Case Report

Intraductal migration of necrotic hepatocellular carcinoma: A possible cause of obstructive cholangitis after chemoembolization

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A B S T R A C T

Acute obstructive cholangitis due to the migration of necrotized tumor fragment(s) has been rarely reported after transarterial chemoembolization (TACE). We report an unusual case of it, which was demonstrated by computed tomography (CT) and endoscopic retrograde cholangiography. We suggest that in the setting of acute biliary obstruction after TACE with a CT-demonstrated new intraductal soft tissue lesion with or without a radiopaque portion, along with no or less visualization of a previous tumor located inside or near the duct, the possibility of intraductal migration of a necrotic tumor fragment should be considered. Both clinicians and radiologists should become familiar with this condition because it may be ignored or misinterpreted as biliary calculi.

Keywords: Carcinoma, hepatocellular; Chemoembolization, therapeutic; Cholestasis

Introduction

Transarterial chemoembolization (TACE) is the most widely used treatment for unresectable hepatocellular carcinoma (HCC). There are several well-known adverse effects following TACE, such as post-embolization syndrome, which manifests as transient fever and pain, hepatic ischemia, liver abscess, and biloma. Bile duct obstruction related to HCC is not common and has a reported incidence of 0.53%–9%. It is usually caused by intraductal tumor ingrowth, hemobilia, or extrinsic compression by the adjacent tumor. Acute obstructive cholangitis due to the migration of necrotized tumor fragment(s) has been rarely reported after TACE, and knowledge of its treatment is even more limited. Here, we report a case of obstructive cholangitis due to detachment of a necrotic tumor fragment and its migration into the common bile duct (CBD) after TACE for HCC with suspicious bile duct invasion, with its detailed clinical course and imaging findings.

Case Report

A 67-year-old male visited our institution complaining of abdominal discomfort lasting for several months. Past medical history was unremarkable, but laboratory findings revealed that he had a chronic infection with hepatitis B virus (positive to hepatitis B surface antigen and immunoglobin G antibodies to core antigen, negative to immunoglobin M antibodies to core antigen, serum hepatitis B virus DNA detected; 1.8 × 10^5 copies/mL). Dynamic liver computed tomography (CT) was performed, and there was a 9.4-cm mass showing hypervascularity and contrast washout in the right posterior section of the liver. The right intrahepatic ducts (IHDs) were positioned inside the mass and were mildly dilated, suggesting the possibility of direct ductal invasion by the tumor. HCC was diagnosed, and he underwent TACE.

Follow-up dynamic liver CT performed 3 months after the first TACE (Fig. 1) revealed an 8.8-cm-sized viable tumor with partial iodized oil uptake in the right posterior section of the liver, along with several new smaller tumors in both hepatic lobes. Both IHDs were dilated, with slight aggravation and irregularity of the right side, again suggesting recurred, ductal-invasive HCC. The portal vein was intact. There were no radiopaque lesions suggesting stones in the bile ducts. Laboratory examinations found normal values for serum total bilirubin and alkaline phosphatase (0.7 mg/dL and 123 IU/L, respectively) but serum C-reactive protein...
was mildly elevated (1.54 mg/dL). The patient was asymptomatic. Based on these findings, a second TACE was planned.

On angiography (Fig. 2), the tumor was found to be supplied from the right hepatic artery, the right inferior phrenic artery, and the right renal capsular artery. After superselection of each feeder with a 2.2 Fr microcatheter, continuous infusion of cisplatin (Ildong, Seoul, Korea) was performed for 15 minutes. The total amount of infused cisplatin was 120 mg. Then, an emulsion of 10 mL iodized oil (Lipiodol; Guerbet, Roissy, France) and 10 mL cisplatin was infused until the compact Lipiodol uptake of the tumor was complete. Next, each feeder was occluded by gelatin sponge particles (Gelfoam; Upjohn, Fort Lee, NJ, USA) until arterial flow stasis was achieved. The final angiogram showed compact Lipiodol uptake of the tumors without residual tumor staining. There
were no events during or immediately after the procedure.

After 2 weeks, the patient visited the emergency department of our institution complaining of acute abdominal pain. He had a mild fever of 37.6°C and elevation of total bilirubin (4.9 mg/dL), alkaline phosphatase (268 IU/L), and C-reactive protein (5.96 mg/dL). Acute cholangitis or cholecystitis was suspected. On CT (Fig. 3), there was a new 3 cm soft tissue lesion with a partial radiopaque portion in the distal CBD, along with diffuse dilatation of the upstream ducts. The soft tissue portion showed no enhancement. The possibility of biliary obstruction due to a migrated necrotic tumor fragment with retained Lipiodol was raised.

Considering the size and location of the lesion, endoscopic removal was planned. The patient underwent endoscopic retrograde cholangiography (ERC), and a filling defect with a similar size to the CT-demonstrated soft tissue lesion was noted in the distal CBD. The upstream ducts were all diffusely dilated (Fig. 4). Before lesion removal, placement of an endoscopic biliary drainage catheter was planned to decompress the dilated ducts. After 2 days, the patient underwent ERC again. The ductal dilatation was slightly improved, but there was still a floating filling defect in the CBD. After sphincterotomy and subsequent endoscopic papillary balloon dilatation using a 12 mm balloon, the lesion was removed with a basket. An ovoid and yellowish lesion was extracted. The pathologic diagnosis of the removed lesion was a severely necrotic HCC (Fig. 5). The patient’s symptoms resolved and his recovery was uneventful. Follow-up CT performed 7 days after the lesion removal showed markedly improved ductal dilatation with no visualization of any Lipiodol-retained soft tissue lesion in the CBD.

Discussion

The incidence of migration of a necrotic tumor fragment into the bile duct after TACE is not well known. Most cases occur after TACE for HCC with biliary invasion or intraductal tumor ingrowth. Ductal invasion with intraductal tumor ingrowth in HCC is uncommon, with a reported incidence of 1.2%–9%, and according to Kim et al, the incidence of intraductal necrotic tumor migration in biliary invasive HCC patients after TACE is 10.4%, which accounts for a very small subset of HCC patients. A considerable number of cases might have been misidentified as biliary stones or ignored in asymptomatic patients. The time interval between TACE and the onset of symptoms may vary, but acute cholestatic symptoms such as jaundice and abdominal pain occur less than 60 days after the TACE.

Ductal invasion with intraductal tumor ingrowth in HCC is one of the main reasons for obstructive jaundice in HCC patients. In almost all cases with intraductal tumor fragment migration after TACE, CT scans performed before TACE show evidence of bile duct invasion, such as irregularly dilated ducts passing through the tumor or intraductal protrusion of the tumor, and Park et al suggested that intraductal invasion would be a major predisposing factor to tumor migration after TACE. Rarely, it may also occur in patients without bile duct invasion because TACE induces marked ischemia in the tumor vascular bed and adjacent biliary tree.

Due to the ischemic effects of Lipiodol and gelfoam particles, tumors become necrotic and the intraductal tumor portion can detach from the main tumor and migrate into the duct. Because
the ductal epithelium underlying the intraductal tumor ingrowth is usually preserved and the intraductal tumor does not attach tightly to the duct,\(^1\) intraductal tumors that become necrotic after chemoembolization can easily detach from the main tumor and migrate into the bile duct.\(^1\)

CT scans can show a new soft tissue lesion with or without a radiodense portion, which suggests a migrated tumor with retained Lipiodol in the distal CBD. The CT attenuation of the lesion may vary, depending on the amount of Lipiodol accumulation. If there is compact Lipiodol uptake, it may mimic calculous biliary stones, and if there is no or sparse Lipiodol accumulation, it may show similar attenuation to that of the surrounding soft tissue.\(^1\)

The soft tissue portion of the lesion may show no or little enhancement, reflecting tumor necrosis and no vascular supply. In addition, previously visualized tumor or Lipiodol deposits located in the bile duct lumen may no longer be seen, which would correlate with the detachment of the tumor portion.

A percutaneous transhepatic or endoscopic approach can be used to remove the lesion, and they are both reported to be effective.\(^10,12\) However, there has been no study of their long-term clinical outcomes. In addition, according to Kim et al.,\(^10\) asymptomatic patients whose tumors spontaneously pass into the gastrointestinal tract can be kept under observation.

We suggest that acute biliary obstruction can occur after TACE, and if CT demonstrates a new intraductal soft tissue lesion with or without a radiopaque portion along with no or less visualization of the previous tumor, it may indicate the migration of a necrotic tumor fragment into the bile duct. Both clinicians and radiologists should become familiar with this condition because it may be ignored or misinterpreted as biliary calculi.

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**Fig. 4.** Endoscopic retrograde cholangiography images. (A) There is an oval-shaped filling defect in the distal common bile duct (CBD) (white arrowheads), with a size similar to that of the computed tomography-demonstrated soft tissue lesion. Upstream bile ducts are diffusely dilated, and there is a scanty amount of contrast medium passing into the duodenum (black arrowhead). An endoscopic drainage catheter was placed to decompress the bile ducts. (B) Sphincterotomy and subsequent endoscopic papillary balloon dilatation using a 12 mm balloon (white arrow) were performed. The floating filling defect is still visible in the CBD (white arrowheads). (C) After sphincterotomy, a basket (black arrow) was used to pull out the filling defect.

**Fig. 5.** (A, B) Endoscopic images obtained during endoscopic retrograde cholangiography. An ovoid-shaped, yellowish mass was extracted through the ampulla with the basket. (C) On microscopic analysis, there are no viable tumor cells and only necrotic materials. Complete coagulative necrosis of the hepatocellular carcinoma is confirmed (H&E stain, x200).
Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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