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Case Report

Hepatocellular Carcinoma with Direct Invasion to the Duodenal Bulb, Presenting with Gastrointestinal Bleeding

Megumi URATA[1,2], Hajime ISOMOTO[2], Saburo SHIKUWA[1], Masayuki OSABE[1], Keiichiro MATSUNAGA[1], Katsuhisa OMAGARI[2], Yohei MIZUTA[2], Kunihiko MURASE[2], Masato TOMITA[3], Isao SHIMOKAWA[3], Ikuo MURATA[4], Shigeru KOHNO[2]

1) Internal Medicine, Omura Municipal Hospital
2) Second Department of Internal Medicine, Nagasaki University School of Medicine
3) First Department of Pathology, Nagasaki University School of Medicine
4) Department of Pharmacotherapeutics, Nagasaki University Graduate School of Pharmaceutical Sciences

Hemorrhage from hepatocellular carcinoma (HCC) directly invading the gastrointestinal tract is very rare. A 71-year-old man, who had been treated with transcatheter arterial embolization and percutaneous ethanol injection for HCC in the right hepatic lobe, presented with melena. Endoscopic examination showed a crater-like ulceration coated with blood clot in the duodenal bulb, and microscopic examination of a biopsy specimen from the duodenal lesion confirmed HCC. Abdominal computed tomography (CT) revealed that the HCC mass containing air-density invaded the duodenum. Recurrent bleeding continued from the lesion and the patient died of liver failure. Postmortem examination revealed massive HCC with hepatoduodenal fistula caused by direct tumor invasion into the duodenum.

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Key Words: hepatocellular carcinoma, duodenal invasion, gastrointestinal bleeding

Introduction

Extrahepatic metastases are found in 50-90% of autopsy cases of hepatocellular carcinoma (HCC), with lungs, adrenal glands, bones and regional lymph nodes being the most commonly involved sites (1). However, involvement of the gastrointestinal (GI) tract by HCC is uncommon forming only 4-12% of the cases at autopsy (2). This uncommon secondary lesion is usually asymptomatic, and most are incidentally found at postmortem examination or during laparotomy (2, 3). Chen *et al.* (2) reported that the incidence of clinical detection of GI tract involvement in HCC patients is only 2%. Direct invasion of HCC to the duodenum has also been rarely reported (2, 4-8). We present a patient with HCC who developed GI bleeding secondary to duodenal wall invasion.

Address Correspondence: Hajime Isomoto, M.D.
Second Department of Internal Medicine, Nagasaki University School of Medicine, 1-7-1 Sakamoto, Nagasaki 852-8501, JAPAN
TEL: +81-95-849-7281 FAX: +81-95-849-7285
E-mail: hhisomot@net.nagasaki-u.ac.jp

Case Report

A 71-year-old Japanese man was admitted to our hospital, with a chief complaint of sudden-onset melena. He had been treated seven months earlier by transcatheter arterial embolization (TAE) and percutaneous ethanol injection therapy (PEIT) for HCC. At that time, he had underwent upper gastroin-

Figure 1. Tumor features on endoscopy conducted 7 month before presentation. Note the presence of a submucosal tumor (SMT) in the duodenal bulb.

Figure 2. Abdominal CT showing a massive hepatocellualr carcinoma (HCC) in the right hepatic lobe.

Figure 3. Duodenoscopy showing a crater-like ulceration in the duodenal bulb.

testinal endoscopy revealing a submucosal tumor (SMT)-like lesion in the duodenal bulb (Figure 1). Abdominal computed tomography (CT) revealed a massive HCC in the right hepatic lobe (Figure 2). Physical examination on admission showed slight anemia and marked hepatomegaly with a palpable nodularity. Laboratory investigation showed anemia (hemoglobin 9.7 g/dl) and elevated serum α-fetoprote in level (1,082 ng/ml, normal range < 20ng/ml). The patient was seronegative for hepatitis B surface antigen but seropositive for antibody against hepatitis C virus. Duodenoscopy revealed a crater-like ulceration coated with fresh blood clot (Figure 3), where the SMT-like lesion had been found previously. There were neither gastric nor esophageal varices. Microscopic examination of a biopsy specimen taken from the edge of the lesion confirmed duodenal invasion of HCC. Abdominal CT showed a recurrent large HCC mass in the right hepatic lobe. The tumor was in direct proximity to the duodenum and contained a large air cavity within

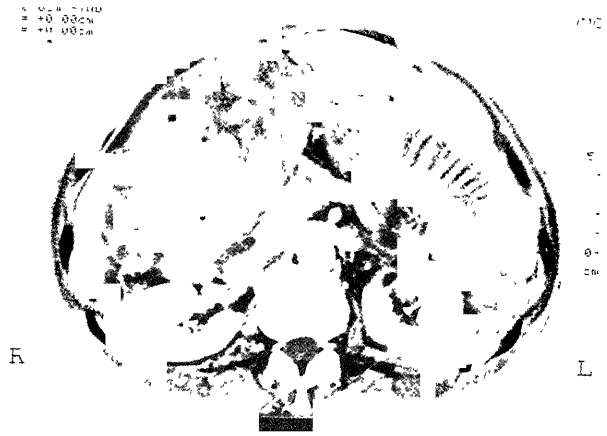

Figure 4. Abdominal CT showing a large recurrent HCC mass containing air cavity within it.

Figure 5. Autopsy specimen of the liver tumor in the right lobe invading the duodenum and forming a hepatoduodenal fistula (arrow, cut surface).

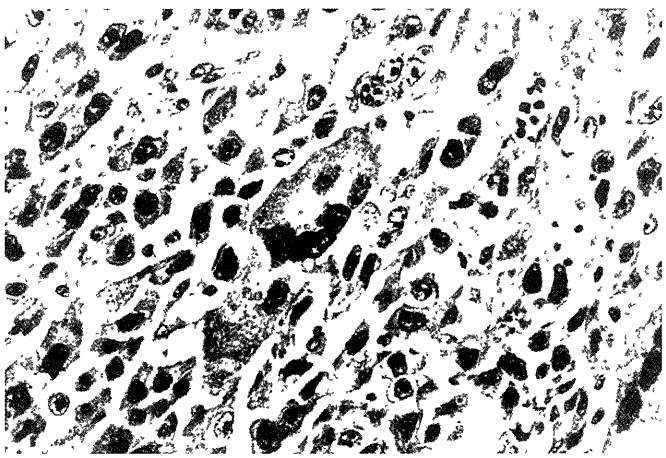

Figure 6. Histopathological examination of the autopsy specimen showing poorly differentiated hepatocellular carcinoma.

it (Figure 4). No free air was seen in the abdomen. Recurrent bleeding continued from the lesion, and the patient died of progressive hepatic failure four weeks

after initial presentation with upper gastrointestinal bleeding.

At autopsy, the liver was cirrhotic. A large mass measuring 12 x 9 cm in diameter encompassed a large cavity and involved the right and quadrate hepatic lobes (Figure 5). The tumor was adherent to the thickened duodenal wall and had eventually invaded through the duodenum to form a hepatoduodenal fistula. On the mucosal side of the duodenum, a giant deep ulcer, 6.5 x 3.4 cm in diameter, was apparent in the duodenal bulb. Microscopically, the tumor comprised poorly differentiated HCC (Figure 6).

DISCUSSION

Upper GI bleeding in patients with HCC is usually caused by variceal rupture, hemorrhagic gastritis or ulcers (9, 10), occasionally related to hemobilia (11). Direct extension of HCC into GI tract can also result in bleeding, but this is extremely rare (2, 6). HCC might extend to the stomach (2), duodenum (2, 4-8) and colon (12). Humbert et al. (4) reported in 1987 the first case of GI bleeding caused by direct duodenal invasion of HCC (4). To date, only 7 cases of HCC presenting with GI bleeding caused by direct invasion to the duodenum have been reported in the English literature (2, 4-8) (Table).

In all these reported cases, gross morphology of the primary liver tumors was exclusively of the massive type, with size ranging from 4 to 13 cm. Of note, 5 cases including ours had previously undergone TAE. Thus, duodenal involvement by contiguous HCC is more likely to develop in patients with relatively large massive-type HCC, particularly after TAE. Chen et al. (2) postulated a possible mechanism for the development of direct invasion of HCC to GI tract after TAE, that the HCC tumor could become adherent to GI tract due to surrounding inflammatory response secondary to TAE, with subsequent induction of direct invasion. The above investigators also indicated that residual viable tumor cells, which usually exist at the tumor periphery, could easily invade GI tract after TAE or intra-arterial chemotherapy (2). The present case had been also treated with PEIT, and we believe a causal association of such regional therapies with GI tract involvement by contiguous HCC.

Regarding endoscopic features of the duodenal lesions in 8 cases including ours, mass or polypoid lesion was seen in 4 cases, ulcer lesion in 2, SMT and ulcerated mass lesion in 1. In the present case, we noted a change in the endoscopic appearances of the duodenal tumors from SMT to crater-like ulcer lesion, throughout the clinical course. A review of literature disclosed various endoscopic features of duodenal involvement by HCC, probably reflecting differences in the stage of the disease including the degree of tumor invasion and growth. During endoscopy, blood clot (5, 6), active bleeding (4) or visible vessels (8) within the involved site were observed in 5 cases, which indicated the lesions as source of bleeding. Moreover, endoscopic biopsy, when performed, revealed the invasion of HCC. Thus, endoscopic examination, together with biopsy, is mandatory for proper diagnosis of such cases.

In our case, air cavity within the HCC tumor was noted on abdominal CT. Postmortem examination revealed hepatoduodenal fistula arising from duodenal invasion of HCC by direct contiguity. Berkelhammer et al. (12) documented intratumor air on the CT in a patient with massive HCC eroding into the ascending colon. In his case, the presence of hepatocolic fistula was demonstrated by water-soluble enema, which showed extravasation of the contrast medium from the colon into the liver. Thus, it is suggested that the presence of intratumor air on CT represents fistula formation resulting from direct tumor invasion to GI tract.

Among the 7 patients in whom the survival periods were described, 4 including ours died within 1 month and no patients survived longer than 6 months. Thus, the prognoses of patients with HCC who develop GI bleeding secondary to direct duodenal invasion seems to be extremely poor, presumably due to advanced stage of the disease, underlying liver cirrhosis and the lack of effective treatment (2). Several authors reported that TAE (7) or an external beam of radiotherapy (6) could successfully result in hemostasis, but severe hepatic failure accelerated by continuous GI bleeding precluded such aggressive therapies in our case.

In conclusion, we presented a rare case of GI bleeding caused by direct duodenal invasion of massive-type HCC after TAE and PEIT. CT finding of intratumor air, together with endoscopy and biopsy, was useful for the diagnosis of this unusual complication of HCC.

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