

Gastric-type extremely well-differentiated adenocarcinoma arising in the blind pouch of a bypassed stomach, presenting as colonic pseudo-obstruction

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Abstract

Gastric carcinoma after gastric bypass is rare. Extremely well-differentiated adenocarcinoma (EWDA) of the stomach is a rare variant that has been mostly reported in Japan. We present a case of a 68-year-old man with EWDA arising in the bypassed stomach that presented as a colonic pseudo-obstruction (CPO). Several imaging, endoscopic and pathologic studies performed in the course of 2 months were non-diagnostic. An iatrogenic duodenal perforation during a diagnostic procedure led to an emergent exploratory laparotomy in which the dilated colonic segment was resected. Pathologic examination showed metastatic EWDA in the colonic wall. Post-operative complications led to the patient's demise. At autopsy the primary tumor was identified in the blind pouch of the bypassed stomach. A literature review on gastric EWDA and carcinomas arising in bypassed stomachs is discussed. EWDA of the stomach is rare, difficult to diagnose, and shows an aggressive clinical course discordant with its near-benign histology. Gastric cancer arising in a bypassed stomach is uncommon; when it occurs it is usually diagnosed at advanced stage. Surveillance of the blind pouch is not currently recommended. Malignant infiltration of the colonic wall should be included in the differential diagnosis of CPO of unclear etiology.

Keywords Stomach neoplasms, extremely well-differentiated adenocarcinoma, minimal deviation adenocarcinoma, gastric bypass, colonic pseudo-obstruction

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Introduction

Gastric carcinoma in the bypassed gastric remnant is rare [1-5]. Extremely well-differentiated adenocarcinoma (EWDA) of the stomach is a rare tumor variant mostly reported in Japan [6,7]. We report a unique case of gastric type EWDA arising in the gastric remnant 7 years after Roux-en-Y gastric bypass (RYGB) surgery, presenting as colonic pseudo-obstruction (CPO).

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Conflict of Interest: None

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Case report

A 68-year-old male consulted for generalized abdominal pain and constipation. Past medical history included a RYGB for morbid obesity 7 years before presentation, and ischemic heart disease. Conservative therapy did not alleviate his symptoms. Computed tomography (CT) scan showed marked ascending colon dilatation (Fig. 1A) without an identifiable lesion indicative of CPO. The differential diagnosis for CPO included functional causes such as cardiac disease, metabolic or electrolyte imbalances, renal insufficiency, medications, and anatomic causes like inflammatory processes and malignancy. Over the course of 2 months several diagnostic procedures were done. Three colonoscopies with multiple biopsies of the right colon showed submucosal mucin extravasation without mucosal abnormalities. On workup for elevated liver enzymes, a magnetic resonance cholangiopancreatography demonstrated intrahepatic biliary dilation with a dilated common hepatic duct and could not rule out a lesion in the bile duct as the cause. A laparoscopically assisted endoscopic ultrasound (EUS) through the remnant stomach showed dilated intrahepatic ducts; a fine needle aspiration of the liver,

performed to assess for a possible hilar lesion observed during the EUS, did not show abnormalities. Endoscopic retrograde cholangiopancreatography (ERCP) was unsuccessful due to distorted anatomy. After the ERCP attempt the patient developed shock and was found to have a perforation of the duodenum during emergent exploratory laparotomy. The perforation was closed and the dilated right colon excised. Shortly thereafter, additional procedures were necessary for intestinal infarction secondary to the perforation induced shock, emergent surgery, and poor cardiac function. He continued deteriorating, opted for comfort measures only and expired a week later. Pathologic examination of the colon showed prominent segmental dilatation but no discrete lesions (Fig. 1B). Microscopically pyloric-type glands with minimal cytologic atypia were present in the muscularis propria and subserosa (Fig. 1C). The tumor did not elicit a desmoplastic response. Architecturally, the tumor glands were well formed with no or minimal branching; the longest axis of the glands always followed the orientation of the collagen they were invading (Fig. 1D). The mucosa was free of tumor. By immunohistochemistry the tumor was positive for cytokeratin (CK) 7, SMAD4, S100P and negative for CK20 and CDX2, consistent with foregut origin. Ki-67 proliferative activity was 25%. At autopsy the primary tumor was located in the antrum of the RYGB, where it caused diffuse thickening of the wall (Fig. 2).

Discussion

After its inception in 1967, the frequency of GB to treat morbid obesity has increased dramatically, with 340,768 operations worldwide in 2011 [8]. The laparoscopic approach has further fostered this trend. Including the current case, only 9 cases of gastric cancer in bypassed stomachs have been reported [1-5]. The cases included 5 females and 4 males; average age at diagnosis was 52 (range 38-71) years; and the interval between GB and diagnosis of cancer ranged from 1 to 22 years. The case diagnosed within 1 year had documented gastric dysplasia prior to RYGB [3]. The most common presenting symptoms were abdominal pain and fullness. Most cases were diagnosed at advanced stage. EWDA, also known as minimal deviation adenocarcinoma, is a rare and under-recognized variant of gastric carcinoma that histologically resembles benign mucosa. When invasive, the tumor elicits minimal or no stromal desmoplasia [6,7]. Common histopathologic classifications of gastric cancer like Laurén and World Health Organization use architecture, differentiation, pattern of invasion and immunophenotype to separate cancers into prognostically significant subgroups. These classifications do not mention this histologic variant. Using the diagnostic criteria of these classifications would fail to recognize that despite its near-benign histology, EWDA pursues an aggressive clinical course and is almost never diagnosed on conventional biopsies; in most cases the malignant nature of this tumor is established after invasion or metastases have occurred [6,7]. Morphologically, this case consisted of pyloric-like glands positive for CK7, S100P,

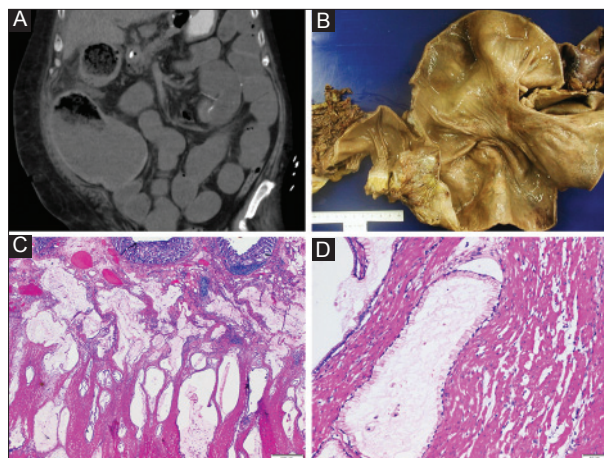


Figure 1 (A) Abdominal computed tomography-scan: the image shows massive dilatation of the ascending colon. (B) Resected ascending colon: The specimen did not show any gross lesions. Colonic wall (hematoxylin & eosin (H&E), 2.5X magnification): the image shows massive infiltration of the muscularis propria and submucosa by dilated glands lacking architectural complexity. The mucosa is free of tumor. (D) Extremely well-differentiated adenocarcinoma (H&E, 40X): the image shows the muscularis propria infiltrated by a simple tubular gland with non-stratified mucinous columnar epithelium with retained nuclear polarity and without cytologic atypia. The tumor does not elicit a desmoplastic or inflammatory response

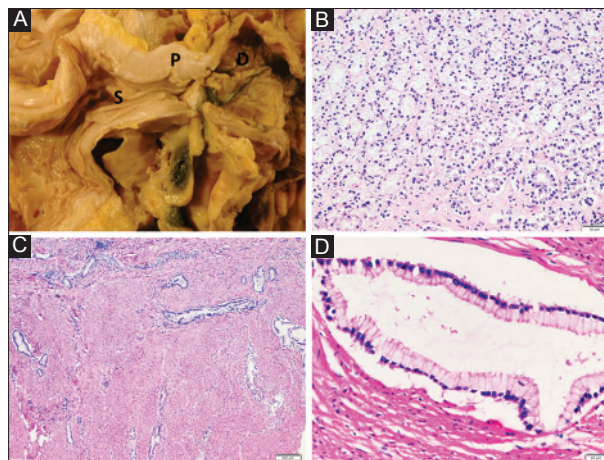


Figure 2 Stomach, autopsy specimen. (A) Bypassed stomach. The image shows a markedly thickened gastric wall at the pylorus. (B) Pyloric mucosa (hematoxylin & eosin (H&E), 20X): The left upper aspect of the image shows normal antropyloric mucosa (solid arrow), the right lower aspect shows intramucosal extremely well-differentiated adenocarcinoma (EWDA) (empty arrow), there is a slight variation in the contents of mucin, nuclear size and gland shape between the normal and neoplastic glands. Mild autolytic changes are present. (C) Pyloric submucosa and muscularis propria (H&E, 5X): The wall is infiltrated by neoplastic glands that assume the orientation of the stroma they invade, leading to either parallel or perpendicular orientation of the tumor glands. (D) EWDA (H&E, 40X): The image shows identical histological features to the tumor found in the wall of the colon S, gastric lumen; P, pylorus; D, duodenal lumen

and negative for CK20, gastrin and p53. This phenotype is identical to the foveolar neck cell phenotype, limiting the

use of immunohistochemistry for separating the normal and neoplastic cells. Most cases of EWDA of the stomach have been reported in Japan [6-8] contributing to lack of recognition of this variant. Most cases have shown an intestinal phenotype and a few a gastric phenotype [6,7]. P53 was negative in this case and the reported cases of gastric type-EWDA, suggesting a functional p53 in these tumors, which may help explain their near normal histology. The CPO was secondary to tumoral invasion of the muscularis propria of the colon causing disruption of the peristalsis. In RYGB the distal stomach is bypassed resulting in abnormal neutralization of gastric acid by ingested food, and bile reflux is a common late complication. Gastritis and intestinal metaplasia in the remnant stomach have been reported in 87% of patients after RYGB [9]. Although it is tempting to speculate that chronic injury associated with these processes may contribute to carcinogenesis, the scant literature on gastric cancer after RYGB does not support a strong causal association. The bypassed segment is not easily accessible by endoscopy; alternative screening methods include radiographic techniques with percutaneous contrast injection in the remnant stomach, placement of gastrostomy tubes, retrograde endoscopy with pediatric colonoscope and double-balloon enteroscopy [10]. Based on the low rates of remnant gastric cancer, this type of surveillance is not considered routine. Some bariatric programs routinely screen patients preoperatively with upper endoscopy to rule out gastric pathology (this patient had a small angiodysplastic lesion on endoscopy prior to RYGB 7 years earlier), but this will only identify the rare pre-existing cancer. As the number of patients with GB increases, more cases may be reported; however, given the difficulty in making a pre-mortem diagnosis, as illustrated by our case, and the overall decline in the frequency of autopsies, under-reporting of this phenomenon appears likely.

In conclusion, EWDA of the stomach is rare, under-recognized, difficult to diagnose, and shows an aggressive clinical course that is discordant with its near-benign histology.

Gastric cancer after GB is uncommon, but when diagnosed it is usually at advanced stage. At this time, surveillance of the blind pouch, technically difficult, is not recommended. CPO has numerous causes; malignant infiltration of the colonic wall should be considered in cases of unclear etiology.

References

1. Escalona A, Guzmán S, Ibáñez L, Meneses L, Huete A, Solar A. Gastric cancer after Roux-en-Y gastric bypass. *Obes Surg* 2005;**15**:423-427.
2. Corsini D, Simoneti C, Moreira G, Lima SJ, Garrido A. Cancer in the excluded stomach 4 years after gastric bypass. *Obes Surg* 2006;**16**:932-934.
3. Harper J, Beech D, Tichansky D, Madan A. Cancer in the bypassed stomach presenting early after gastric bypass. *Obes Surg* 2007;**17**:1268-1271.
4. Watkins B, Blackmun S, Kuehner M. Gastric adenocarcinoma after Roux-en-Y gastric bypass: access and evaluation of excluded stomach. *Surg Obes Relat Dis* 2007;**3**:644-647.
5. Wu C, Lee W, Ser K, et al. Gastric cancer after mini-gastric bypass surgery: a case report and literature review. *Asian J Endosc Surg* 2013;**6**:303-306.
6. Niimi C, Goto H, Ohmiya N, et al. Usefulness of p53 and Ki-67 immunohistochemical analysis for preoperative diagnosis of extremely well differentiated gastric adenocarcinoma. *Am J Clin Pathol* 2002;**118**:683-692.
7. Nokubi M, Kawanowa K, Kawata H, Hanatsuka K, Hosoya Y. Extremely well differentiated adenocarcinoma of the gastric cardia: a unique case with columnar cells and laminated stones. *Pathol Int* 2004;**54**:854-860.
8. Buchwald H, Oien D. Metabolic/bariatric surgery worldwide 2011. *Obes Surg* 2013;**23**:427-436.
9. Flickinger E, Sinar D, Pories W, Park H, Gibson J. The bypassed stomach. *Am J Surg* 1985;**145**:151-156.
10. Sakai P, Kuga R, Safatle-Ribeiro A, et al. Is it feasible to reach the bypassed stomach after Roux-en-Y gastric bypass for morbid obesity? the use of double balloon enteroscopy. *Endoscopy* 2005;**37**:566-569.