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Hepatogastric Fistula following Transcatheter Arterial Chemoembolization of Hepatocellular Carcinoma

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Key Words
Hepatogastric fistula · Transcatheter arterial chemoembolization · Hepatocellular carcinoma · Endoscopy

Abstract
Hepatogastric fistula (HGF) formation following transcatheter arterial chemoembolization (TACE) leads to increased morbidity and mortality. A 51-year-old Caucasian male with chronic hepatitis B virus-associated cirrhosis and unresectable hepatocellular carcinoma (HCC) presented to the Interventional Radiology Unit for TACE to achieve tumor necrosis. Following the procedure, the patient was admitted with symptoms of fever, epigastric and right upper quadrant pain secondary to the development of an abscess. The abscess was drained; however, an exceedingly rare HGF resulted that was favored to represent a direct invasion of HCC. HGF, the rare complication following TACE, leads to grave consequences and vigilant monitoring, for the development of this entity is recommended to reduce patient mortality. We present a case and literature review of HGF development following TACE for HCC.

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Introduction

Hepatocellular carcinoma (HCC) is the third leading cause of death from cancer worldwide and is the ninth leading cause of cancer-related deaths in the United States [1]. Hepatogastric fistula (HGF) development is a rare complication of transcatheter arterial

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chemoembolization (TACE) of the hepatic artery for HCC. TACE is performed as a palliative measure for unresectable malignant tumors to reduce pain and slow growth of the mass by producing vascular compromise leading to necrosis of the mass. Such tissue hypoxia can be destructive to normal tissue and can increase the tumor burden leading to metastatic disease [2]. An unfortunate complication of TACE is an abscess development that occurs in less than 1% of the cases [3]. It is hypothesized that the ischemic necrosis that follows the TACE procedure may partially be responsible for the occurrence of HGF [4]. The complications from this aberrant communication of visceral organs lead to rapid status decline and to patient opting for hospice care. We present a case and literature review of HGF following TACE, which was performed to provide palliative care for an unresectable hepatitis B virus-related HCC tumor.

Case Report

A 51-year-old Caucasian male with chronic hepatitis B virus-associated cirrhosis and biopsy-proven HCC was treated with TACE for an unresectable malignant liver mass. At his initial presentation, the patient complained of right upper quadrant pain, a 20-lb unintentional weight loss (initial weight: 180 lbs, weight at presentation: 160 lbs), and an epigastric mass. Physical examination showed a cachectic-appearing male with jaundice and hepatomegaly. The laboratory results were significant for anemia of chronic disease, elevated liver enzymes with a total bilirubin of 2.2 mg/dl, marked thrombocytopenia, and an elevated international normalized ratio of 1.72. The patient was Child Class B and had a Model for End-Stage Liver Disease (MELD) score of 21. An abdominal computed tomography (CT) scan showed a heterogeneous, hypervascular mass arising in the lateral segment of the lower left lobe of the liver (segments II and III) measuring 11.5 × 9.5 × 5.3 cm in size suggestive of HCC. His α-fetoprotein levels were markedly elevated. General surgery was consulted and found the mass to be unresectable. Their recommendations included palliative measures with TACE and pain management. The patient subsequently underwent TACE of the hepatic mass, which later was complicated by a liver abscess. Out of concern for infectious etiology, the hepatic abscess was drained by interventional radiology.

Approximately 6 months following the first TACE, the patient presented for his second TACE. At that time, he reported a recent history of melena and coffee ground emesis, which were suggestive of an upper gastrointestinal hemorrhage. Unfortunately, the patient could not accurately correlate the symptoms in relation to the first TACE. A gastroenterology consultation was requested, and the team suspected a fistulous connection between the HCC mass and the stomach, which was seen on the abdominal CT (fig. 1). The patient underwent esophagogastroduodenoscopy that revealed a 2-cm ulcer to the lesser curvature of the stomach communicating with the liver, forming a HGF (fig. 2). This ulcer and surrounding tissue were believed to represent recurrent HCC or metastatic HCC. Surgical consultation again recommended supportive care after considering the patient's advanced disease status and poor candidacy for surgical intervention. Gastroenterology recommended the use of proton pump inhibitors and the avoidance of nasogastric and orogastric tubes to prevent further complications while hospitalized. CT and esophagogastroduodenoscopy results along with poor prognosis secondary to the advanced disease were discussed with the patient, following which, the patient opted for hospice care.

Discussion

Direct invasion of HCC to adjacent organs is one of the most common routes of metastasis along with hematogenous and lymphatic spread [4]. The most common site of direct tumor invasion is the stomach followed by the duodenum and colon [5]. Most metastases to the gastrointestinal tract (GIT) are found incidentally secondary to their asymptomatic presentation, but bleeding from the upper GIT is the most common initial presentation [6, 7]. HGF following TACE is an extremely rare complication of the procedure. Careful patient selection is a must for the TACE procedure. Risk factors for the development of HGF include liver cirrhosis, local or regional radiation, previous TACE of the liver or stomach, large lesions from HCC which are close to the GIT, and hepatic abscess. Indications for TACE include: confirmed diagnosis of HCC, absence of extrahepatic metastases, targeted tumor involving 50% or more of the liver parenchyma, disease recurrence after potentially curative treatment, and if ablation is unfeasible [8, 9]. A further indication is given in a potential transplant recipient requiring bridge therapy to minimize the drop-off rate from the transplant list. Contraindications to TACE include: portal vein thrombosis, portal flow reversal, and Child Class C cirrhosis [10, 11]. Contraindications to the chemotherapeutic agent and anaphylactic reactions to the contrast media also remain to be considered.

When considering TACE as a therapy option, the metabolic status of the candidate must be evaluated. Serum creatinine must be ≤2 mg/dl, platelet count ≥50,000/mm^3, and prothrombin activity ≥50% [12]. Few case reports of HGF following TACE exist, and the mechanism is not clearly understood, with even less literature available concerning treatment options. While there is no widely accepted pathophysiologic mechanism for HGF development, a review of the literature suggests that a direct invasion of HCC to the stomach is more likely to develop in patients with a history of loco-regional treatment such as TACE or intra-arterial chemotherapy [13, 14]. As such, we can hypothesize that the direct tumor invasion might result from the adhesion of HCC after loco-regional treatment. TACE for HCC might induce an inflammatory reaction along with local tissue hypoxia in the proximity, which causes the serosal side of the stomach to become adherent to a tumor capsule [13, 15]. Park et al. [4] reported that the main factors for the direct invasion were growth pattern, tumor size, and location rather than a previous history of loco-regional treatment. In the case documented above, the patient was treated with repeated TACE, and there was a fistulous connection noted between the left lobe of the liver and the stomach following the procedure. All the factors discussed above and the abscess formation might have contributed to a direct gastric invasion by HCC and resulted in the formation of HGF.

Regardless of the etiology, this inappropriate communication between the stomach and the liver results in hepatogastric irritation and inflammation that leads to symptoms such as pain, hemorrhage, melena, and hematemesis. Closer surveillance is warranted in patients undergoing successive TACE or radiotherapy for HCC close to the GIT, as complications including fistula, abscesses, hemorrhage, and perforation can develop leading to devastating consequences. More studies are needed to indicate the potential benefits of routine surveillance with ultrasound or CT scan for an early detection of asymptomatic fistulas that represent disease metastasis. Quality of life and surgical risks should also be taken into consideration before undertaking additional procedures.

In conclusion, HGF secondary to an invasion by HCC is rare and should be included in the differential diagnosis of patients presenting with upper GIT bleed who have undergone TACE for advanced HCC.

Informed consent was obtained from the patient.

Disclosure Statement

The authors have nothing to disclose.

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Fig. 1. Abdominal CT scan showing a fistulous connection between the lesser curvature of the stomach and the liver (arrow).

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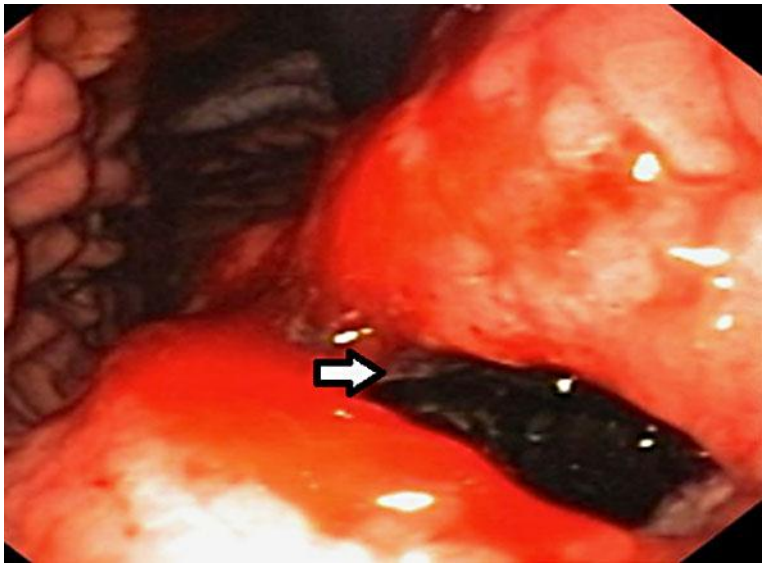

Fig. 2. Upper gastrointestinal endoscopy showing a protrusion of the tumor into the gastric lumen and the opening of a HGF (arrow).