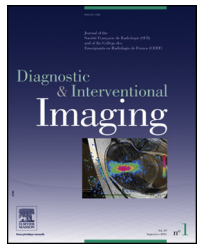
Diagnostic and Interventional Imaging (2015) **96**, 1169—1175



ORIGINAL ARTICLE / *Technical*

Biliary complications of arterial chemoembolization of hepatocellular carcinoma

E. Dhamija, S.B. Paul*, S.R. Gamanagatti, S.K. Acharya

Departments of Radio Diagnosis and Gastroenterology, All India Institute of Medical Sciences, 110 029 New Delhi, India

KEYWORDS
Hepatocellular carcinoma (HCC);
Transarterial chemoembolization (TACE);
Biliary complications;
Biloma

Abstract
Rationale and background: Transarterial chemoembolization (TACE) is the most frequently used palliative therapy for unresectable hepatocellular carcinoma (HCC). It is a safe and effective procedure with few major and minor complications. Rarely, biliary complications are also encountered following TACE. The goal of our study was to investigate the incidence and the presentation of biliary complications following TACE in patients with HCC.
Material and methods: In this retrospective study, data of patients with HCC who underwent TACE between June 2002 to December 2014 were obtained from the records. Their detailed information about the procedure of TACE, diagnosis of biliary complications and subsequent management details were reviewed.
Result: One hundred and sixty-eight patients with HCC underwent 305 procedures of TACE. Of these, biliary complications of various severities developed in 6 (3.6%) patients leading to an incidence of 1.9% (6/305). Minimal intrahepatic biliary dilatation (IHBD) occurred in three, biliary stricture in one and intrahepatic biloma in two patients. Supportive management was undertaken for IHBD patients while percutaneous aspiration and naso-biliary drainage was performed for the infected bilomas.
Conclusion: Biliary complications following TACE are infrequent. Diagnosis should be suspected clinically and confirmed with imaging. Treatment depends on the severity. Enforcing specific measures can minimize its frequency.

Abbreviations: TACE, transarterial chemoembolization; HCC, hepatocellular carcinoma; AFP, alpha-fetoprotein; MDCT, multi-detector computed tomography; MRI, magnetic resonance imaging; EASL, European Association for the Study of Liver; BCLC, Barcelona clinic of liver cancer; IHBD, intrahepatic biliary dilatation; mRECIST, modified response evaluation criteria in solid tumors.

* Corresponding author.
E-mail address: shashi.aiims@gmail.com (S.B. Paul).

http://dx.doi.org/10.1016/j.diii.2015.06.017

Introduction

Transarterial chemoembolization (TACE) is a well-established therapy for unresectable hepatocellular carcinoma (HCC) worldwide [1]. It is a minimally invasive, effective and safe technique with minor and few major complications. Post-embolization syndrome is the most frequently occurring complication, which is self-limiting and managed conservatively. Rarely, biliary complications of various severities may occur following TACE, which may be fatal if unrecognized [2—4]. It is thus important for the interventional radiologist to be aware of these life threatening adverse events following a procedure that is widely used. Once biliary damage is diagnosed, the repeat procedure of TACE is preferably avoided. The goal of our study was to investigate the incidence and the presentation of biliary complications following TACE in patients with HCC.

Materials and methods

This retrospective work is a part of the ongoing study on TACE at our centre, which has been approved by the Institute ethics committee. Between June 2002 to December 2014, patients of unresectable HCC, who underwent TACE, were studied. Their data pertaining to the clinical, demographic profile, biochemical parameters, imaging findings and treatment details with follow-up were retrieved from the case records. The laboratory tests included complete hemogram, liver function tests, serum alpha-fetoprotein (AFP) and viral markers for hepatitis B and C. Findings of ultrasonography, multi-detector computed tomography (MDCT) and magnetic resonance imaging (MRI) were analyzed. The diagnosis of HCC was based on the European Association for the Study of Liver (EASL) criteria [5]. Staging with treatment allocation of TACE was done on the basis of Barcelona Clinic of Liver cancer (BCLC) staging [6].

TACE was performed on HCC patients with BCLC-B/C stage, having underlying Child's A or B cirrhosis, normal main portal vein, tumor burden involvement less than 50% of the liver and patients willing for therapy and follow-up. Few patients of BCLC-A stage unsuitable for curative therapy were also included. Patients of HCC having extrahepatic disease; coagulopathy, intrahepatic biliary dilatation (IHBR) and associated co-morbid illness like coronary artery disease, congestive heart failure, chronic renal failure, etc. were excluded.

TACE was undertaken through the transfemoral route. Initially, a superior mesenteric artery and celiac axis arteriogram were obtained using 5F RC1 (reverse curve, Cook, Bloomington, IN, USA) or C1 (Celiac, Cook, Bloomington, IN, USA) diagnostic catheter and 0.035-inch j-tip terumo guidewire (Terumo; Terumo Corporation, Tokyo, Japan). Whereas, for reaching the distal tumor bed, we used either 4F slip catheter (VERT slip-cathBeacon Tip Catheter; Cook, Bloomington, IN, USA) after exchanging with 5F catheter (Cook, Bloomington, IN, USA) or 2.7F micro-catheter (Progreat 2.7 F micro-catheter, Terumo; Terumo Corporation, Tokyo, Japan) as co-axial system through 5F catheter. These diagnostic 4F or 5 F catheters were partially occlusive. We used two chemotherapeutic drugs (doxorubicin 50 milligram [mg] and cisplatin 100 mg) till 2008, and later changed over to a single drug (epirubicin 60 mg). The chemotherapeutic drug emulsion was prepared with 10 ml of iodinated/nonionic contrast media and 20 ml of iodized oil (Lipiodol, Guerbet, Roissy-Charles de Gaulle, France) and this emulsion was delivered by placing the catheter tip as close as possible to the tumor. In masses less than 5 centimeters in diameter, we used the chemotherapeutic emulsion prepared with a smaller amount of Lipiodol® (10 ml). Following the injection of the drug emulsion, the same feeding artery was embolized using gel foam slurry made from shaved gelfoam mixed with contrast material. No aggressive embolization was done. The gelfoam slurry was injected till there was sluggish blood flow seen as to and fro movement of contrast column in the feeding artery on real time fluoroscopy. Intra-arterial lidocaine (10 mg) (xylocard 2%, AstraZeneca, Bangalore, India) was given between 10-ml aliquots of chemoembolization material to minimize the pain occurring post-embolization. Gradually, over a period of time, the micro-catheter co-axial system became available at our centre and then this was used to access narrow tortuous feeders.

Follow-up post-procedure was carried out at 1, 3, 6 and 12 months. Clinical, laboratory and imaging evaluation was performed at each visit. Patients reported earlier if any untoward symptom appeared and they were then subjected to an abdominal ultrasonography/MDCT or MRI depending upon the indication. The findings of the treated mass and complications if any were recorded. MRI was undertaken in inconclusive situations or to delineate the site of narrowing if any focal intrahepatic biliary dilatation was observed on ultrasonography/MDCT.

Diagnosis of intrahepatic bilomas was made on ultrasonography when a well-defined cystic mass was detected in the liver that was anechoic (when sterile), or had echogenic contents (if infected or had hemorrhage within). On MDCT, biloma was seen as a well-defined hypodense lesion (attenuation less than 20 Hounsfield Unit) communicating with the IHBR [7] (Fig. 1A—D). On MRI, biliary channels were seen as hyperintense branching structures while a biloma was seen as a hyperintense collection with or without communication with the bile ducts (Fig. 2A and B). We used heavily T2-weighted MR sequence, Half-Fourier Acquisition Single-Shot Turbo Spin-Echo (HASTE) and T2-weighted fat-saturated sequence for evaluating the biliary radicals. Narrowing of the bile duct was suggestive of stricture. Tumor response was classified according to the modified Response Evaluation Criteria in Solid Tumors (mRECIST) criteria [8].

In patients who developed biliary complications, the predisposing factors were studied and analyzed. Statistical analyses was done using Stata 12.1, Stata Corp, 4905 Lakeway Drive, College Station, Texas 77845 USA.

Results

Table 1 illustrates the demographic and biochemical profile of the 168 HCC patients enrolled. These were 146 men and 22 women, with a mean age of 52 ± 12.6 (SD) years, [range: 16—75 years], Child-Pugh status A 122/167 (72.6%), Child's B 46/167 (27.4%) and had HCC of BCLC stage A, B and C. The masses were single in 73/168 (43.4%) and multiple in 95/168 (56.6%) patients. The mean