

Early Gastric Cancer Widespread Invading the Duodenum: A Case Report

Hao Fu¹; Aifeng Pan²; Shengjie Zhou³; Guangxu Zhu^{1*}

¹Department of General surgery, Weifang People's Hospital, Weifang, Shandong, China.

²Department of Pathology, Weifang People's Hospital, Shandong Weifang, China.

³Department of Anesthesiology, Weifang People's Hospital, Shandong Weifang, China.

Abstract

Background: Gastric cancer has been observed to infrequently infiltrate the duodenum, with a prevalence of duodenal involvement ranging from 11.9%-23.8% [1] among patients with cancer in the gastric antrum. However, it is important to note that the majority of these instances pertain to advanced gastric cancers, as the occurrence of duodenal invasion in early gastric cancer is exceedingly uncommon.

Case presentation: A 62-year-old female patient presented with peripyloric thickening of the gastric antrum near the pyloric ring on gastroscopy. The lesion extended into the duodenum, appearing as a nodular and uneven intraduodenal lesion near the pyloric ring. The majority of the lesion exhibited a type 0-IIa flat elevation covered by White Opaque Substance (WOS). A CT scan with enhanced examination revealed no evidence of enlarged metastatic lymph nodes or distant metastasis. Biopsy of the intragastric lesion indicated high-grade intraepithelial neoplasia, with no surrounding enlarged metastatic lymph nodes observed. The lesion exhibited softness during the endoscopic insufflation test, indicating its conformity with Early Gastric Cancer (EGC) characterized by the encircling invasion of the duodenum. A laparoscopic-assisted major gastrectomy (D2) procedure was conducted, accompanied by B-II anastomosis. The surgical intervention and subsequent recuperation proceeded without complications, and there was no evidence of metastatic recurrence within a 13-month postoperative period.

Conclusion: This case presents an unusual instance of early gastric cancer, providing additional evidence to support the notion that early gastric cancer can indeed infiltrate the duodenum by directly penetrating the mucosal layer.

Case presentation

The patient sought medical attention at the outpatient clinic due to experiencing epigastric discomfort persisting for a duration of 20 days. Subsequent gastroscopy conducted at the outpatient clinic revealed the presence of circumferential thickening in the gastric antrum and encroachment of the duodenal bulb across the pyloric ring. Additionally, biopsy of the intragastric lesion indicated the presence of high-grade intraepithelial neoplasia. Upon admission, the patient reported postprandial bloating and

discomfort, accompanied by a loss of appetite. However, there were no reports of nausea, vomiting, or weight loss. Abdominal examination did not reveal any signs of abdominal pain, and the remainder of the physical examination yielded no noteworthy findings. The patient presented with a documented history of hypertension spanning three years, effectively managed through standardized medication. No additional gastrointestinal symptoms were reported. Laboratory tests, including admission blood routine, biochemical routine, and gastrointestinal tumor markers,

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Correspondance: Guangxu Zhu, Department of General surgery, Weifang People's Hospital, Weifang, Shandong, China.

Email: qx2042zgx@qq.com

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did not reveal any abnormalities. Furthermore, the serum antibody test for *Helicobacter pylori* yielded a negative result.

Following that, a meticulous examination of the upper gastrointestinal endoscopy was conducted, revealing the thickening of the distal gastric sinus and pyloric ring, accompanied by an unevenly elevated surface (type 0-I and 0-IIa) (Figures 1a,1b). Notably, no ulceration or erosion was observed. Further assessment through Narrow-Band Imaging Magnification Endoscopy (NBI-ME) demonstrated that the gastric sinus exhibited a background of atrophic mucosa, while the overall mucosa of the lesion displayed a distinct “tea brownness color”. Additionally, irregular widening of the ducts, covered by White Opaque Substance (WOS) (Figures 1c,1d). During the endoscopic insufflation test, the lesion demonstrated softness and displayed normal functionality of the pyloric ring. The lesion extended into the duodenal bulb, where it exhibited a characteristic flat and elevated appearance (type 0-IIa) with a distinct boundary, resembling the morphology of a Laterally Spreading Tumor (LST) in the colon (Figure 2e). Magnification observation using NBI revealed that a significant portion of the lesion’s surface was extensively attached with WOS. The glandular ducts exhibited Irregular Microvascular Pattern (IMVP) and Irregular Microsurface Pattern (IMSP), while the blood vessels displayed varying thickness and disorganized alignment (Figures 2f,2h). However, the level of disorganization observed was comparatively lower than that observed in the gastric sinus lesions. Regrettably, the unavailability of indigo carmine staining and ultrasonic endoscopy hindered their utilization in this study due to material constraints in the endoscopy department. The abdominal CT scan revealed a marginal thickening of the gastric sinus, with no evidence of distant metastasis or enlarged perigastric lymph nodes. Multiple biopsies were obtained from intragastric and duodenal lesions, indicating high-grade intraepithelial neoplasia in the gastric sinus, low-grade intraepithelial neoplasia in the duodenum, and focal high-grade neoplasia.

Treatment programs

Following a Multidisciplinary Team (MDT) evaluation encompassing gastrointestinal surgery, gastroenterology, imaging and pathology departments, a unanimous consensus was reached indicating a high likelihood of EGC for the lesion under consideration. However, due to the lesion’s extensive size and circumferential growth involving the pylorus and duodenum, endoscopic treatment posed significant challenges, with potential complications such as stenosis and perforation difficult to avoid after Endoscopic Submucosal Dissection (ESD). Consequently, surgical intervention emerged as the preferred treatment option. Subsequently, the patient underwent laparoscopic-assisted major gastrectomy with B-II anastomosis and D2 lymph node dissection. Following the postoperative pathological examination of the tumor, it was determined that the gastric sinus lesion exhibited characteristics of highly differentiated adenocarcinoma, while the duodenal lesion displayed primarily low-grade intraepithelial neoplasia. The lesion measured approximately 6.5 cm x 4.6 cm and was confined to the mucosal muscular layer, with cancer cells extending to the duodenum. The distance from the anal side to the pyloric ring was 2.6 cm (Figure 3), and the margins were devoid of cancer cells. Notably, there was no evidence of lymph or venous invasion, nor any metastasis to peripheral lymph nodes. Based on these findings, the tumor was classified as pT1aN0M0 Ia

stage. The surgical specimen revealed the presence of High-Grade Intraepithelial Neoplasia (HGIN) with localized moderately differentiated adenocarcinoma (Figures 4a-4f). Immunostains suggests that the lesion as a whole is strongly positive for Muc5ac and partially positive for CDX2 (Figures 4g,4h). P53 exhibited weak staining (1+) in 30% of cells, and the Ki-67 proliferation index was measured at 60%. Following surgical intervention, the patient experienced a successful recovery and was discharged from the hospital after 11 days. Subsequently, during a 13-month follow-up period, the patient remained in a stable condition without any signs of recurrence.

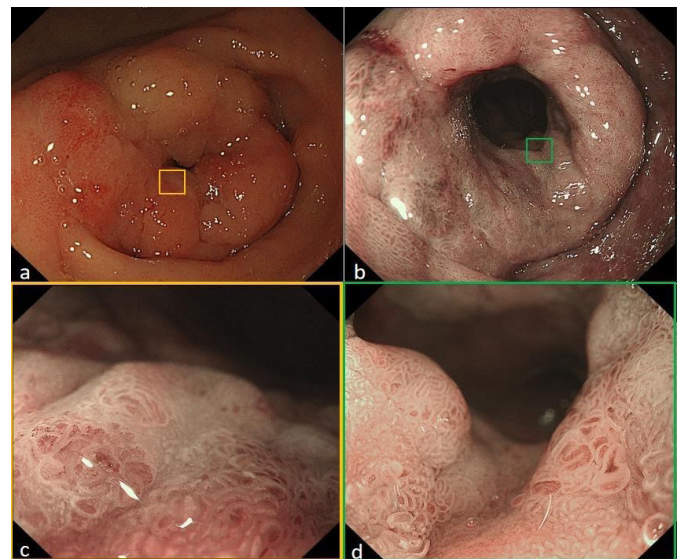


Figure 1: The distal gastric antrum and peripyloric ring display heterogeneous thickening, characterized by an irregularly elevated surface (0-I+0-IIa) (a). The lesion exhibited softness during the endoscopic insufflation test (b). NBI-ME demonstrated that the overall mucosa of the lesion displayed a distinct “tea brownness color”, irregular widening of the conduit, the surface of the lesion is covered with WOS (c,d).

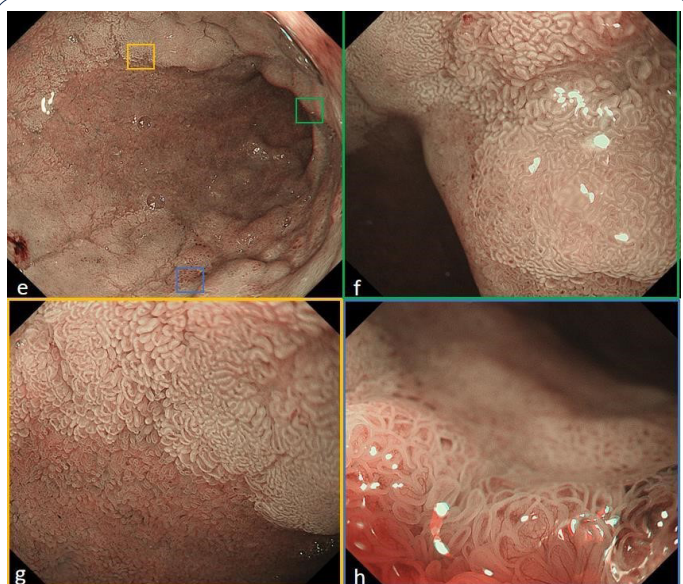


Figure 2: The duodenal bulb lesion exhibits a flat elevated pattern that is a direct extension of the gastric sinus lesion, characterized by clear demarcations and extensive attachment with WOS (e,f,g). Upon closer examination, the lesion displays IMVP and IMSP (h).

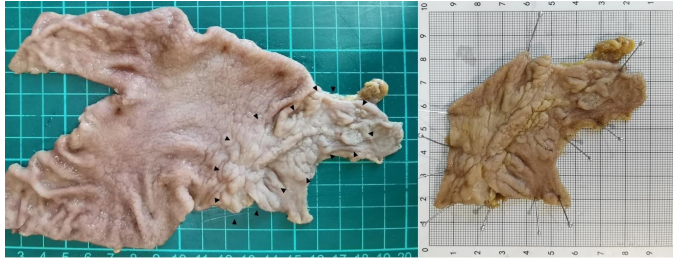


Figure 3: Macroscopic examination of the resected specimen showed an irregular flat elevated lesion spreading from the gastric antrum to the duodenum beyond the pyloric ring.

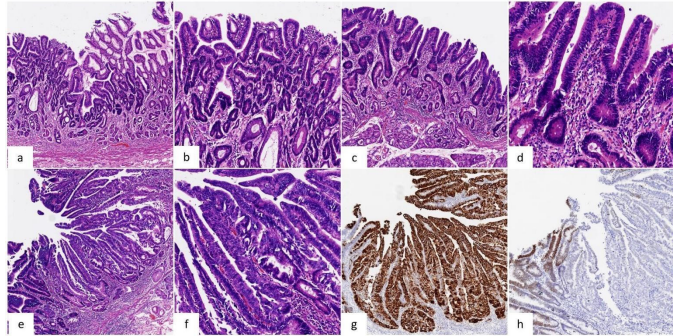


Figure 4: The surgical specimen revealed the presence of HGIN in the gastric antrum region, characterized by disrupted glandular duct architecture and loss of polarity, without infiltration into the muscular layer of the mucosa at 100× (4a), high magnification 200×, the observed nuclei exhibit a rod-like morphology and display intense staining and a stacked arrangement comprising multiple layers. These cells maintain their inherent cell polarity (4b). Irregular morphology of the duodenal glands, characterized by villous changes while maintaining an intact muscular layer of the mucosa, with a general appearance of HGIN (4c), 300x showed crowded, rod-shaped nuclei, abnormal cytoplasmic ratio, and massive inflammatory cell infiltration in the interstitial connective tissue (4d). The moderately differentiated adenocarcinoma is situated within the thickened region of the pyloric ring, exhibiting poor differentiation (4e,4f). Immunostains suggests that the lesion as a whole is strongly positive for Muc5ac and partially positive for CDX2 (4g,4h).

Discussion

The etiology of gastric cancer is influenced by a combination of genetic predisposition and environmental factors [2]. EGC patients are usually asymptomatic. In the case, the patient with early gastric cancer exhibited peripheral growth in the distal gastric sinus and pyloric ring, only resulting in discomfort such as abdominal bloating rather than the typical symptoms associated with malignant tumors in the distal stomach. This highlights the significance of utilizing endoscopy for the early diagnosis of gastric cancer. Advanced gastric cancer in the antrum has been found to occasionally invade the pyloric ring and duodenum, with a majority of cases demonstrating submucosal vertical invasion. The occurrence of EGC invading the duodenum while being confined to the mucosa is extremely rare. Namikawa T et al. [3] examined reports from the Japanese Centra database spanning 33 years after 1975, identifying 13 similar cases. The average tumor diameter was measured at 6.3 cm, with the mean length of duodenal infiltration recorded at 0.9 cm (ranging from 0.2 to 3.8

cm). Based on the Japanese pathologic staging system for early gastric cancer, the predominant tumor types observed in these cases were Tub (differentiated) and Sig (signet ring) tumors. Our case aligns with Tub1 classification, as confirmed by immunohistochemistry indicating gastric type gastric cancer. Furthermore, the extent of duodenal invasion in our case exceeded the mean diameter reported in existing literature. A comprehensive search of the Medline database spanning the past two decades yielded a mere four pertinent reports [3-5]. In contrast, this case was extensively documented, presenting a series of consecutive magnified endoscopic and histopathologic images that effectively illustrate not only the macroscopic morphological alterations of the lesion, but also offer a comprehensive Magnifying Endoscopy (NBI-ME) perspective of the flat and depressed regions within the lesion.

The clinical definition of the boundary between the stomach and duodenum poses challenges due to its lack of clear demarcation [6]. In practice, the pyloric ring is commonly employed as a reference point to distinguish between the two anatomical structures. However, this demarcation is better characterized as a region of pyloric annulus, as the criteria for delineating this line are not as stringent as those applied to the boundary between the stomach and esophagus in clinical settings. From a clinicopathological perspective, the commencement of Brunner's gland is frequently employed as the demarcation boundary between the stomach and the duodenum [7]. The prevalence of malignant neoplasms at the gastroduodenal junction in clinical settings is considerably lower compared to those occurring at the esophagogastric junction. Is there a correlation between the distinctive structure of the pyloric region and the recurrence of Early Gastric Cancer (EGC)? A Japanese scholar [8] reported a case that EGC recurred in the pyloric region, occurring eight months after Endoscopic Mucosal Resection (EMR). The recurrence was accompanied by extensive infiltration in the duodenal mucosa, leading to the suspicion that the disruption of the microstructure of the gastroduodenal mucosa caused by EMR facilitated the invasion of cancer cells into the duodenal mucosa. This prompts the question of whether there exists a barrier between the mucosa and submucosa of the gastroduodenum that hinders the progression of gastric tumors towards the distal end? Scholars [1] have noted that Brunner's glands can remain unaffected even when cancer cells directly infiltrate the duodenal mucosa. Therefore, it can be hypothesized that Brunner's glands may potentially impede the advancement of gastric cancer cells from the gastric mucosa to the duodenum. Brunner's glands, situated in the submucosa of the duodenum [9], serve the purpose of producing an alkaline fluid that counteracts gastric acid. Additionally, these glands secrete various substances such as epidermal growth factor, trefoil peptides, bactericidal factors, proteinase inhibitors, and surface-active lipids. These components effectively bind to the mucus layer, safeguarding it and the underlying mucosa from degradation caused by gastric acid, pancreatic enzymes, and other surfactants present in the area. However, the medical community has not provided detailed elucidation on the potential involvement of Brunner's gland in tumor suppression. From a molecular pathology standpoint, it has been proposed that the demarcation between gastric and duodenal regions lies in the expression boundary of SOX2 and CDX2 [10]. Additionally, abnormal CDX2 expression in the stomach is believed to be associated with intestinal metaplasia, which in turn is closely linked to the development of

intestinal-type gastric cancer. This provides evidence, in part, for the molecular expression boundary theory. It is worthwhile to investigate the presence of crucial proteins in the duodenum that possess the ability to impede tumorigenesis.

The utilization of endoscopic techniques has become increasingly prominent in the management of gastric and duodenal early cancers [11]. As per the sixth edition of the Japanese Guidelines for the Treatment of Gastric Cancer [12], intramucosal carcinoma exceeding a diameter of 2 cm (cT1a), differentiated carcinomas, and ULO are regarded as definitive indications for endoscopic intervention. However, in the case of lesions situated in specific regions, such as sizable Early Gastric Cancers (EGCs) found in the pylorus, cardia, and duodenum, while Endoscopic Submucosal Dissection (ESD) is theoretically viable as a treatment option, it necessitates a surgeon with advanced proficiency in this intricate technique, as well as thorough readiness to manage potential postoperative gastrointestinal perforation and stenosis. Nakayama et al. [13] reviewed 24 cases of invasion of the duodenum in Japan and found that duodenal infiltration was detectable preoperatively in only 4 cases. Their findings revealed that preoperative detection of duodenal infiltration was only possible in four cases. Consequently, when dealing EGCs located in close proximity to the pylorus, it is crucial to thoroughly evaluate lesion margins prior to endoscopic treatment and exercise caution when selecting the appropriate resection method. The presence of a tubular structure in the pyloric region poses additional challenges to endoscopic treatment, necessitating a careful assessment of the risk of positive margins before opting for EMR treatment. ESD mitigates the likelihood of margin positivity; however, it is imperative to conduct the procedure subsequent to magnification endoscopy for the purpose of accurately delineating the tumor boundary. In this case, the decision to opt for laparoscopic-assisted surgery instead of ESD treatment was based on a thorough assessment of the tumor's location and dimensions. Furthermore, Laparoscopic Endoscopic Cooperative Surgery (LECS) [14] has been documented as an investigative therapeutic alternative for specific sites of EGC, offering superior preservation of healthy tissues and organs compared to standalone surgery. In summary, it is imperative to thoroughly assess lesions in the pyloric region prior to surgery in order to determine the potential risk of duodenal invasion, irrespective of the stage.

Conclusion

In summary, further investigation of additional cases is warranted to enhance our understanding of the underlying mechanism of early gastric cancer with duodenal invasion. Our study has revealed that early gastric cancers situated in the gastric antrum, particularly in the prepyloric region, possess the ability to directly infiltrate the duodenal mucosal layer.

Declarations

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