

CHINESE MEDICAL SCIENCES JOURNAL

CASE REPORT

Sclerosing Cholangitis after Transcatheter Arterial Chemoembolization: a Case Report

Kai Qu¹, Chang Liu^{1*}, Qi-fei Wu¹, Bo Wang¹, Aasef Mohamed Ali Mansoor¹,
Hao Qin², Qiang Ma², and Ya-min Liu²

¹Department of Hepatobiliary Surgery, ²Department of Cardiovascular Intervention, the First
Affiliated Hospital, Medical School of Xi'an Jiaotong University, Xi'an 710061, China

Key words: sclerosing cholangitis; transcatheter arterial chemoembolization; bile duct;
complication; treatment

SCLEROSING cholangitis represents progressing jaundice or/and paroxysmal symptom of cholangitis, finally developing to end-stage of liver disease. When compared with primary sclerosing cholangitis (PSC), there are no apparent differences in pathology and clinical manifestation in secondary sclerosing cholangitis (SSC). But unlike PSC, SSC always has underlying causes, the most common being biliary obstruction, surgical trauma and ischemic injury of bile duct during liver transplantation.^{1,2} Repeated transcatheter arterial chemoembolization (TACE) leading to progressive SSC was rarely reported. Because of its rapid and irreversible progression, once SSC begins, it is difficult to deal with. Therefore, clinicians need to pay more attention to it.

CASE DESCRIPTION

A 23 years old man on physical examination was found to have a neoplastic lesion in the left liver lobe and alpha-fetoprotein (AFP) was 567.3 µg/L on May 2007. Whereafter, left lobe resection was performed and pa-

thology confirmed it was a primary hepatocellular carcinoma (Stage II). One month after surgery the patient was followed up. His AFP level was significantly elevated at 443.0 µg/L, but no positive signs were found in CT scans. Considering hepatic tumor recurrence, we advised this patient to undergo hepatic arterial infusion.

After selective hepatic angiography, chemotherapeutic agents (epirubicin 60 mg and fluorodeoxyuridine 1.25 g dissolved into 150 mL saline solution) were injected. No fever, chills, abdominal pain, diarrhea and jaundice were observed after the procedure. The patient totally underwent another two interventional therapy procedures with a similar approach performed by the same professional radiologist (Table 1). Thirty months after surgery, we performed the 4th TACE and injected emulsion (epirubicin 50 mg+fluorodeoxyuridine 1.0 g+iodized oil 15 mL) and gelfoam particles (diameter, 500-1000 µm) for abnormal staining seen in the right hepatic lobe and the caudate lobe (Fig. 1).

One month after the 4th TACE, fever and progressive aggravating jaundice were observed in this patient. White blood cell count was elevated and AFP was 240 µg/L. Cholestasis parameters including alkaline phosphatase (1951.4 U/L), γ-glutamyl transpeptidase (828 U/L), total bilirubin (425.8 µmol/L), and direct bilirubin (175.2 µmol/L) were significantly elevated. Autoimmune parameters such

Received for publication November 25, 2010.

*Corresponding author Tel: 86-29-85263190, Fax: 86-29-85263190,
E-mail: eyrechang@126.com

Table 1. Interventional treatment for four times

No.	Time (mon)	AFP level (μg/L)	DSA presentation	Interventional therapy
1	1	433.0	Right hepatic artery was normal and no tumor staining was seen	HAI (FUDR 1.25 g+Epi 60 mg)
2	17	620.4	Right hepatic artery was normal and no tumor staining was seen	HAI (FUDR 1.25 g+Epi 60 mg)
3	26	313.9	Right hepatic artery was thinner and abnormal staining was seen in the right lobe (Fig. 1A)	HAI (FUDR 1.0 g+Epi 40 mg)+TACE (Epi 20 mg+iodized oil 5 mL)
4	30	634.9	Right hepatic artery was thinner, and abnormal staining was seen in the right and the caudate lobe (Fig. 1C)	TACE (FUDR 1.0 g+Epi 50 mg+iodized oil 15 mL)+gelfoam particles

AFP: alpha fetoprotein; DSA: digital subtraction angiography; HAI: hepatic arterial infusion; FUDR: fluorodeoxyuridine; Epi: epirubicin; TACE: transcatheter arterial chemoembolization.

as antinuclear antibody, smooth muscle antibody, anti-mitochondrial antibody and perinuclear antineutrophil cytoplasmic antibodies were all negative. CT scans after the 4th TACE showed multiple round lesions with central necrosis (Fig. 2). Endoscopic retrograde cholangiopancreatography (ERCP) suggested diffuse intrahepatic and extrahepatic bile duct occlusions and rarefaction of the small bile ducts (Fig. 3A). Pancreatic ducts were entirely normal. Histological findings of needle biopsy of liver showed that there was an inflammatory response of infiltrated lymphocytes and plasma cells and fibroid degeneration in the portal regions. Cholestasis with interlobular bile duct proliferation was also observed (Fig. 4).

Ursodeoxycholic acid (UDCA) (10 mg/kg body weight) and antibiotics were used in our patient. To relieve jaundice of this patient, we performed endoscopic nasobiliary drainage (ENBD) and flushing of the bile duct with a continuous infusion

of saline solution. After ENBD, both clinical manifestation and biochemical values of this patient were mitigated (Fig. 5). The patient was discharged on the 15th day after removed ENBD tube and with remarkable improvement of bile duct stricture (Fig. 3B). A seventeen months follow-up of patient showed that, at present, he is in a relatively stable condition without clinical sign of hepatic failure.

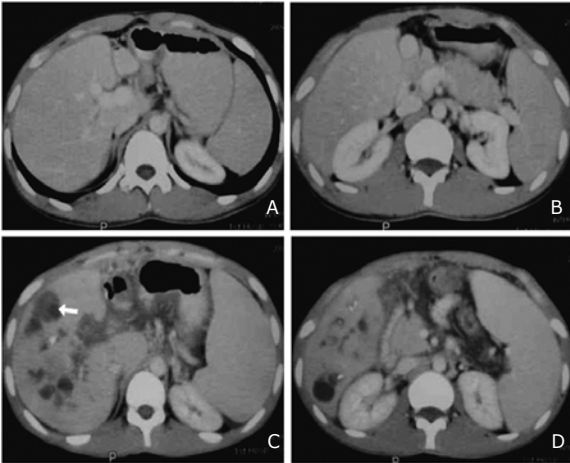


Figure 2. CT scan images pre- and post-4th TACE.
A, B. Transverse CT images before the 4th TACE are normal.
C, D. Transverse CT images one month after the 4th TACE show multiple low-density lesions with sharp margin in the hepatic parenchyma (the size of biggest one is 3.3 cm×2.5 cm, arrow).

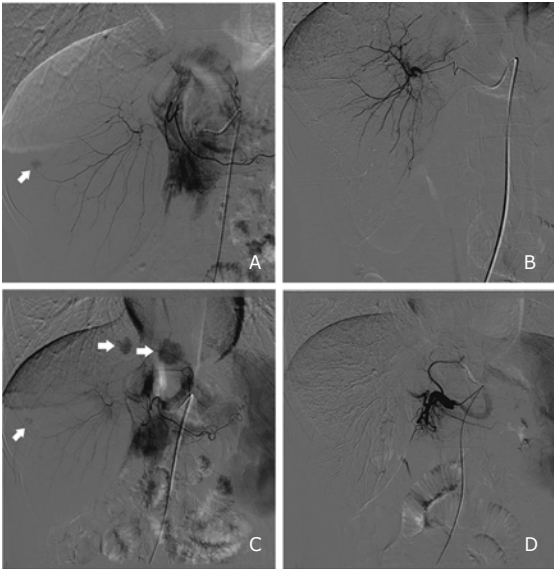


Figure 1. DSA presentations of the 3rd and 4th TACE.
A. Abnormal staining was seen in the right lobe in the 3rd TACE (arrow).
B, D. Presentations of hepatic angiography after the 3rd and 4th TACE, respectively.
C. Abnormal staining was seen in the right hepatic lobe and the caudate lobe in the 4th TACE (arrows).

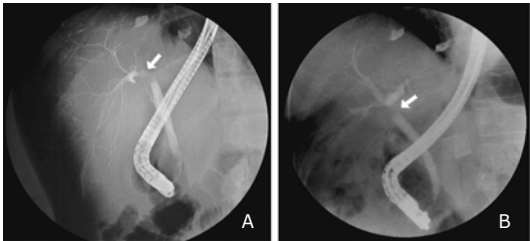


Figure 3. Endoscopic retrograde cholangiopancreatography (ERCP) shows common hepatic duct at the level of the hilum denotes a stricture (about 0.5 cm in length, arrow), and intrahepatic bile ducts are thin and their route is stiffened (A). ERCP shows the stricture becomes wider after endoscopic nasobiliary drainage (B, arrow).

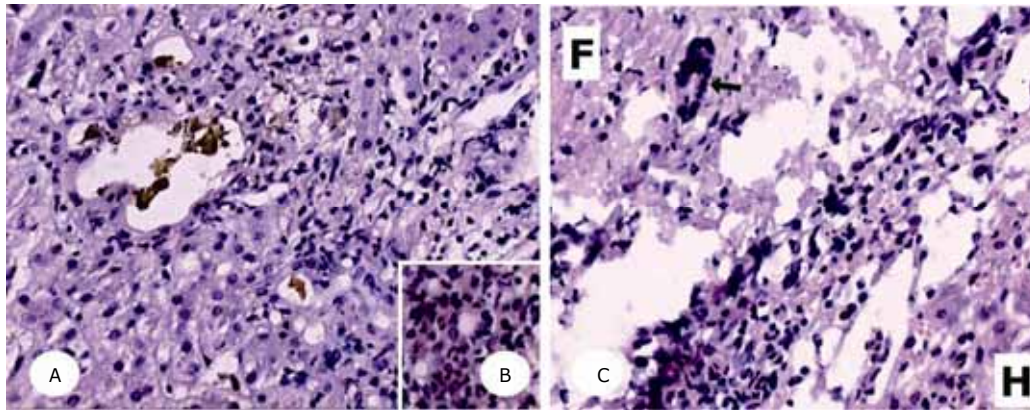


Figure 4. Histological findings of hepatic biopsy.

A. A bile duct with a mixed inflammatory infiltration and cholestasis. HE $\times 200$

B. The magnified image depicts interlobular ducts of the biopsy sample which are surrounded by inflammatory cells. HE $\times 400$

C. Portal fibrosis with periductular fibrosis (arrow) and inflammatory response of the portal region (F: fibrosis; H: hepatocyte).

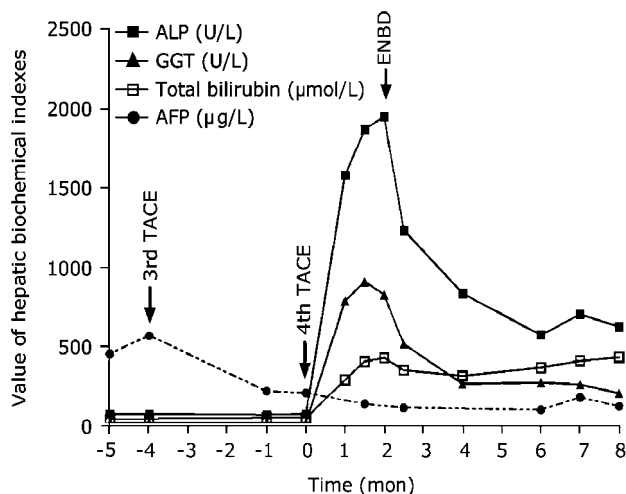


Figure 5. Change of values of hepatic biochemical indexes before and after the 4th TACE.

Serum levels of alkaline phosphatase (ALP) and γ -glutamyl transpeptidase (GGT) rapidly rise after the 4th TACE, and level of bilirubin is also elevated but less pronounced than ALP and GGT. Hepatic biochemical values were significantly decreased after endoscopic nasobiliary drainage (ENBD) performed.

DISCUSSION

Since 1976 Goldstein reported about how to treat malignant tumors of the liver by TACE, it has been accepted as the primary approach of non-operative treatment. Increased number of complications with the wide use of TACE gradually attracted people's attention. Other than the common post-embolization syndrome, sclerosing cholangitis secondary to TACE being the most difficult to deal with was rarely reported.^{3,4} Review of the literature, only Richardet *et al*⁵ has reported two cases of sclerosing

cholangitis after TACE whose clinical presentation and images are similar to us.

The pathogenesis of SSC is still unknown, but ischemic injury caused by damage of the peribiliary capillary plexus during TACE procedure may be the fundamental cause.⁶ Animal experimental studies showed that occlusion of arteries less than 200 μm in diameter rather than larger arteries may cause ischemic cholangiopathy.^{7,8} Some clinical survey showed that a few predisposing factors of this patient such as history of hepatocellular carcinoma without cirrhosis, repeated TACE procedures and prior liver resection lead to high risk of bile duct complications.^{9,10} Interestingly, all of these predisposing factors were related with microvascular abnormality. In the following TACE treatment, embolic agent acted as an embolus and contributed to ischemic injury of the peribiliary capillary plexus that developed sclerosing cholangitis finally.

So far, therapy options for SSC patients are limited and continuous drainage of bile duct is the key treatment. Endoscopic therapy including ENBD as an effective method of palliation is recommended¹¹ and was also proved by this case. Clinical manifestation and biochemical values usually improve after the foregoing treatment. Therefore although endoscopic treatment will only improve liver function temporarily, but it should be considered as a primary treatment protocol even if we are unsure if it has any beneficial effect on the disease prognosis. Complications with biliary tract infection should be treated with antibiotics and doses should be high enough that an effective concentration is maintained in the bile duct. Besides high-dose UDCA seems reasonable in some clinical drug trials.¹² For this patient, long-term treatment of high-dose UDCA combined with ENBD had showed good effect.

REFERENCES

1. Ruemmele P, Hofstaedter F, Gelbmann CM. Secondary sclerosing cholangitis. *Nat Rev Gastroenterol Hepatol* 2009; 6:287-95.
2. Abdalian R, Heathcote EJ. Sclerosing cholangitis: a focus on secondary causes. *Hepatology* 2006; 44:1063-74.
3. Xia J, Ren Z, Ye S, et al. Study of severe and rare complications of transarterial chemoembolization (TACE) for liver cancer. *Eur J Radiol* 2006; 59:407-12.
4. Sakamoto I, Iwanaga S, Nagaoki K, et al. Intrahepatic biloma formation (bile duct necrosis) after transcatheter arterial chemoembolization. *Am J Roentgenol* 2003; 181: 79-87.
5. Richardet JP, Lons T, Sibony M, et al. Secondary sclerosing cholangitis and chemoembolization with lipiodol. *Gastroenterol Clin Biol* 1994; 18:168-71.
6. Kobayashi S, Nakanuma Y, Terada T, et al. Postmortem survey of bile duct necrosis and biloma in hepatocellular carcinoma after transcatheter arterial chemoembolization therapy: relevance to microvascular damages of peribiliary capillary plexus. *Am J Gastroenterol* 1993; 88:1410-5.
7. Deltenre P, Valla DC. Ischemic cholangiopathy. *J Hepatol* 2006; 44:806-17.
8. Kemeny MM, Battifora H, Blayney DW, et al. Sclerosing cholangitis after continuous hepatic artery infusion of FUDR. *Ann Surg* 1985; 202:176-81.
9. Chung JW, Park JH, Han JK, et al. Hepatic tumors: Predisposing factors for complications of transcatheter oily chemoembolization. *Radiology* 1996; 198:33-40.
10. Yu JS, Kim KW, Jeong MG, et al. Predisposing factors of bile duct injury after transcatheter arterial chemoembolization (TACE) for hepatic malignancy. *Cardiovasc Intervent Radiol* 2002; 25:270-4.
11. Alazmi WM, McHenry L, Watkins JL, et al. Chemotherapy-induced sclerosing cholangitis: long-term response to endoscopic therapy. *J Clin Gastroenterol* 2006; 40:353-7.
12. Lindor KD, Kowdley KV, Luketic VA, et al. High-dose ursodeoxycholic acid for the treatment of primary sclerosing cholangitis. *Hepatology* 2009; 50:808-14.