Biloma after Transcatheter Arterial Chemoembolization with Drug-Eluting Beads Managed with Sclerotherapy and Stent Placement

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――――――――― **Abstract** ―――――――――

We report a case of successful treatment of an intractable large biloma induced by transcatheter arterial chemoembolization with beads for hepatocellular carcinoma. First, percutaneous drainage was performed for the biloma but the volume of discharge continued at > 300 ml per day for 12 days. We were unable to approach the proximal bile duct from the biloma. We performed sclerosis of the biloma with ethanolamine oleate, after which the volume of drained bile was markedly decreased. After this sclerotherapy, we were able to advance the catheter into the proximal bile duct from the biloma. Subsequently, internal drainage with a metallic stent was successful, and the biloma was resolved. The patient's course has been uneventful for the 2 years since the stent placement.

Key words: biloma, ethanolamine oleate, drug-eluting beads

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Introduction

Transcatheter arterial chemoembolization (TACE) is accepted as a standard therapy for unresectable hepatocellular carcinomas (HCCs) [1]. Although the incidence of liver abscess and biloma formations after TACE is low, high mortality rates, ranging from 13.3% to 50%, have been reported after TACE with an abscess as a complication [2, 3]. A bilioenteric anastomosis has a significant effect on the development of a liver abscess [3]. Small biloma can be conservatively treated in most cases, but in patients with an infected biloma, percutaneous drainage should be performed promptly [4]. For bilomas that are refractory to percutaneous drainage alone, no consensus has been reached regarding the optimal treatment intervention.

We treated a patient who developed an intractable large biloma following drug-eluting beads-transcatheter arterial chemoembolization (DEB-TACE) for hepatocellular carcinoma (HCC) using percutaneous sclerotherapy with ethanolamine oleate and biliary stent placement.

Case Report

A 67-year-old man with alcoholic cirrhosis underwent a hepatic segmentectomy for HCC at another hospital 2 years before he was admitted to our hospital. Fourteen months after the surgery, recurrence of multiple HCCs was observed on computed tomography (CT). The patient first underwent conventional TACE and then additional radiofrequency ablation (RFA) for the HCCs without sufficient lipiodol accumulation in segments 4 and 5. Four months after the RFA, perihilar bile duct stricture developed, and the patient underwent an endoscopic placement of two metallic stents with papillotomy. At that time, the multiple HCCs remained (>10 tumors, largest tumor: 5 cm), and he was referred to our hos-

Fig. 1. Contrast-enhanced CT image showing the development of a liver abscess, with a size of up to 8 cm in diameter.

Fig. 2. A 10-Fr. external-internal drainage catheter was placed into the common bile duct, over the guidewire (*arrow*).

pital for further treatment of the recurrent HCCs.

At the first visit to our hospital, the patient had well-compensated liver function (Child-Pugh class A) and no clinical symptoms of cholangitis. Treatment with sorafenib (Nexavar; Bayer Yakuhin, Osaka, Japan) was started instead of TACE, as he had a high risk of liver abscess formation because of stent placement. However, at 6 months after the start of the sorafenib therapy, a CT scan revealed an increase in tumor size (largest tumor: 8 cm); thus, the therapeutic response was not satisfactory.

Treatment options, including hepatic arterial infusion chemotherapy (HAIC), conventional TACE, and DEB-TACE, were discussed. HAIC was excluded because the patient had a replaced right hepatic artery, which conferred to the patient the risk of biloma due to the embolization for arterial redistribution. Conventional TACE was excluded because the previous conventional TACE failed to control the patient's HCCs. We eventually decided to perform DEB-TACE. We speculated that the risk of abscess formation after DEB-TACE would be decreased by prophylactic antibiotic therapy.

We performed DEB-TACE via the right posterior segmental artery, which fed most of the tumors, using a 1.9-F-tip microcatheter (Tellus; Asahi Intecc, Nagoya, Japan) passed through a 4-F catheter. DEB-TACE was performed using 100- to 300-mm microspheres (DC-Beads; Eisai, Tokyo) loaded with 50 mg of epirubicin (Nippon Kayaku, Tokyo). The angiography after DEB-TACE showed substantial tumor vascularity reduction.

After the DEB-TACE, the patient had neither abdominal pain nor fever. A prophylactic antibiotic (ceftriaxone sodium hydrate; Pfizer, Tokyo) was administered before and for 5 days after the DEB-TACE. However, on day 7, the patient became febrile, with a body temperature of >38.5℃. The emergency CT performed on the same day revealed a cystic low-density area in the right posterior segment (**Fig. 1**). On the same day, ultrasonography-guided transhepatic abscess

drainage with 8.5-Fr catheter was performed. We removed 90 ml of bile-like fluid that was yellow in color. After percutaneous drainage, the patient's fever subsided; however, the volume of drainage continued at >300 ml per day for 12 days. Endoscopic tube stent placement in the perihilar bile duct resulted in no reduction of bile discharge.

On day 19, a CT examination with contrast medium injection in the biloma revealed the communication between the biloma and the peripheral intrahepatic bile duct. We tried to advance a guidewire into the proximal bile duct through the biloma but failed because we could not identify the communication in the very large biloma cavity.

On day 40, we performed biloma sclerotherapy. We selected ethanolamine oleate (Oldamin; 10 mg/vial; Takeda Pharmaceutical, Osaka, Japan) as the sclerotic agent, as we suspected that the inflammation induced by the sclerotherapy caused the occlusion of the connection between the biloma and the biliary tree. The biloma was opacified by injection of contrast medium to verify the absence of communication between the biloma and the proximal biliary tree. One vial of ethanolamine oleate (Oldamin) was dissolved in 10 ml of nonionic contrast medium (Omnipaque; Daiichi-Sankyo, Tokyo) as a 5% ethanolamine oleate mixture. We injected 8 ml of the 5% ethanolamine oleate mixture in the biloma cavity, as was done for the previous tubogram. The patient's bile discharge began to decrease to <150 ml per day after the initial sclerotherapy. Altogether, four sessions of ethanolamine oleate sclerotherapy were performed over a period of 3 weeks. During these sclerotherapies, the patient reported no complaints. On day 66, a tubogram after the fourth session of sclerotherapy showed significant shrinkage of the biloma and proximal right hepatic bile duct. On that day, we advanced a 10-Fr. external-internal drainage catheter with multiple sideholes (Create Medic, Yokohama, Japan)
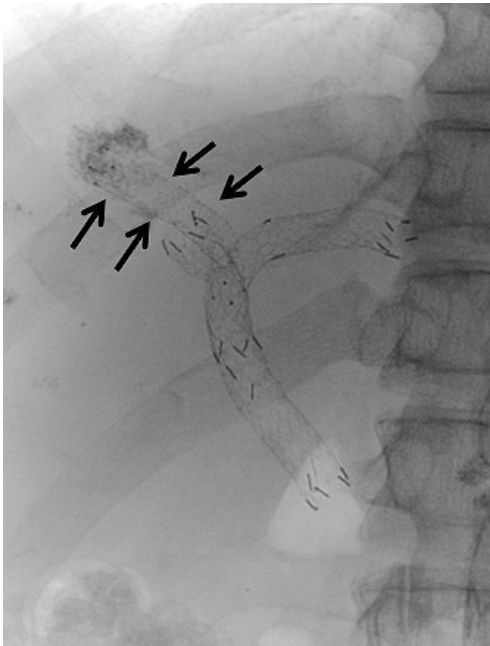
Fig. 3. A metallic stent was placed from the biloma to the proximal common hepatic duct (*arrow*, Zilver stent).

Fig. 4. CT image 18 months after stent placement, showing significant shrinkage of the biloma (*arrow*).

into the common bile duct over the guidewire (**Fig. 2**). The catheter was left for 2 days as a bougie dilatation.

On day 69, we placed a self-expandable metallic stent (Zilver 635; 8-mm diameter, 60-mm long; Cook Medical, Bloomington, IN) connecting the biloma and common hepatic duct (**Fig. 3**). The bile discharge from the catheter then ceased. After confirming a good flow of contrast material on cholangiography, we removed the catheter in the biloma cavity on day 71. At that time, the HCC was in its intermediate stage (>10 tumors, without vascular invasion); however, the patient did not want further therapy.

A CT image obtained 18 months after metallic stent placement showed significantly decreased collection in the cavity (**Fig. 4**). The patients had no complications such as recurrence of biloma, cholangitis, or liver abscess for 24 months after the procedure.

Discussion

The biliary tree is supplied primarily by arterial blood alone; therefore, ischemia of the bile ducts can easily occur after TACE [1, 4]. In our patient, we performed DEB-TACE via the proximal right posterior segmental artery supplying the peribiliary plexus artery; thus, it is possible that the greater amount of embolization agent perfused a larger liver area, resulting in the large biloma. In biliary abnormalities such as bilioenteric anastomosis, endoscopic papillotomy, and biliary stenting, the bile ducts can become contaminated by enteric bacteria retrogradely, and TACE may transform this contamination into an obvious infection [3].

In our patient, the bile inflow in the biloma was continued from the peripheral bile duct, and the bile outflow in the biloma was blocked by a proximal bile duct stricture

caused by the DEB-TACE, which led to a persistent bile leak. Percutaneous drainage was not effective. Internal biliary drainage was not technically feasible at first.

We selected ethanolamine oleate as a sclerotic agent because of its higher safety and tolerance [5]. Ethanolamine oleate has been used successfully for simple hepatic and renal cysts, and polycystic liver disease [5]. It destroys cystic epithelial cells, bringing about cyst resolution. The biloma wall is not thought to be composed of epithelial cells, like the polycystic liver. However, we speculated that the connection between the patient's biloma and the biliary tract became stenosed or even occluded by inflammation induced by the sclerotherapy. The biloma cavity decreased markedly, and the communication between the biloma and the proximal bile duct became clear. Subsequently, biliary internal drainage with a metallic stent was successful, and the biloma shrank. After 2 years of follow-up, the metallic stent is still functioning well and prevented biloma, cholangitis, and liver abscess.

To avoid biliary complications such as biloma, embolization should be performed as selectively as possible. We think that the reason for development of biloma was ischemia of the peribiliary plexus by non-selective DEB-TACE and retrograde biliary infection induced by the previous biliary stenting. We should perform stepwise selective DEB-TACE because the patient had multiple tumors. The management of an intractable biloma is problematic. In our patient, the combined interventions for biloma sclerotherapy with ethanolamine oleate and internal biliary stenting to make a bridge from the biloma to the common bile duct proved useful in the treatment of a biloma that was refractory to drainage alone.

Conflict of interest: The authors declare that they have no conflicts of interest.

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