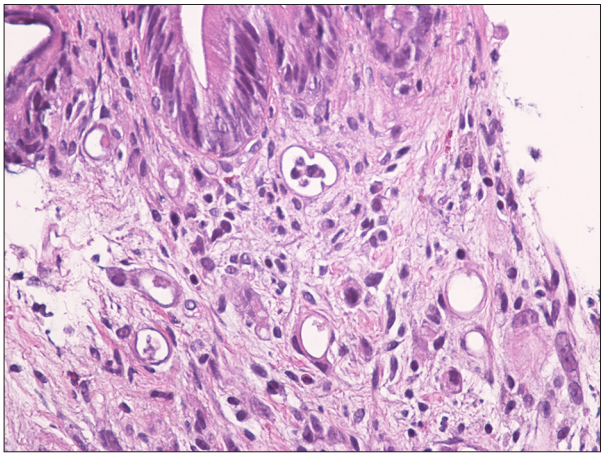

Figure 2. Gastric mucosa. The lamina propria contains individual infiltrating, discohesive signet ring cells of diffuse-type adenocarcinoma (hematoxylin and eosin ×200).

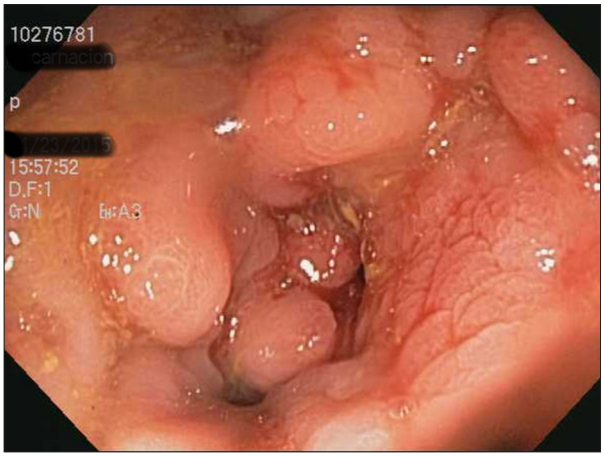

Figure 3. Rectal mass as seen on colonoscopy.

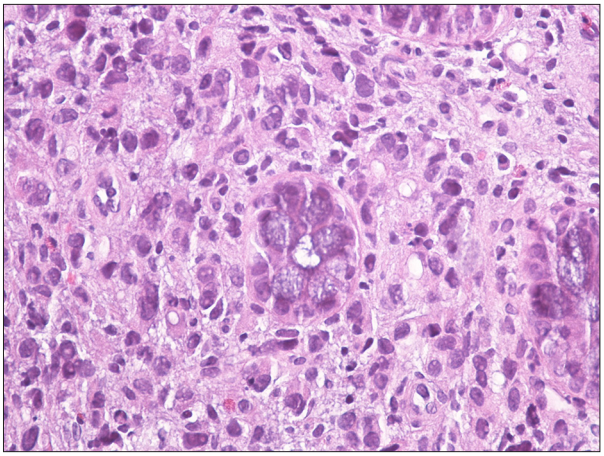

Figure 4. Rectal mass showing individual infiltrating and discohesive cells, consistent with signet ring cell adenocarcinoma. The cytomorphological features and immunoprofile (CK 7+) supports a gastric primary site (hematoxylin and eosin ×200).

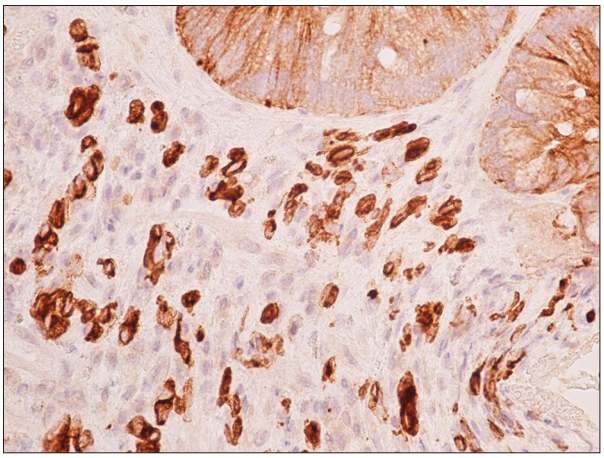

Figure 5. Gastric mucosa with signet ring cell adenocarcinoma. The neoplastic infiltrating cells show strong immunoreactivity with cytokeratin 7 (×400).

the rectal mass and showed diffuse circumferential rectal wall thickening without perirectal lymph node involvement. Histopathological examination of rectal mass biopsy specimen showed poorly differentiated invasive signet ring cell adenocarcinoma (Figure 4). On Immunohistochemistry (IHC) stain, the gastroesophageal tumor cells were positive for AE1/AE3, CK7, and CDX2, and focally positive for CK20 antibodies, consistent with poorly differentiated adenocarcinoma (Figure 5). IHC staining on the rectal mass biopsy specimen demonstrated positive staining for CK7, CK20, CDX2, and CEA, and was negative for LCA antibodies (Figure 6). Cancer cells at the 2 sites (lower esophagus and rectum) were identical on cytomorphologic and immunohistologic examinations (CK7 immunoreactivity), confirming gastroesophageal carcinoma as the primary site with metastatic involvement of rectum.

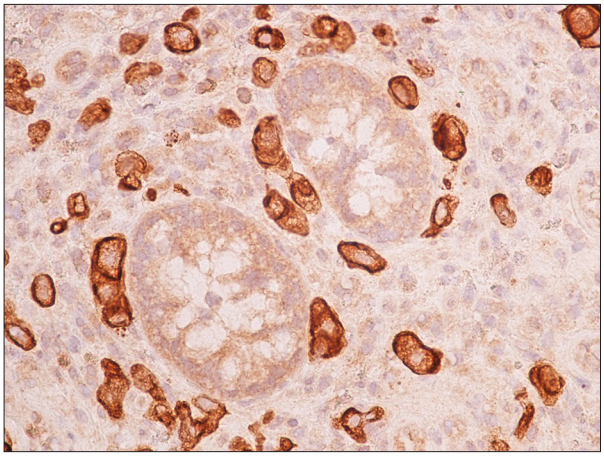

Figure 6. Rectal mass. Immunohistochemical stain cytokeratin 7 demonstrates strong positivity in the infiltrating signet ring cells (×400).

Metastatic work-up with head, chest, and abdomino-pelvic CT scan showed multifocal osteoblastic lesions of the left frontal bone and skull base, 2 pulmonary nodules, and numerous osteoblastic lesions in the thoracic spine. Bilateral malignant pleural effusion as confirmed by pleural fluid examination was also found.

The patient was treated with Docetaxel, Cisplatin, and 5-Fluorouracil with Leucovorin for 10 cycles over a period of 8 months, during which she had improvement in her appetite and overall well-being. Her CEA levels diminished to 10.6 ng/ml. Twelve months after her diagnosis of metastatic gastroesophageal cancer, she was admitted with complicated parapneumonic pleural effusion and developed acute respiratory failure. She declined endotracheal intubation and resuscitation and died due to complicated parapneumonic effusion, sepsis, and respiratory failure.

Discussion

In the last 3 decades, the incidence and prevalence of gastroesophageal junction carcinomas has dramatically increased in Western countries, while it is decreasing in Eastern countries [1,3]. In the United States, the incidence of gastroesophageal junction cancer was 1.22 per 100 000 population in 1973–1978 and it increased to 1.94 in 2003–2008 [4]. The incidence of gastroesophageal junction carcinomas is about 4.7 times higher in men as compared to women. Among men, white men have a 1.88 times higher risk than black men.

Risk factors for gastroesophageal junction cancers include smoking, obesity, and gastroesophageal reflux disease (GERD). Our patient was obese and had undergone sleeve gastrectomy, which may increase GERD [5]. On the other hand, a decline in

obesity-related cancers has been seen after bariatric surgery. A meta-analysis by Yang et al. in 2011 showed decreased incidence of obesity-related cancers in patients who have undergone bariatric surgery. However, effects of bariatric surgery on gastric, esophageal, or gastroesophageal cancers were not reviewed in this meta-analysis [6]. Infection with *Helicobacter pylori* and high dietary fiber intake has been found to be protective and linked to lower disease risk.

Early-stage gastroesophageal cancers are usually asymptomatic. Symptoms of advanced gastroesophageal junction result from a mass causing difficult transit of the food bolus. Dysphagia is a common symptom. Weight loss, which was one of the presenting complaints in our patient, is mostly due to interference with dietary habits. However, in advanced cancers, weight loss is the result of toxicity from the tumor.

In 1996, Siewert et al. classified adenocarcinoma of the gastroesophageal junction based upon anatomic topography [7]. Recently, all the tumors that arise within 5 cm proximal and distal to the anatomic cardia are considered as adenocarcinoma of the gastroesophageal junction, and it has now been sub-divided into: a) Type I, which arise from an area of intestinal metaplasia in the distal esophagus and invade the gastroesophageal junction from above; b) Type II, which arise from the gastric cardiac epithelium or metaplastic junctional epithelium; and c) Type III, which are cancers that originate from the subcardial region and invade the gastroesophageal junction from below [1]. Type I tumors are less frequent in Eastern countries than in Western countries. The difference may be due to lower prevalence of obese patients with GERD in Eastern countries compared to Western countries [3].

Surgery is the mainstay of treatment in patients who have no evidence of distant metastasis and are fit for surgery. Extended transthoracic surgery is recommended only for type I tumors. A transhiatal extended gastrectomy is the preferred approach for type II and type III tumors [3]. Perioperative chemotherapy contributes to survival when combined with a limited nodal dissection [8]. A Germany study showed that patients who received preoperative chemoradiation had a higher 3-year survival rate compared to those who received preoperative chemotherapy alone, although the difference did not reach statistical significance [9]. Prognosis is better when perioperative chemoradiation is combined with limited nodal dissection; however, when combined with extensive nodal dissection, the prognosis remains unknown. Patients who have advanced disease with systemic metastases are recommended to receive systemic chemotherapy, which is usually a combination of Fluorouracil and Cisplatin. If the gastroesophageal tumors are HER-2 positive, Fluoropyrimidine, Cisplatin, and Trastuzumab could be a standard chemotherapy.

Gastric tumors have been divided into intestinal and diffuse types according to Lauren classification. The intestinal type exhibit cell adhesion and form glands, are associated with intestinal metaplasia, and are known to cause lymphatic and vascular invasion. The diffuse type lacks adhesion, forms signet ring cells, and are associated with peritoneal metastasis [10]. Our patient did have signet cell formation in the histopathology, but CT abdomen failed to reveal any peritoneal metastasis. In general, there are 5 main routes of metastasis of esophageal and gastric cancer: 1) direct invasion 2) lymphatic spread 3) hematogenous 4) transperitoneal, and 5) intraluminal implantation [11]. Gastroesophageal junction cancers usually cause liver and peritoneal metastases. Colorectal metastasis from any cancer is very uncommon. Colorectal metastasis is usually from cancers of the breast, stomach, skin (melanomas), kidney, prostate, or ovaries [12]. There have been case reports of gastric or gastric stump carcinoma metastasizing to the colon and presenting as solitary or multiple colonic polyps [12–14]. However, there have been no reported cases of gastroesophageal junction tumors metastasizing to the rectum. The most plausible explanation for the spread of gastroesophageal cancer to the rectum is lymphatic spread, as has been proposed widely in cases of Krukenberg tumor [15], and integrins expressed on exosomes of tumor cells contribute to organ-specific metastasis [16].

We presented a rare case of gastroesophageal junction cancer with metastasis to the rectum. When multiple lesions are found in a patient, it is of prime importance to identify the primary lesion and differentiate the synchronous lesions from metastatic lesions to define the further treatment plan. Interestingly, tumor marker CEA, well known to be associated with colorectal cancers, can also be elevated in other malignancies [17,18] and hence cannot differentiate between these entities. A study by Terada on cytokeratin profile based on immunohistochemical stain has demonstrated that gastric signet cell carcinoma is more likely to express CK7 and not CK20, whereas colon signet cell carcinoma express CK20 more often than CK7 [19]. In our case, tumor cells at the gastroesophageal junction and rectum had positivity for CK7, supporting the primary gastric site.

Conclusions

Our case is the first report of adenocarcinoma of the gastroesophageal junction with metastasis to the rectum. This case illustrates an unusual site of metastasis of a gastroesophageal cancer and heightens our awareness in suspecting an unusual primary site if such rectal lesions are found. It is of utmost importance to identify the primary tumor sites because management depends on knowing the primary site. Briefly, rectal cancers at early-stage can be treated with surgical excision alone,

whereas at the advanced stage they need neoadjuvant chemotherapy followed by adjuvant chemoradiation. On the other hand, treatment of early locoregional gastroesophageal cancer involves neoadjuvant chemoradiation and surgical excision. More advanced disease is treated with chemotherapy alone.

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Conflict of interest

The authors have no conflicts of interest to disclose.