Acute Obstructive Cholangitis Complicated by Tumor Migration after Transarterial Chemoembolization: A Case Report and Literature Review

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Intraductal tumor invasion of hepatocellular carcinoma (HCC) is considered rare. Transarterial chemoembolization (TACE) is effective for tumor thrombus of HCC in the bile duct. However, a few cases of obstructive jaundice caused by migration of a tumor fragment after TACE have recently been reported. The aim of this study was to identify factors that affect tumor migration after TACE. At this writing, a review of the medical literature disclosed seven reported cases of biliary obstruction caused by migration of a necrotic tumor cast after TACE. We, herein, report on an additional case of acute obstructive cholangitis complicated by migration of a necrotic tumor cast after TACE for intrabiliary duct invasion of HCC, in a 71-year-old man. The tumor cast in the common bile duct was removed successfully using a basket during ERCP and was pathologically confirmed to be a completely necrotic fragment of HCC. The patient’s symptoms showed dramatic improvement. In summary, physicians should be aware of acute obstructive cholangitis complicated by tumor migration in a patient undergoing TACE. We suggest that an intrabiliary duct invasion would be a major predisposing factor of tumor migration after TACE and drainage procedures such as ERCP or percutaneous transbiliary drainage could be effective treatment modalities in these patients. (Korean J Gastroenterol 2014;63:171-175)

Key Words: Hepatocellular carcinoma; Biliary obstruction; Chemoembolization; Migration; Bile duct

INTRODUCTION

Transarterial chemoembolization (TACE) is one of the most common treatment modalities as a palliative or preoperative method for patients with advanced hepatocellular carcinoma (HCC). Common post TACE complications include postembolization syndrome (fever, abdominal pain, nausea, vomiting) and transient impairment of liver and kidney functions. Less frequently, ischemic liver failure may occur in patients with partial portal vein thrombosis or if TACE has not been selectively performed. Various complications of TACE have been reported, however, acute biliary obstruction due to migration of a tumor fragment after TACE is rare.

In previously reported cases, bile duct thrombosis (BDT) was one of the main reasons for development of obstructive jaundice after TACE. However, diagnosis is usually difficult, due to the low incidence rate, ignorance of this disease, and the difficulty of imaging diagnosis to find the BDT. The aims
of this study were to identify factors that affect tumor migration after TACE. Here, we describe a patient with acute obstructive cholangitis complicated by migration of a necrotic tumor cast after TACE for intrabiliary duct invasion of HCC and provide a review of the literature.

CASE REPORT

A 71-year-old man, who had been followed for alcoholic liver cirrhosis for 10 years, was admitted to our hospital for evaluation of a liver mass detected during HCC surveillance. The relevant laboratory results at the time of admission were as follows: white blood cell count, 4,400/mm³ (normal range, 4,000-10,800/mm³); hemoglobin, 14.1 g/dL; platelet count, 154,000/mm³ (normal range, 130,000-450,000/mm³); AST, 48 U/L (normal range, 7-38 U/L); ALT, 20 U/L (normal range, 6-42 U/L); ALP, 152 U/L (normal range, 39-117 U/L); GGT, 239 IU/L (normal range, 11-75 IU/L); total bilirubin, 2.18 mg/dL (normal range, 0.35-1.3 mg/dL); and serum albumin, 2.9 g/dL (normal range, 3.1-5.2 g/dL). Coagulation profiles were within normal limits. Serologic tests for hepatitis viruses A, B, and C were negative. The AFP serum level was 3,002 IU/mL (normal range, <5.8). Indocyanine green retention value at 15 minutes was 30.9%. Abdominal CT showed a hypervascular mass measuring 2.5 cm in diameter in segment IV, with partial tumor thrombosis in the left portal vein. On MRI, the left intra-hepatic bile duct was slightly dilated by tumor invasion (Fig. 1). These laboratory and imaging findings were consistent with HCC. Due to limited hepatic function, the patient was not a suitable candidate for surgical resection. Therefore, TACE was performed through the left hepatic arterial branch in segment IV without serious complications. Abdominal CT obtained 28 days after TACE showed a defective lipiodol uptake lesion measuring 1.8 cm in size in segment IV and lipiodol uptake of tumor thrombosis in the left intrahepatic bile duct (IHBD) (Fig. 2). Therefore, we considered performance of additional TACE. However, 45 days after TACE, he presented with epigastric pain and fever. His serum bilirubin level increased from 2.18 to 4.5 mg/dL. Abdominal CT showed acute obstructive cholangitis asso-

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Fig. 1. Hepatobiliary phase transverse T1-weighted MRI at the time of diagnosis shows a hepatocellular carcinoma (white arrow) measuring approximately 2.5 cm in segment IV of the liver, with invasion to the left portal vein and intrahepatic bile duct (black arrows).

Fig. 2. Abdominal CT scan obtained 28 days after transarterial chemoembolization. (A) Transverse section. (B) Coronal section. It shows newly a defective lipiodol uptake lesion measuring 1.8 cm in segment IV and lipiodol uptake (black arrow) of tumor thrombosis in the left intrahepatic bile duct.
Fig. 3. Abdominal CT scan obtained 45 days after transarterial chemoembolization. Lipiodol uptake of tumor thrombosis previously seen in the left intrahepatic bile duct has disappeared (A; white arrow) and migrated to the distal common bile duct (CBD) (B; black arrow). It shows acute obstructive cholangitis associated with a migrated lipiodolized tumor fragment in distal CBD.

Fig. 4. (A) ERCP shows an elongated filling defect (black arrow) in the lower part of the common bile duct (CBD) and a protruding mass like filling defect (white arrow) in the dilated left intrahepatic bile duct. (B) After a sphincterotomy, a dark green colored, friable material was extracted from the CBD. (C) The mass measured 2.5×1.0 cm in size, and was friable and dark green in color.

associated with a lipiodolized tumor fragment that had migrated into the distal common bile duct (CBD) (Fig. 3). One day later, an ERCP showed an elongated filling defect in the lower part of the CBD and a protruding mass like filling defect in the dilated left IHBD (Fig. 4A). After a sphincterotomy, a dark green colored, friable material was removed from the CBD (Fig. 4B, C). Histological examination showed that the material was completely coagulative necrosis of HCC. There were no viable tumor cells and only necrotic materials with bile. Silhouettes of a few hepatocytes with nucleoli are noted in the center area (Fig. 5). After removal of the necrotic tissue, he was free of symptoms, and his serum bilirubin level returned to normal. Later, the newly developed tumors at segment IV were treated successfully by additional TACE and the patient was followed up at the outpatient department.

DISCUSSION

Intraductal tumor invasion of HCC is considered rare. Obstructive jaundice in a patient with intraductal invasive HCC is an uncommon manifestation at the time of diagnosis, which usually occurs in later stage. Such cases are clinically classified as ‘icteric type hepatoma’. BDT is one of the main reasons for obstructive jaundice, and the previously reported incidence is 1.2-9%. The expected survival of patients with intraductal invasive HCC is significantly shorter than that of patients without bile duct invasion. However, not all patients with intraductal invasive HCC are terminally ill, and good palliation and occasional cure may be possible with proper management.10-16

The ideal treatment in these patients is surgical resection. However, because tumors with bile duct invasion are gen-
erally large and located near the hepatic hilum, most tumors are not resectable, and such patients usually have poor hepatic functional reserve. According to some reports, TACE is effective as an alternative treatment strategy and should be tried as a first choice of treatment. \textsuperscript{15,17} TACE induces marked ischemic necrosis in bile duct thrombus as well as HCC and the BDT is easily detached and dropped into CBD after TACE. \textsuperscript{18} In our case, sequential abdominal CT scans performed after TACE showed a lipiodolized tumor cast in the left IHBD and subsequent migration into the distal CBD. In addition, histological examination showed that the lipiodolized tumor cast was a necrotic fragment of HCC. This finding demonstrates that TACE has an apparent therapeutic effect and can achieve complete necrosis in the intraductal tumor thrombus. A few cases of detachment of a necrotic tumor from the bile duct wall after TACE, which migrated into the distal CBD and caused obstructive jaundice, have been reported. Our review of the literature identified eight apparent cases (including ours) of obstructive jaundice caused by tumor fragments from HCC after TACE (Table 1). \textsuperscript{5-9} The patients (including ours) ranged in age from 62 to 82 years (mean age, 70.5 years) and consisted of five men and three women. Most patients showed bile duct invasion (six of the eight patients) and bile duct dilatation (six of the eight patients) on initial CT finding. The tumor was located mainly in segment IV or near the hilum. Five patients had undergone TACE more than two times in the past. Days to biliary obstruction due to tumor migration after TACE were 7 to 60 (means, 26.3). All patients were treated successfully by ERCP (seven patients) or percutaneous transbiliary drainage (PTBD, one patient). However, the long-term course of each patient was not described, therefore, no detailed information was provided.

We suggest that an intrabiliary duct invasion would be a major predisposing factor of migration of a tumor fragment after TACE and drainage procedures such as ERCP or PTBD are effective treatment modalities in such patients. However, because TACE induces marked ischemic necrosis to the adjacent biliary tree as well as the tumor vascular bed, it may also occur in a patient without bile duct invasion. \textsuperscript{5} Otherwise, migration of a tumor fragment appears to be correlated with the total number of TACE, bile duct dilatation on initial CT finding.

**Table 1. Summary of Reported Cases of CBD Obstruction Caused by Tumor Thrombus after TACE in HCC**

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Author</th>
<th>Age (yr) /sex</th>
<th>Location (size, cm)</th>
<th>Bile duct dilatation</th>
<th>Bile duct invasion</th>
<th>TACE (total, n)</th>
<th>Days to obstruction after TACE</th>
<th>Treatment modalities</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Spahr et al. \textsuperscript{5}</td>
<td>78/M</td>
<td>Segment IV (5)</td>
<td>Rt IHBD</td>
<td>No</td>
<td>1</td>
<td>50</td>
<td>ERCP</td>
<td>Successful</td>
</tr>
<tr>
<td>2</td>
<td>Hiraki et al. \textsuperscript{6}</td>
<td>69/M</td>
<td>Medial segment (1.7)</td>
<td>Lt IHBD</td>
<td>Lt IHBD</td>
<td>2</td>
<td>18</td>
<td>ERCP</td>
<td>Successful</td>
</tr>
<tr>
<td>3</td>
<td>Choi et al. \textsuperscript{7}</td>
<td>62/M</td>
<td>Segment III, IV</td>
<td>Proximal CHD</td>
<td>Proximal CHD</td>
<td>1</td>
<td>14</td>
<td>PTBD</td>
<td>Successful</td>
</tr>
<tr>
<td>4</td>
<td>Choi et al. \textsuperscript{8}</td>
<td>70/M</td>
<td>Rt lobe</td>
<td>Pt hepatic duct NA</td>
<td>Lt hepatic duct</td>
<td>3</td>
<td>60</td>
<td>ERCP</td>
<td>Successful</td>
</tr>
<tr>
<td>5</td>
<td>Okuda et al. \textsuperscript{9}</td>
<td>61/F</td>
<td>Segment IV (1.5)</td>
<td>Lt IHBD</td>
<td>Lt IHBD</td>
<td>3</td>
<td>7</td>
<td>ERCP</td>
<td>Successful</td>
</tr>
<tr>
<td>6</td>
<td>Okuda et al. \textsuperscript{9}</td>
<td>82/F</td>
<td>Hilum (4)</td>
<td>Rt IHBD</td>
<td>Rt IHBD</td>
<td>4</td>
<td>10</td>
<td>ERCP</td>
<td>Successful</td>
</tr>
<tr>
<td>7</td>
<td>Okuda et al. \textsuperscript{9}</td>
<td>71/F</td>
<td>Multiple, both lobes</td>
<td>NA</td>
<td>Rt hepatic duct</td>
<td>8</td>
<td>7</td>
<td>ERCP</td>
<td>Successful</td>
</tr>
<tr>
<td>8</td>
<td>Present case</td>
<td>71/M</td>
<td>Segment IV (2)</td>
<td>Lt IHBD</td>
<td>Lt IHBD</td>
<td>1</td>
<td>45</td>
<td>ERCP</td>
<td>Successful</td>
</tr>
</tbody>
</table>

CBD, common bile duct; TACE, transarterial chemoembolization; HCC, hepatocellular carcinoma; Rt, right; Lt, left; NA, not available; IHBD, intrahepatic bile duct; CHD, common hepatic duct; PTBD, percutaneous transbiliary drainage.
ing, and tumor location.

TACE is generally contraindicated for patients with hyperbilirubinemia. In addition, HCC in patients with hyperbilirubinemia is often overlooked with terminal illness. However, as seen in the cases, good palliative and occasional cure may be possible with proper management such as ERCP or PTBD in patients with obstructive jaundice caused by migration of a tumor fragment. Several recent reports have demonstrated an association of effective biliary drainage achieved by use of an appropriate biliary drainage procedure in patients with obstructive jaundice caused by HCC with an improvement in survival. However, evidence of the usefulness of prophylactic biliary drainage in patients with biliary obstruction due to migration of a tumor fragment has been insufficient. Therefore, we think that biliary drainage should be considered in cases involving development of a symptomatic migrated tumor. In our review of the literature, although the long-term course of each patient was not described, effective biliary drainage would affect clinical outcomes by improving Child-Turcotte-Pugh class and allowing additional treatment for HCC.

In summary, intrabile duct invasive HCC is considered rare and TACE as the alternative treatment strategy could be effective in non resectable tumors. Physicians caring for patients treated with TACE should be aware of acute obstructive cholangitis complicated by tumor migration. As seen in the literature review, we suggest that an intrabile duct invasion would be a major predisposing factor of tumor migration after TACE and drainage procedures such as ERCP or PTBD are effective treatment modalities in these patients. However, it remains undetermined due to the limited number of patients. Additional study is required in order to evaluate clinical outcomes of TACE in patients and to identify factors that could affect tumor migration.

REFERENCES


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