Hepatocellular Carcinoma with Direct Invasion to the Stomach Causing Gastrointestinal Hemorrhage

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Abstract

A 54-year-old man had undergone transcatheter arterial embolization (TAE) three times to treat hepatitis B virus-related hepatocellular carcinoma (HCC), but recurrence was found in June 2005. A large tumor in the left lateral portion of the liver showed extrahepatic growth and was attached to the gastric wall. TAE was performed a fourth time. In September 2005, the patient was admitted with worsening anemia. Computed tomography and upper gastrointestinal endoscopy revealed that the HCC had directly invaded the stomach and caused gastrointestinal hemorrhage. Endoscopic hemostasis was effective, but the patient died because of worsening hepatic failure.

Key words: gastrointestinal tract involvement, hepatocellular carcinoma, bleeding

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Introduction

Involvement of the gastrointestinal (GI) tract in patients with hepatocellular carcinoma (HCC) rarely occurs, being found in only 0.7% to 2% of cases. In this report, we describe a case of HCC with direct invasion to the stomach which caused GI hemorrhage. We also present a review of the literature.

Case Report

A 54-year-old man was admitted to our hospital for evaluation of a hepatic tumor in June 2005. He had a history of chronic hepatitis positive for hepatitis B surface antigen. HCC had first been diagnosed in 2002, then he had undergone transcatheter arterial embolization (TAE) three times. No recurrence had been observed until June 2005, when a 50-mm-diameter tumor in the left lateral portion of the liver was demonstrated by computed tomography (CT). Multiple enlarged lymph nodes, from 17 to 40 mm in diameter, were also demonstrated around the celiac artery (Fig. 1). The patient was admitted for a thorough evaluation.

At the time of admission, physical examination showed no particular abnormalities other than high body temperature, ranging from 36.5 degrees C to 38.8 degrees C, which had been observed since 5 weeks before admission. Laboratory examination revealed slight elevation of aminotransferase levels and slight normocytic anemia (red blood cell count, 404×10⁴/μl; hemoglobin, 12.0 g/dl; and hematocrit, 36.5%). Serum levels of α-fetoprotein (AFP) and protein-induced vitamine K absence-II were within the normal ranges. AFP-L3 fraction was not examined. Contrast-enhanced CT showed that the hepatic tumor had extended extrahepatically toward the stomach and attached to the gastric wall. This tumor was well stained on hepatic arteriography, as is typical for HCC (Fig. 2). Upper GI fiberoptic endoscopy revealed external compression on the greater curvature of the upper body of stomach (Fig. 3). The biopsy specimen from the compressed portion showed normal gastric mucosa. For mass reduction, TAE was performed for the lesion in the left lobe of the liver.

In September 2005, the patient was readmitted because of worsening anemia and postprandial epigastric pressure. Physical examination revealed anemia, exhaustion, and abdominal distention due to ascites. Laboratory studies re-

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revealed worsening of the normocytic anemia (red blood cell count, 295×10⁴/μl; hemoglobin, 8.4 g/dl; hematocrit, 26.3%) and synthetic liver dysfunction (serum albumin, 2.1 g/dl; cholinesterase, 68 IU/l [normal 322-762 IU/l]; prothrombin activity, 72%). Contrast-enhanced CT showed that the HCC in the left lateral part of the liver had increased in size from 50 mm to 75 mm in diameter and had fused with the gastric wall (Fig. 4). Upper GI fiberoptic endoscopy revealed increased external compression on the upper body of stomach. In the area, a tumor was protruded massively into the gastric lumen, but no sign of active bleeding was observed (Fig. 5). Pathological examination from the invasive lesion revealed epithelial malignant cells forming sheet like arrangement that were positive against immunological staining for AFP (Fig. 6), but negative for cytokeratin and epithelial membrane antigen. Because other hepatocyte specific markers, such as hepatocyte paraffin 1, were not examined, the possibility of AFP-producing gastric adenocarcinoma could not be excluded pathologically. However, from clinical course, especially from imaging findings, it was obvious that the tumor progressed from the liver toward the gastric wall. Therefore, we concluded that the HCC in the left lateral part of the liver had directly invaded the stomach and caused the
postprandial symptoms. The patient refused additional TAE. On the 17th hospital day, hematemesis suddenly developed, hemoglobin decreased to 5.6 g/dl, and blood transfusion was done. Upper GI endoscopy revealed bleeding from the portion of the gastric body with HCC invasion, leading to a diagnosis of GI hemorrhage from a HCC directly invading the stomach. Hemostasis was achieved with endoscopic clipping. However, signs of hepatic failure, such as jaundice, ascites, and encephalopathy, developed. The patient died on the 59th hospital day. A request for an autopsy was refused.

**Discussion**

GI tract involvement by HCC is rare. Chen et al found 8 such cases (2%) in 396 patients with HCC (1). The major sites of involvement were the stomach, duodenum, and colon (1-3). Direct invasion by contiguous neoplasm was assumed (1, 2). In the present case, worsening anemia at the time of readmission suggested recent GI hemorrhage. When GI hemorrhage occurs in a patient with HCC, esophageal varices or peptic ulcer is usually suspected. When hematemesis occurred, we also expected that a hypervascular HCC directly invading the stomach might bleed. Indeed, several cases of gastric bleeding from direct invasion of HCC have been reported previously (4). Hemostasis was immediately achieved with endoscopic clipping in the present case, but it is generally difficult. Successful endoscopic hemostasis has not been reported previously. Furthermore, overt GI bleeding is a rare presentation of GI tract involvement. According to Park et al, in only 1 of 18 cases, GI tract involvement by HCC was found after upper GI bleeding (2). GI tract involvement was detected in 9 patients on the basis of epigastric discomfort, including pain, nausea, and vomiting, and in 5 patients on the basis of palpable mass.

Because of the rarity of direct invasion, several predisposing factors have been suggested. Chen et al (1) have reported that most of their patients with HCC and GI tract invasion had received regional therapy, such as TAE, before invasion occurred. They have speculated that when a large HCC attached to the GI tract is treated with TAE, the wall of the GI tract might be affected by the inflammatory response and become adherent to the liver or tumor capsule. Thereafter, the viable tumor tissue could easily invade the GI tract at the time of tumor recurrence (1). However, Park et al (2) have reported that 7 of 12 patients with HCC and direct invasion had not received any treatment before GI tract invasion was diagnosed. They assumed that the main factors in direct invasion are the growth pattern, size, and location of the masses rather than previous regional treatment. In most cases of direct invasion, the HCC masses are large, located in the subcapsular area, and have an exophytic growth pattern (2). The present patient had all these characteristics. The HCC mass, greater than 5 cm in diameter, was located in the subcapsular area of the left part of the liver and had an extrahepatic growth pattern. TAE was performed four times, and the fourth time the mass in the left liver was targeted.

Surgical removal of a bleeding tumor should be considered first if the patient has an appropriate hepatic reserve (5, 6). However, the prognosis of patients with HCC accompanied by GI involvement is poor because of massive bleeding, hepatic failure, or both. Non-surgical techniques to maintain hemostasis include TAE, endoscopic injection of ethanol or adrenalin or both, and radiotherapy (7-9). Fuji et al have summarized 28 patients with HCC and direct invasion to the GI tract in the English language literature. The median survival of patients who received nonsurgical thera-
pies (11 patients), curative surgery (7 patients), and supportive therapy (10 patients), were 3.0, 9.7, and 1.2 months, respectively (3). The patients who had undergone curative surgery survived for significantly longer than did the other patients. In the present case, since curative surgery was impossible because of metastasis to multiple lymph nodes, endoscopic clipping was attempted to achieve hemostasis. Despite the successful treatment of hematemesis, the patient died of hepatic failure.

In conclusion, although GI tract hemorrhage due to involvement by HCC is rare, it should be considered in addition to the more common causes of GI bleeding, such as variceal rupture and peptic ulcer, in patients of HCC who have hematemesis or melena, or both. Because repeated TAE, intraarterial chemotherapy, and radiology have recently lengthened the survival of patients with unresectable HCC, GI tract involvement by HCC is expected to become more common in the future.

References