Percutaneous Drainage of an Infected Biloma Secondary to Transcatheter Arterial Chemoembolization for Hepatocellular Carcinoma: Report of Two Cases

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ABSTRACT
Bilomas are localized collections of bile located outside the biliary tree. Infected biloma is a rare complication of transcatheter arterial chemoembolization (TACE) for hepatocellular carcinoma (HCC). We present two patients with HCC complicated by infected bilomas secondary to TACE. The clinical history, the location, and the CT scan appearance of the lesion may suggest the diagnosis of bilomas. Definite diagnosis of biloma was confirmed by ultrasound-guided aspiration, and placement of the drainage catheter was performed thereafter. Two patients improved clinically after percutaneous drainage and intravenous antibiotics regimen, thus obviating the need of surgical exploration. The clinician must be aware of this potential and fatal complication of TACE. Prompt diagnosis is necessary for optimal management.

Key words: biloma, transcatheter arterial chemoembolization (TACE), hepatocellular carcinoma (HCC)
INTRODUCTION

Transcatheter arterial chemoembolization (TACE) is now widely used for the treatment of hepatocellular carcinoma (HCC) in Taiwan. Various complications associated with TACE for HCC include hepatic failure, hepatic infarction, liver abscesses, bilomas, cholecystitis, gastrointestinal mucosal lesions, and multiple intrahepatic aneurysms [1]. Bilomas denote localized cystic collections of bile extravasated after bile duct injury and necrosis [2]. The incidence of bilomas formation following TACE for HCC has been shown to be 0.32%~1.1% [3,4]. TACE using an emulsion of an oil-soluble anti-cancer agent (mitomycin-C), iodized oil (lipiodol) and gelfoam cubes may cause destruction of the wall of the bile duct by obstructing the peribiliary arterial plexus of the duct, leading to leakage and subsequent pooling of the bile [5].

We report the percutaneous management of infected bilomas following TACE in two HCC patients.

CASE REPORTS

CASE 1
A 76-year-old man with liver cirrhosis and HCC was discharged uneventfully 1 week after the 4th TACE for HCC, but was readmitted because of fever and right upper quadrant pain 2 weeks later. Laboratory findings revealed leukocytosis (12190/mm$^3$), thrombocytopenia(107000/mm$^3$), and hypoalbuminemia(2.5gm/dl). Abdominal ultrasound showed a subcapsular fluid collection abutting the right lobe of the liver. Computed Tomography (CT) scan was performed which demonstrated a subcapsular fluid collection adjacent to the right
lobe of the liver [Fig 1]. Under ultrasound guidance, placement of 8 French pigtail (Angiomed Co; USA) was successfully done which drained out about 480 ml of bilious fluid. Aspirated subcapsular fluid analysis revealed total bilirubin of 33.91 mg/dl, and direct bilirubin 14.55 mg/dl. Culture of the drained specimen yielded Citrobacter youngae. Parenteral antibiotics therapy with pefloxacin was given for 12 days. Endoscopic retrograde cholangiography (ERC) was subsequently performed but which failed to demonstrate the bile leak [Fig2]. He remained afebrile on the 15th hospital day. Follow-up abdominal CT scan after 2 months documented a significant decrease in the size of the biloma cavity [Fig 3]. However, the patient died of progressive hepatic failure 6 months later.

CASE 2
A 40-year-old man with liver cirrhosis and HCC underwent TACE for HCC of the left lobe. Selective left hepatic artery catheterization was performed and TACE was carried out thereafter using mitomycin-C 20 mg mixed with lipiodol 10 ml. Gelfoam cubes were then slowly infused to occlude the feeding artery. He presented with fever and epigastric pain one week later. Abdominal CT scan revealed a hypodense lesion in the lateral segment of the left lobe, suggestive of fluid mixed with some air bubbles located at the left subphrenic area [Fig 4]. Laboratory tests revealed the following values: WBC count 7600/mm³, hematocrit 47%, alanine aminotransferase 155 U/L(normal range 0-40 U/L), aspartate aminotransferase 114 U/L (normal range 10-35 U/L). The biloma was aspirated under ultrasound guidance, the catheter was left in place for further drainage. Culture of the bilious fluid yielded
Escherichia coli. Parenteral antibiotics therapy with cefuroxime was given for 10 days. Follow-up abdominal CT scan documented a markedly regression in the size of the biloma cavity by day 4 [Fig 5], the patient was discharged uneventfully 2 weeks later.

DISCUSSION
The term “biloma” was defined as a loculated collection of bile located outside the biliary tree[6]. Kulgowska et al extended the term “biloma” to include intrahepatic as well as extrahepatic collections of bile[7]. In a postmortem survey of bile duct necrosis and biloma following TACE for HCC, biloma was defined as a round, softened lesion with bile imbibition and histologically showed coagulation necrosis of the hepatic parenchyma imbibed by bile extravasated from the necrotic ducts [5]. Bilomas mainly result from iatrogenic, traumatic, or spontaneous rupture of the biliary tree. Bile duct necrosis or biloma was not uncommon in cirrhotic livers with HCC after TACE, the mechanism of biloma formation after TACE is believed to be due to ischemic injuries of the peribiliary plexus, which uniquely supplies blood to the bile ducts [5].

The reported incidence of bilomas formation following TACE for HCC ranges from 0.32% to 1.1% [3,4]. While the postmortem incidence of bile duct necrosis or biloma following TACE for HCC was much higher and about 12.5%[5], because they were not detected or suspected antemortem. One of our patients had undergone multiple TACEs before the development of biloma. Repeated performance of TACE causes peripheral hepatic arterial occlusion due to chemical arteritis or gelfoam...
cubes embolization, resulting in intrahepatic biloma formation. The possible mechanisms are focal hepatic infarction accompanied by secondary bile leak formation or peripheral bile duct injury with chemoembolization agents [3]. ERC is probably the optimal procedure to document an active bile leak, while ultrasound and CT scan are the best methods to identify and localize a bile collection [2]. Bilomas should be added to the differential diagnosis of cystic, intrahepatic, or perihepatic abnormal fluid collections [7]. The typical sonographic appearance is that of a purely cystic, encapsulated mass with space-occupying and space-conforming characteristics in an upper abdominal cavity, contiguous with the liver or biliary structure [8]. The epithelization of the biloma might be only detected on ultrasound as septations, and was not seen on CT scans [9]. Abdominal CT scan is the optimal examination to identify and localize a biloma and to show its regional anatomy. The CT numbers of the biloma fluid are less than 20 H, but may be higher when the bile is mixed with blood or exudates [2]. Magnetic resonance imaging is also useful in the differential diagnosis of bilomas. Bilomas are heterogeneously intense on T1-weighted images, and homogeneously hyperintense on T2-weighted images [10]. Needle aspiration is essential in confirming the diagnosis of biloma. The simplest method for diagnosing the collection specifically as a biloma is either the use of commercially available multistix or determination of bilirubin levels in the chemistry laboratory [11]. We report 2 patients with biloma in whom the diagnosis was confirmed by sonographic guidance needle aspiration and treated successfully by percutaneous catheter drainage. The 2nd patient received another nasobiliary drains
endoscopically after percutaneous transhepatic drainage, it offered bile diversion and it’s also an accepted form of therapy to reduce the amount of biloma.

Komatsu et al reported a patient who developed a giant hepatic biloma following TACE for hepatic metastases from malignant pheochromocytoma, that was treated by biliary reconstruction using a metallic stent, which decrease the size of biloma [12]. Chen et al also treated 2 cases of infected biloma, but the biloma persisted despite percutaneous aspiration and drainage [4].

Our chemoembolization protocol includes mitomycin-C 20 mg mixed with 10 ml of lipiodol, and gelfoam cubes. Of these three agents, we cannot determine which agent causes the occurrence of bile duct necrosis and biloma formation.

The occurrence of peripheral bile duct necrosis has been reported after hepatic artery embolization with small-sized embolic particles such as silicone rubber and gelatin powder [13], thus the use of gelfoam cubes or other medium-sized particles can probably prevent ductal necrosis. The use of microwave coagulation therapy for HCC resulting in intrahepatic bile duct necrosing and biloma formation has been reported in the literature [14]. Soon et al had also reported a case of intra-arterial injection of 5-fluorodeoxyuridine that causes bilomas after hepatic cryotherapy [15]. They hypothesize that increasing biliary pressure caused by sclerosing cholangitis secondary to 5-fluorodeoxyuridine resulted in bile leakage into the necrotic areas of liver.

In conclusion, biloma formation following TACE was more difficult to treat and had a detrimental effect on the prognosis of HCC. Early diagnosis and a precise localization of the biloma allow the possibility of
a percutaneous drainage, obviating surgical intervention. However, when the patient did not respond after the percutaneous drainage and antibiotics administration, surgical drainage should be considered.

REFERENCE
Percutaneous Drainage of Infected Biloma

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肝癌經導管動脈化學栓塞併發感染性膽液瘤—經皮引流:兩病例報告

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摘　要

膽液瘤乃腹腔局部膽液蓄留。肝癌經導管動脈化學栓塞後發生感染性膽液瘤為罕見的併發症。有兩位肝癌病患接受經導管動脈化學栓塞後發生感染性膽液瘤。臨床病史、病變位置及電腦斷層分析可診斷膽液瘤。兩位病人接受超音波導引抽吸及引流導管留置後，避免外科手術。熟悉感染性膽液瘤對臨床醫師是有必要的，尤其是在肝癌患者接受經導管動脈化學栓塞後能正確地診斷此併發症及適當地治療之。

關鍵語: 膽液瘤，經導管動脈化學栓塞，肝癌。

FIGURE LEGENDS

Fig 1. Abdominal CT (case 1) showing a subcapsular fluid collection
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(arrow) adjacent to the right lobe of the liver.

**Fig 2.** Endoscopic retrograde cholangiography (case 1) failing to demonstrate the bile leak, and percutaneous drainage catheter locating in infected biloma (arrow).

**Fig 3.** Follow-up abdominal CT scan (case 1) showing a significantly decrease in the size of the biloma cavity (arrow).
Fig 4. Abdominal CT (case 2) revealing an infected biloma (arrow) in the lateral segment of the left lobe.

Fig 5. Follow-up abdominal CT scan (case 2) showing a markedly regression in the size of the biloma cavity, and percutaneous drainage catheter (arrow) locating in it.