Gastric ulcer penetrating to liver diagnosed by endoscopic biopsy

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Abstract
Liver penetration is a rare but serious complication of peptic ulcer disease. Usually the diagnosis is made by operation or autopsy. Clinical and laboratory data were no specific. A 64-year-old man was admitted with upper gastrointestinal bleeding. Hepatic penetration was diagnosed as the cause of bleeding. Endoscopy showed a large gastric ulcer with a pseudotumoral mass protruding from the ulcer bed. Definitive diagnosis was established by endoscopic biopsies of the ulcer base.

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INTRODUCTION
Penetration into the liver is a rare complication of peptic ulcer disease and may lead to unusual complications such as abscess formation or upper gastrointestinal hemorrhage[1,2]. The absolute frequency of this complication in patient with peptic ulcers is not known.

We reported on a patient who presented with upper gastrointestinal bleeding due to a gastric ulcer penetrating into the liver. Diagnosis was based on histologic examination of endoscopic biopsy materials. We also reviewed 13 other reported cases of endoscopically and histologically diagnosed peptic ulcer penetration into the liver[3-13].

CASE REPORT
A 64-year-old man was admitted because of a 2-wk history of weakness, dizziness, and melena. One week before his admission, the patient noted intermittent mild mid-epigastric pain and nausea after meals. He had undergone a highly selective vagotomy and primer suture 13 years before for peptic ulcer perforation. Physical examination demonstrated that he was afebrile with a regular heart rate at 88 beats/min and a blood pressure of 110/60 mm Hg. The abdomen was soft, nontender, nondistended, and without organomegaly or masses. Bowel sounds were hyperactive. Rectal examination revealed no masses and the stool was melenic. A nasogastric tube was passed in emergency room, “coffe grounds” material were aspirated from the stomach. Initial laboratory evaluation showed mild leukocytosis (white blood cell counts, 15800/mm³; normal, 4-1010³/mm³) and severe anemia (hemoglobin, 4.7 g/dL; normal hemoglobin, 14.1–17.2 g/dL; hematocrit, 13.8%; normal hematocrit, 36.1-50.3%; mean red cell volume, 68.2 fl; normal red cell volume, 82.2-99 fl). The stool was positive for occult blood. Coagulation parameters and liver function tests were within normal limits. The patient had no gastrointestinal symptoms and was not receiving aspirin or nonsteroidal antiinflammatory drugs (NSAIDs). Emergency endoscopy showed a large (4.5 cm) ulcer on the anterior wall of the gastric antrum, with malignant appearance (Figure 1). The ulcer base was covered with fibrin, and the margins were irregular. No active bleeding was present at the time of investigation, but stigmata of recent hemorrhage were detected. Sonographic examination demonstrated the “target” sign of the gastric antral area with suggestion of eccentric “tumour” extension into liver (Figure 2). The center of the target was echogenic. Multiple biopsies were taken separately from the ulcer margins and the pseudotumoral mass. Histologic examination of the specimens showed gastric mucosa with granulation tissue and also normal-appearing hepatocytes (Figure 3).

Figure 1 Endoscopic photograph showing a giant deep ulcer (about 4.5 cm in diameter) with malignant appearance (arrow).

Figure 2 Longitudinal ultrasound scan showing the target like appearance (arrows) representing the giant ulcer seen on gastroscopy.
Figure 3 Endoscopic biopsy showing granulation tissue (arrowhead) adjacent to normal-appearance hepatocytes (arrow) (HE ×20).

Urease (CLO test) for *Helicobacter pylori* was negative. Treatment was started with 40 mg of omeprazole twice per day. He received 4 units of packed red blood cells by transfusion. The symptoms improved. The surgery service was then consulted for potential resection, however the patient and family refused surgical intervention. On the 17th day of hospitalization, he died of gastrointestinal bleeding.

**DISCUSSION**

We reported a very rare case of an endoscopically and histologically proven liver penetration by a gastric ulcer in an older man. In general, penetration into the liver by a peptic ulcer is not a frequent event. We have found only a few reports of liver penetration by gastric ulcer diagnosed by endoscopy. None of them was clinically or radiologically recognised prior to endoscopy. There were thirteen previous case reports of liver penetration in patients with peptic ulcer disease. Four of these cases were for duodenal ulcer and nine were for gastric ulcer. Three of these cases could be diagnosed at the time of surgery, but the other cases were diagnosed on the basis of histologic finding of hepatic tissue on endoscopic biopsies. All of the patients, including ours, showed severe gastrointestinal bleeding. Abdominal pain was described in only 4 patients [7,8,11,13], thus in our case, abdominal pain did not seem to be a common finding. These case reports, including the present one, are summarized in Table 1.

Endoscopically, 3 of the patients had a large ulcer crater with a pseudotumoral mass protruding from the ulcer bed, however no histologic signs of malignancy were seen [9,10,11]. Another patient had only a mass without any ulcer [12]. The rest of them had ulcers ranging from 2.5 cm to 9 cm x 3 cm in diameter.

The correct diagnosis was established in all the cases by the presence of liver tissue in the histologic examination of endoscopic biopsies. In contrast to the cases, described by Guerrieri and Waxman [9], the liver tissue in this case did not show severe inflammation or inflammatory atypia. The hepatic histological changes found in our case were consistent with those reported by others. All reported cases except two [6,9] had normal liver function tests. This may reflect that local hepatic injury does not cause abnormalities in liver functions. The diagnostic value of liver function tests in cases of ulcer penetration into the liver is very limited.

**Table 1** Comparison of published reports of liver penetration by peptic ulcer

| Source             | Age/Gender | Epigastric Pain/ tenderness | Main clinical feature | Location | Endoscopic appearance | NSAIDs       | Treatment |
|--------------------|------------|----------------------------|-----------------------|----------|-----------------------|--------------|-----------|
| Martinez-onsurbe (10) | 91/ Female | -                          | GI bleeding           | Anterior wall of antrum ulcer | ?           | ?         |
| Guerrieri (9)      | 53/ Male   | -                          | GI bleeding           | Lesser curve of antrum ulcer with mass | ?           | Antiacids,Op (BII) |
| Goldman (6)        | 65/ Male   | Tenderness                 | Nause, anemia         | Lesser curve of stomach ulcers | ?           | Op (BII)  |
| Park (4)           | 52/ Male   | -                          | GI bleeding           | Lesser curve of antrum giant ulcer | ?           | H$_2$RA    |
| Sperber (3)        | 69/ Male   | Tenderness                 | GI bleeding           | Lesser curve of corpus ulcer with ? | Op          |
| Jimenez-Perez (2)  | 61/ Male   | Tenderness                 | GI bleeding           | Lesser curve of corpus ulcer with | ?           | Op        |
| Castellano (11)    | 77/ Male   | -                          | GI bleeding           | Posterior wall of duodenal bulb ulcer posterior wall of antrum ulcer | ?           | Op (BII)  |
| Castellano (11)    | 70/ Male   | Epigastric pain            | GI bleeding           | Posterior wall of duodenal bulb Giant ulcer ulcer | ?           | H$_2$RA,Op |
| Matsuoka (12)      | 53/ Male   | Tenderness                 | GI bleeding           | Lesser curve of corpus Giant ulcer ulcer | ?           | H$_2$RA,Op |
| Novacek (8)        | 33/ Female | Epigastric pain            | GI bleeding           | Posterior wall of duodenal bulb Giant ulcer ulcer | ?           | PPI,Op    |
| Padda's (5)        | 78/ Male   | -                          | GI bleeding           | Anterior wall of duodenal bulb Mass without ulcer | ?           | H$_2$RA,Op |
| Brullet (7)        | 89/ Female | Epigastric Pain            | GI bleeding           | Anterior wall of gastric antrum ulcer with mass | ?           | Op (BII)  |
| Mostbeck (13)      | 53/ Male   | Epigastric pain            | -                     | Anterior wall of duodenal bulb Giant ulcer | ?           | ?         |
| Present case       | 61/ Male   | -                          | GI bleeding           | Anterior wall of gastric antrum giant ulcer | ?           | PPI       |

GI Bleeding: gastrointestinal bleeding; Op (BII): subtotal gastrectomy with Billroth II reconstruction; H$_2$RA: histamine H$_2$-receptor antagonist; PPI: proton pump inhibitor.
Larger lesions of the upper gastrointestinal tract have some characteristic sonographic patterns. These have been described variously as ring sign, pseudo-kidney, target-like and bull’s-eye.\textsuperscript{[13,14]} Ultrasonographic examination of the present case showed a ‘target’ lesion with echogenic centre in the gastric antral area with suggestion of exogastric extension into the liver, leading to the suspicion of hepatic penetration by a gastric tumor as described by Sperber\textsuperscript{[3]}. The center of the ulcer appeared as cavity lesions (hypoechoic area) which were considered secondary to fluid secretions within the cavity of the giant ulcer. Endoscopic ultrasonography is useful for the diagnosis and treatment of a variety of gastrointestinal diseases. We could not perform endoscopic ultrasonography because of its absence in our unit. Endoscopic ultrasonography may be helpful for the diagnosis of gastric ulcer complications such as penetration into an adjacent structure\textsuperscript{[10]}. Only one of the patients was treated successfully with a histamine \textsubscript{H\textsubscript{2}}- receptor antagonist\textsuperscript{[4]}, but an operation was necessary for all other patients. A subtotal gastrectomy with Billroth II reconstruction was performed in 5 cases\textsuperscript{[6,7,9,11]}. In the present case, the patient did not require an emergency operation and was initially treated with a proton pump inhibitor. All patients had uneventful postoperative courses except for 2 patients, of them one died of a sepsis\textsuperscript{[3,10]}. The outcome was not given in 3 cases\textsuperscript{[5,10,13]} These reports indicate that penetration as a serious complication of peptic ulcer disease often required operative treatment. Results of a recent study have not shown a decrease in severe ulcer complications despite the use of histamine \textsubscript{H\textsubscript{2}} receptor antagonists\textsuperscript{[10]}. This was likely due to the increase, mean population age in developed countries and the high prevalence of nonsteroidal anti-inflammatory drug use. Lanas et al, found that NSAID use was the most important independent risk factor for upper and lower gastrointestinal perforation\textsuperscript{[17]}. Endoscopic studies have shown an increase in the prevalence of peptic ulcers and gastrointestinal perforation in patients who took NSAIDs regularly\textsuperscript{[18]}. Only three of these cases were regularly using NSAIDs\textsuperscript{[5,8,11]}. Nonsteroidal antiinflammatory drugs, therefore, seem to be the most important risk factor for ulcer penetration into the liver.

Finally, as in other reported cases, results of the liver function tests in our patient were unremarkable and so did not focalise our attention on the probability of liver process. Endoscopic view of the lesion did not make us suspect penetrating peptic ulcer disease. However, ultrason was the first procedure to raise suspicion of hepatic penetration by a gastric ulcer. This diagnosis was subsequently confirmed by endoscopic biopsy. A high index of suspicion to make the diagnosis is necessary.

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