CASE REPORT

Recurrent giant longitudinal duodenal ulcer with massive hemorrhage in a *Helicobacter pylori*-negative patient

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Abstract : A 67-year-old man, in whom a linear ulcer running from the duodenal bulb to the descending part had been noted 3 years previously, was admitted to our hospital because of abdominal pain and melena. Duodenoscopy revealed a bleeding giant longitudinal ulcer, which was more extensive than before. Tests for *Helicobacter pylori* (Hp) were negative. The ulcer was cured by endoscopic hemostasis and repeated blood transfusions. Attention must be paid to Hp-negative post-bulbar duodenal ulcers because of the frequent complications including hemorrhage. J. Med. Invest. 48 : 210-215, 2001

Keywords **:** *duodenal ulcer, massive hemorrhage, Helicobacter pylori*

INTRODUCTION

Post-bulbar duodenal ulcers are relatively rare and are noted in only 2-10% of endoscopically diagnosed duodenal ulcers (1). Most duodenal ulcers are positive for *H. pylori* (Hp), and the frequency of Hp-negative duodenal ulcers is very low (2). The frequency of bleeding ulcers in the post-bulbar duodenum is as high as 37-72% compared with 20-25% for the duodenal bulb ; moreover, the bleeding is often intractable to endoscopic hemostasis (3). Recently, we encountered a giant ulcer, which ran longitudinally from the duodenal bulb to the lower end of the descending part of the duodenum and bled frequently. The disease had an unusual course with a relapse of similar lesions at an interval of 3 years. It is suggested that this case had a disease that indicated the need for special attention in the follow-up of Hp-negative duodenal ulcers and thus deserves description.

Received for publication January 29, 2001 ; accepted April 23, 2001.

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CASE REPORT

The patient was a 67-year-old man who had pulmonary tuberculosis at about 25 years of age. He had been taking Bromhexine for the treatment of silicosis from the age of 50. He was usually afebrile, and had no habit of smoking. He visited our hospital complaining of abdominal pain and melena in March, 1997. Endoscopy of the upper gastrointestinal tract revealed no noteworthy abnormalities in the stomach and a linear ulcer running longitudinally from the duodenal bulb to the descending part of the duodenum (Fig. 1A). Histopathologic examination of the mucosa around the scarred ulcer showed nonspecific inflammatory cell infiltration (Fig. 1B). For the following 3 years he took an H_2-blocker continuously, and he had no subjective symptoms. In January, 2000 he suddenly had abdominal pain, vomiting and melena, which required emergency admission to our hospital. The physical findings on

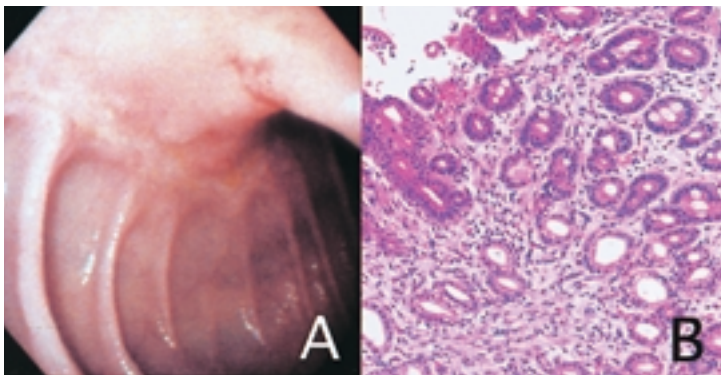

Fig. 1. Upper gastrointestinal endoscopy (March, 1997, A) and histopathology of biopsy material (B)
A linear ulcer running longitudinally from the duodenal bulb to the descending part of the duodenum (A). Histologically, a nonspecific inflammatory cell infiltrate is seen (B). (H&E×10)

admission included a mild fever (body temperature 37.2°C) and anemia in the palpebral conjunctivae. His blood pressure was 131/77 mmHg, and his pulse rate 92/min. Breathing sounds were normal. There was tenderness in the right upper quadrant. A hematological examination showed anemia with an Hb level of 8.2 g/dl and an increased inflammatory reaction with a WBC of 18,370 cells/μl and a CRP of 1.4 mg/dl. The blood gastrin level (25 pg/ml) was normal, and tumor markers (CEA and CA19-9), other blood biochemical tests, and immunological examinations were unremarkable (Table 1).

Upper gastrointestinal endoscopy showed no noteworthy abnormalities in the stomach and an ulcerative lesion around the circumference of the duodenal bulb mucosa (Fig. 2A), which was contiguous with an additional giant discrete ulcer running longitudinally on the ampulla side from the duodenal bulb to the lower end of the descending part of the duodenum (Fig. 2B). Blood was noted oozing from several points of the ulcer floor. The mucosa around the ulcer was normal. On H & E stains of the mucosa surrounding the ulcer lesion there were nonspecific inflammatory changes (Fig. 2C). A urea breath test with C^{13} for Hp, and a urease test and culture were all negative, and no tubercle bacilli were detectable

Table 1. Laboratory findings on admission

Peripheral blood		Serological test	
WBC	18,370 cells/μl	CRP	1.4 mg/dl
RBC	270×104 cells/μl	ANA	< 1 : 20
Hb	8.2 g/dl	RF	5 IU/ml
Ht	24.9%	LE test	(−)
Plt	9.3×10^4 cells/μl	IgG	567 mg/dl
Blood coagulation test		IgA	140 mg/dl
PT	12.7 sec	IgM	49 mg/dl
APTT	25.2 sec	CEA	0.3 ng/ml
Blood chemistry		CA-19-9	0.0 U/ml
TP	5.4 g/dl	Hormonal examination	
Alb	3.1 g/dl	Gastrin	25 pg/ml
ALT	10 IU/l	Viral examination	
AST	7 IU/l	HBs-Ag	(−)
LDH	290 IU/l	HCV-Ab	(−)
ALP	128 IU/l	Fecal examination	
γ-GTP	16 IU/l	Occult blood	(++)
Ch-E	204 IU/l	Significant bacteria	(−)
CPK	44 IU/l	Urinalysis	
T-bil	0.2 mg/dl	Protein	(−)
T-cho	144 mg/dl	Sugar	(−)
BUN	34.5 mg/dl		
Cre	1.2 mg/dl		

from biopsy materials, gastric juice, feces or sputa. Fecal examination did not disclose any pathogenic microorganisms.

After admission, nothing by mouth was allowed, and the patient received intravenous hyperalimentation. Intravenous administration of ranitidine (40 mg/day), an H_2-blocker, was started. His fever subsided on the 2nd hospital day, and inflammatory responses subsided on the 4th hospital day. However, the anemia exacerbated to an Hb of 5.8 g/dl, which required a blood transfusion and emergency endoscopy. On the ulcer floor, an exposed vessel was seen to be spurting blood (Fig. 3A), for which endoscopic hemostasis by local injection of 1% polidocanol was

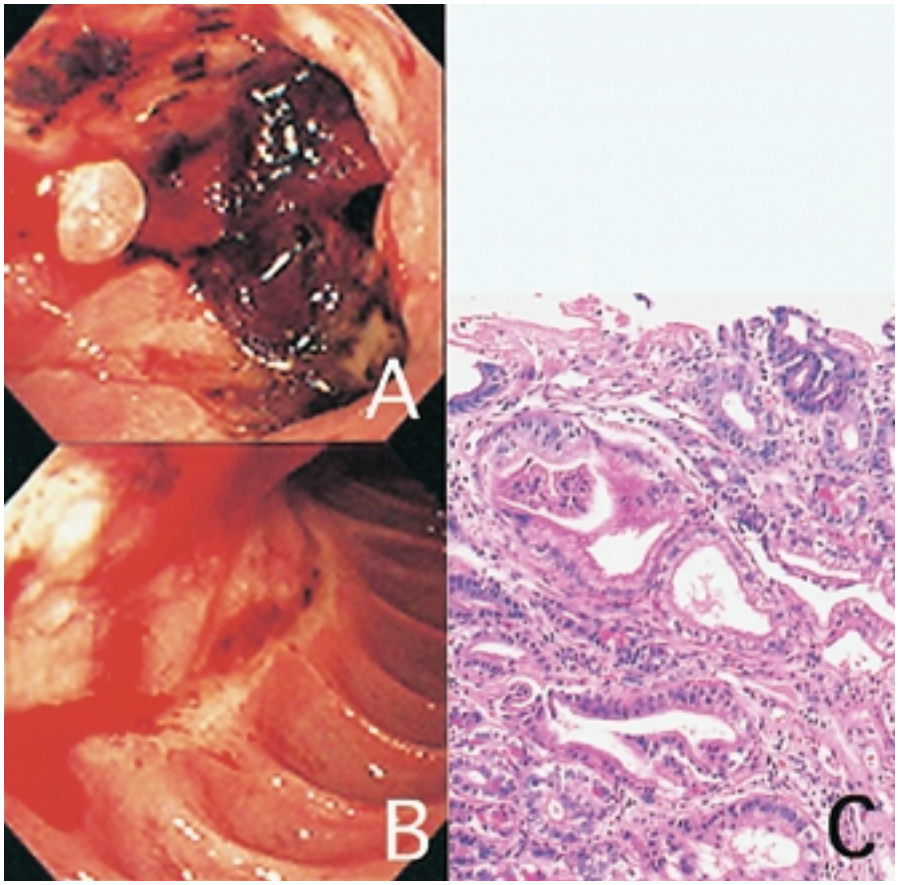

Fig. 2. Upper gastrointestinal endoscopy on admission (January, 2000, A and B) and pathology of biopsy material from the mucosa surrounding the ulcer (C)
A solitary giant ulcer running longitudinally on the ampulla side from the duodenal bulb (A) to the lower end of the descending part of the duodenum (B) and oozing blood from several points on the ulcer floor. Histopathologically, inflammatory cell infiltration and erosions are observed with no evidence of ischemic changes (C). (H & E×10)

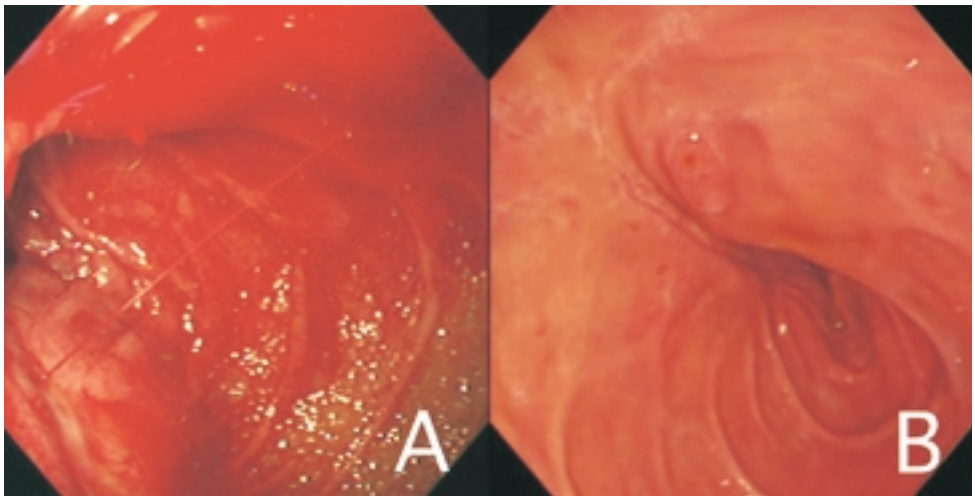

Fig. 3 Upper gastrointestinal endoscopy
On the 19th hospital day, exposed vessels spurting blood were observed on the ulcer floor. Endoscopic hemostasis via local injection of 1% polidocanol and electrocautery with a heater probe was performed (A). On the 56th hospital day, the exposed vessels have virtually disappeared, and the ulcer has healed with scar formation (B).

performed. Later, hemoglobin dropped to approximately 8.0 g/dl on the 5th, 6th and 19th hospital days, when emergency endoscopy revealed vessels exposed and spurting blood at a total of 5 locations along the longitudinal ulcer floor. In addition to the local injection of 1% polidocanol, endoscopic hemostasis via electrocautery with a heater probe was performed, and the intravenous H_2-blocker was discontinued and replaced by oral sodium rabeprazole (20 mg/day), a proton pump inhibitor. On the 26th hospital day, the anemia improved to an Hb of 10.2 g/dl, and endoscopy showed that the exposed vessels had disappeared and that the duodenal ulcers had healed with scar formation (Fig. 3 B). During the course of the disease, a total of 24 units (4,800 ml) of blood were transfused. Transillumination of the small intestine and endoscopy of the large intestine showed no abnormalities, including ulcers or scarred ulcers. Abdominal CT, MRI and ERCP did not show any noteworthy abnormalities. Abdominal angiography did not reveal any vascular malformations, arteriovenous fistulas, or occlusions (Fig. 4).

Since the lesion was a recurrent giant ulcer, we considered surgical removal. However, since we had previously noted the ulcer healing with scar formation, were unable to obtain consent from the patient, and considering the magnitude of surgical trauma to the duodenum, we decided to closely follow the patient thereafter and, with full informed consent, discharged him from the hospital in March, 2000. No recurrence of the ulcer has been noted to date, 6 months after discharge.

DISCUSSION

Most reported examinations have shown that the post-bulbar duodenal ulcers are located between the upper horizontal part of the duodenum and the papilla of Vater, and that duodenal stenosis is likely to occur at the site of ulceration (1, 4-6). However, in this case, the patient had a giant ulcer without Hp running longitudinally along the descending part of the duodenum beyond the ampulla of Vater, which resulted in no deformity at the site of the post-bulbar duodenal ulceration. Moreover, the disease conditions causing Hp-negative duodenal ulcers include 1) inflammatory intestinal diseases in the broad sense, such as Crohn's disease, ischemic enteritis and intestinal tuberculosis, 2) collagen diseases such as Behçet's disease, 3) vascular lesions such as arteriovenous malformations (7), 4) Zollinger-Ellison syndrome, 5) drug-induced lesions due to nonsteroidal anti-inflammatory and other drugs, and 6) misswallowing of foreign bodies like fish bones. In the present case, however, the possibility of vascular lesions, Behçet's disease, Zollinger-Ellison syndrome, drug-induced lesions, and lesions due to misswallowing were ruled out, because a giant longitudinal duodenal ulcer with massive hemorrhage recurred after an interval of 3 years, during which time medication with an H_2-blocker and a therapeutic agent for silicosis remained almost unchanged ; no ingestion of nonsteroidal anti-inflammatory drugs, alcohol, or other gastroduodenal irritants, that cause of hemorrhagic gastroduodenitis, had been taken during the few weeks prior to this

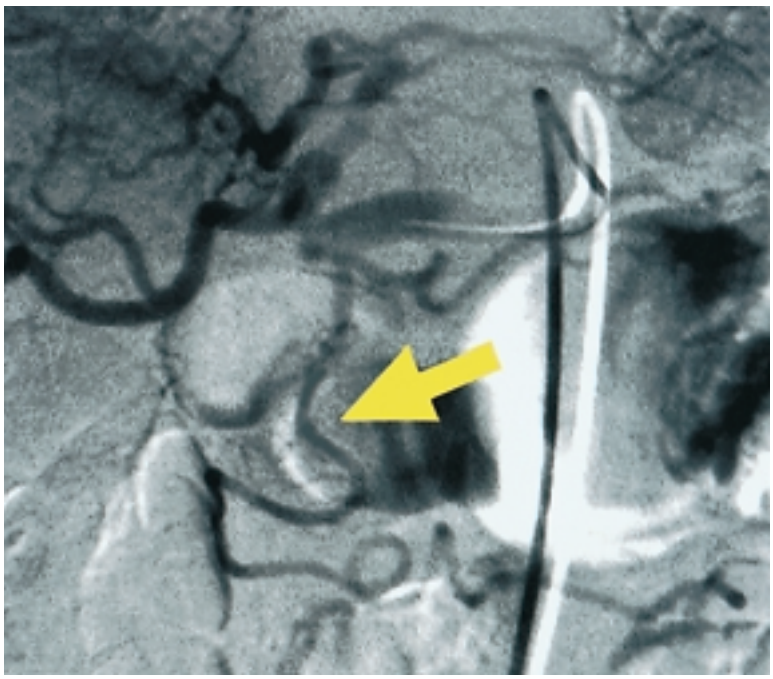

Fig. 4. Abdominal angiography
A catheter was inserted selectively into the gastroduodenal artery via the celiac artery to visualize the duodenal artery (arrow). No vascular malformations, arteriovenous fistulas, or occlusions are observed.

patient's admission ; the blood gastrin level was normal ; there were no symptoms or signs of Behçet's disease in the clinical course ; and abdominal angiography showed no abnormalities such as vascular malformations or arteriovenous fistulas.

In ischemic colitis, longitudinal ulcerative lesions are found frequently in the large intestine (8). The advanced age of the patient (67 years) and the morphologic features of the longitudinal ulceration suggested the possibility of ischemic changes. However, histopathologic examination of endoscopic biopsy material did not show features of ischemic colitis. Furthermore, a bleeding ulcer requiring transfusion of as much as 24 units (4,800 ml) of blood is not compatible with ischemic changes. The possibility, however, cannot be excluded that, as in ischemic colitis, circulatory disturbances such as occlusion or recanalization of the intra-or submucosal microvasculature, barely visualized by angiography, are at least some of the factors involved in the onset of the ulcer reported here.

The frequency of gastroduodenal lesions in Crohn's disease with longitudinal ulcers is only about 2-4%, and solitary lesions have been less frequently reported (9). Although in the present case the ulcer in the posterior part of the duodenal bulb showed a longitudinal shape, no nodular changes or cobblestone appearance was observed. We were not able to identify either aphtha-like lesions in the mucosa surrounding the ulcer, or to note anything suggestive of Crohn's disease. However, one report previously described the occurrence of a lesion in another location 14 years after the identification of a solitary gastroduodenal lesion in Crohn's disease (10), therefore, further follow-up is important.

In the present case, the patient had a history of tuberculosis and had a mild fever on admission. Intestinal tuberculosis exhibits local ulcerative lesions (11). However, no tubercle bacilli were detectable from biopsy material, gastric juice, feces or sputa, and the duodenal ulcerative lesion remitted without antituberculous therapy. Although the cause of the fever on admission was unknown, it subsided, and then immune responses returned to normal ; nevertheless, the duodenal ulcerative lesion was exacerbated. Therefore, there appeared to be no apparent association between the ulcer and tuberculosis.

As far as we are aware, the recurrent longitudinal duodenal ulcer with massive hemorrhage and nonspecific pathology in the present case has not previously been described. Recently, Adachi *et al*. reported a case of an unclassifiable recurrent intestinal ulcer (12), which required a series of 4 intestinal resections during the course of about 3 years because of the ineffectiveness of medical treatment. The lesion was a longitudinal ulcer extending from the terminal ileum to the colon and histopathologically did no show any specific changes, suggesting the possibility of an unclassifiable intestinal ulcer. Thus, the present case also might be an "unclassifiable" duodenal ulcer.

At present, the concepts that have been reported on ulcer disease are not useful to explain the pathogenesis of the disease condition reported here, and we have not reached a definitive diagnosis. We considered surgical resection for further histopathologic study, but because there was little evidence suggesting malignant disease, and since the ulcers that had bled twice before were in a state of remission with scar formation at least for the time being, and the lesion was in a location that will inevitably sustain significant surgical trauma, no future surgical resection was suggested proposed. There is a significant possibility that the duodenal ulcer will recur in the future, therefore, close follow-up will be necessary.

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