

Case Report

Acute Obstructive Jaundice Complicated by Sloughing of Intraductal Tumor Thrombus in Hepatocellular Carcinoma after Transarterial Chemoembolization: Two Case Reports and Literature Review

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Received: 07 May 2020

Accepted: 27 May 2020

Published: 08 June 2020

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1. Abstract

Transarterial chemoembolization (TACE) is relatively useful for tumor thrombus of HCC. Still, certain infrequent side effects and complications, such as obstructive jaundice, may occur after TACE. Herein, we reported two cases of patients with acute obstructive jaundice complicated by excretion of necrotic bile duct tumor thrombus after transarterial chemoembolization (TACE). After Percutaneous Transhepatic Cholangiography (PTCD) or ERCP, and the patients gradually recovered.

2. Keywords: Hepatocellular carcinoma; Biliary obstruction; Transarterial chemoembolization; Bile duct tumor thrombus; Obstructive jaundice

3. Introduction

Bile Duct Tumor Thrombus (BDTT) of hepatocellular carcinoma (HCC) is a rare entity [1], with poor prognosis (less than three months). In patients who undergo palliative treatment, the average survival time is 3-13 months [2-7]. Transarterial chemoembolization and radiotherapy are the best treatment options for HCC with BDTT [2]. Transarterial chemoembolization (TACE) is relatively effective for tumor thrombus of HCC in the bile duct. Yet, only a few cases of obstructive jaundice caused by migration of a tumor fragment after TACE have been reported. Compared to obstructive jaundice caused by direct invasion of bile duct cancer thrombus, jaundice caused by the fallen-off bile duct cancer thrombus after TACE is rarer; however, if handled properly, it may have a better prognosis than the former one. Thus, it is crucial to distinguish the type of obstructive jaundice in order to provide better prognosis and treatment. Herein, we reported two cases of patients with acute obstructive jaundice complicated by excretion of necrotic bile duct tumor thrombus after TACE. In order to alleviate obstructive jaundice, Percutaneous Transhepatic Cholangiography (PTCD) or Endoscopic Retrograde Cholangiopancreatography (ERCP) was performed timely, and the patients gradually recovered.

4. Case Presentation

4.1. Case 1

A 48-year-old Asian male consulted our institute due to pain in the upper abdomen that lasted for a few months. Physical examination revealed mild tenderness and rebound pain in the right upper abdomen. Laboratory test indicated the following: total bilirubin of 28.5 $\mu\text{mol/L}$, alanine aminotransferase of 151U/L, glutamic oxaloacetylase of 115U/L and alpha-fetoprotein (AFP) of 1750ng/ml. Abdominal Magnetic Resonance Imaging (MRI) results showed hepatic masses compatible with HCC (10.0 \times 8.0 cm in segment V and VIII) with the right branch of the portal vein and intrahepatic bile duct invasion. The liver function of the patient was Child-Pugh class B, and tumor stage was BCLC stage C. After multidisciplinary discussion, we found that the mass was unresectable. The patient subsequently underwent two TACE procedures.

About 3 weeks, the patients with obstructive jaundice revisited our hospital. Ultrasound showed hyper echoic lesions at the lower end of the common bile duct, and dilatation of the common bile duct and intrahepatic bile duct. Abdominal plain CT scan showed that lipiodol was deposited

in the right liver and hilar lesions; the left intrahepatic bile duct and common bile duct were significantly dilated, and dot-like high-density lesions were seen at the lower end of the common bile duct, thus suggesting that the bile duct cancer thrombus fell off and caused obstructive jaundice (Figure 1). Laboratory suggested high total bilirubin(193 $\mu\text{mol/L}$).

In order to alleviate obstructive jaundice, percutaneous transhepatic cholangiography (PTCD) was performed under the B-ultrasonic localization. The patient's bilirubin decreased after drainage of intrahepatic and extra hepatic bile ducts for 10 days. The patient then underwent an additional TACE. At last follow up (6 months), the patient was still alive.

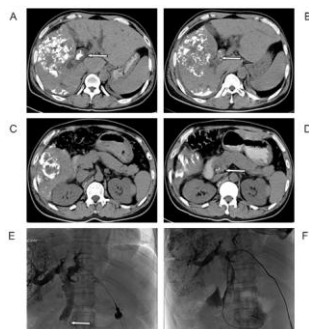


Figure 1: (case 1). (A, B) Abdominal plain CT before TACE showing cancer thrombus containing lipiodol duct (white arrow) in the upper common bile duct.. (C) No mass was observed in the lower end of the common bile duct before TACE. (D) Approx. 3 weeks after TACE, the bile duct cancer thrombus dropped to the lower end of the common bile duct (white arrow). (E, F) The cholangiography image showed a filling defect at the lower end of the common bile duct (white arrow) and placement of internal and external drainage tube.

4.2. Case 2

A 48-year-old Asian female was hospitalized in the local hospital 2 months ago due to abdominal pain and was consequently diagnosed with primary liver cancer. Laboratory test results were all normal, except for alpha-fetoprotein (AFP) that was $>20000.0\text{ng/mL}$. MRI results showed multiple lesions in the liver, the largest in the IV segment (7.5 \times 6.7 cm) with the left branch of the portal vein and intrahepatic bile duct invasion (Figure 2). After multidisciplinary consultation, it was decided that TACE should be performed after stereotactic radiotherapy of portal vein tumor thrombus and adjacent liver tumor area. The patient subsequently underwent four times TACE and radioactive particles implantation.

After treatment, her laboratory test indicated the following: total bilirubin of 91 $\mu\text{mol/L}$, alanine aminotransferase of 78U/L, and glutamic oxaloacetylase of 133U/L. Three days post-TACE, abdominal plain CT scan showed dot-like high-density lesions at the lower end of the common bile duct, suggesting that the bile duct cancer thrombus fell off and caused obstructive jaundice (Figure 3).

For obstruction of bile duct cancer thrombus, ERCP and internal drainage of common bile duct were performed. During ERCP operation,

we tried to get the tissue of bile duct tumor thrombus, but the tissue fell into the intestine. Consequently, her laboratory test results showed: total bilirubin of 36.8 $\mu\text{mol/L}$, alanine aminotransferase of 49U/L, and glutamic oxaloacetylase of 39U/L. considering that the patient recovered well after the operation, she was discharged from the hospital.

One month later, the patient consulted the hospital due to severe pain in the abdomen. Laboratory test results showed: total bilirubin of 20.7 $\mu\text{mol/L}$, alanine aminotransferase of 30U/L, glutamic oxaloacetylase of 17U/L, C-reactive protein 79.1mg/l, white blood cell count $6.5\times 10^9 / \text{L}$, procalcitonin 1.19ng/ml, and D-dimer 5230 $\mu\text{g} / \text{L}$.The abdominal enhanced CT showed free gas in the right subphrenic and gallbladder fossa that indicated on the perforation of the digestive tract, which was considered first (Figure 3). A 7F drainage tube was then placed under the guidance of ultrasound, and about 2ml of light yellow liquid was extracted for examination. We infused methylene blue 20mg into the stomach tube; no liquid was detected in the abdominal cavity, which suggested there was no perforation of the digestive tract. Finally, the patient was diagnosed with suppurative biliary perforation as a complication of ERCP. After treatments, the patient gradually recovered and was discharged 5 days later. The patient underwent conservative treatment. At last follow up (18 months), the patient was still alive.

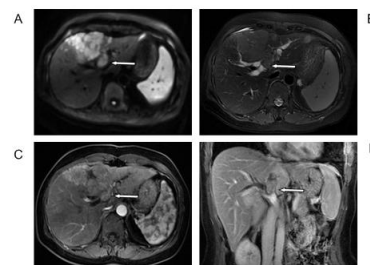


Figure 2: (case 2).Diffusion-weighted image (A), T2 weighted image (B), and enhanced magnetic resonance image (C, D) showing left liver lobe mass (black arrow), with intrahepatic bile duct invasion (white arrow).

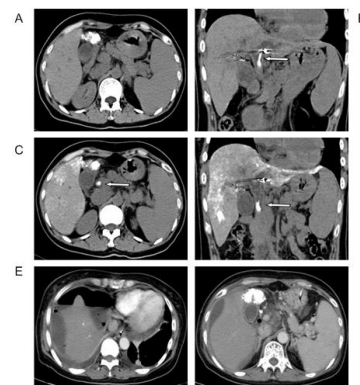


Figure 3: Case 2 : (A, B) Abdominal plain CT before TACE showing cancer thrombus containing lipiodol (white arrow) in the common bile duct. (C, D) Abdominal plain CT after TACE suggested that the bile duct cancer thrombus dropped to the lower end of the common bile duct (white arrow). (E, F) The abdominal enhanced CT showed free gas in the right subphrenic and gallbladder fossa (black arrow).

5. Discussion

Intraductal tumor invasion of HCC is a relatively rare event. Obstructive jaundice in a patient with intraductal invasive HCC is an uncommon manifestation at the time of diagnosis, which usually occurs in a later stage [8]. The expected survival of patients with intraductal invasive HCC is significantly shorter than that of patients without bile duct invasion. Moreover, the complication of obstructive jaundice resulting from the sloughing of intraductal tumor thrombus of hepatocellular carcinoma after transarterial chemoembolization is very uncommon.

TACE induces marked ischemic necrosis in bile duct thrombus as well as HCC. Yet, during this procedure, the BDTT can easily detach and fell off into the common bile duct (CBD) [9]. Histological examination performed in previous studies have shown that the lipiodolized tumor cast is a necrotic fragment of HCC, which further suggests that TACE has an apparent therapeutic effect on intraductal tumor thrombus [10-15].

Main intraductal invasion and complete necrosis in the intraductal tumor thrombus should be considered as major predisposing factors of tumor fragment migration. In a previous study, sequential abdominal CT scans performed after TACE showed a lipiodolized tumor cast in the left intrahepatic bile duct and subsequent migration into the distal CBD. In our patients, the migration of a tumor fragment was analyzed using abdominal CT, precisely coronal CT images. In addition, MR imaging is useful for the diagnosis of biliary tumor thrombi from HCC and for evaluating the extension of thrombi and biliary hemorrhage [16]. In these two patients, left and right branches of the hepatic duct and common hepatic duct were invaded by the tumor; after which MR images showed complete necrosis in the intraductal tumor thrombus.

Drainage procedures, such as ERCP or PTCD, are effective treatment modalities for such patients [10]. In our first case, PTCD was performed under the B-ultrasonic localization, and the prognosis was good. In the second case, we tried to obtain the tissue of bile duct tumor thrombus during ERCP operation, but the mass fell into the intestine. Despite ERCP and internal drainage of the common bile duct, suppurative perforation of the bile duct occurred. This suggests that combined internal and external drainage may be more effective than internal drainage alone.

In summary, the possibility of tumor thrombus migration should be considered when acute obstructive jaundice occurs after TACE. Intraductal invasion and complete necrosis in the intraductal tumor thrombus should be considered as major predisposing factors of tumor fragment migration. Abdominal CT can be used as the primary diagnostic method, mainly to observe the displacement of lipiodol tumor thrombus. Drainage procedures such as ERCP or PTCD are effective treatment modalities for such patients.

6. Ethics Statement

Clinical data was obtained from Second Affiliated Hospital of Zhejiang University School of Medicine with written consent of each individual and approved by the Research Ethics Board of the Second Affiliated Hospital of Zhejiang University. Data were collected anonymously and the clinical study was carried out in accordance with the Declaration of Helsinki.

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