— **Case Report** —

Intraoperative Bile Duct Disruption Treated Using Intrahepatic Biliary Ablation with Ethanol: A Report of Two Cases

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Abstract

We report two cases of intraoperative bile duct disruption. In case 1, an isolated bile duct in the remnant of the anterosuperior liver segment after right hepatic lobectomy for cholangiocarcinoma caused bile leakage. In case 2, bile leakage continued from a disrupted accessory hepatic duct during pancreaticoduodenectomy for pancreatic carcinoma. In both patients, a mixture of ethanol and iodized oil at a 10:1 ratio was injected into the disrupted bile duct under balloon occlusion. In case 1, the mixture was injected through a balloon catheter under balloon occlusion overnight. No severe complications developed in either case. Bile leakage stopped postoperatively and did not recur until the patients' death from tumor progression 14 and 16 months after surgery, respectively.

Key words: intraoperative bile duct disruption, intrahepatic biliary ablation, ethanol, iodized oil

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Introduction

Bile duct injury is a major complication of hepatobiliary and pancreatic surgeries, with a reported frequency of up to 15.6% [1-3]. Percutaneous, endoscopic, and/or surgical interventions are often required, but they occasionally fail to improve bile leakage. If the leaking bile duct communicates with the common bile duct (CBD), endoscopic biliary drainage can be performed first. However, for a leaking bile duct without a fistula communicating it to the CBD, such as a disrupted bile duct, percutaneous interventions are mainly performed [2]. Although a standard treatment for the disrupted bile duct has not been established, usefulness of intrahepatic biliary ablation with ethanol for refractory bile leakage has been reported [4, 5]. We encountered two cases of bile leakage due to intraoperative bile duct disruption successfully treated with intrahepatic biliary ablation. Our experience is described in this case report.

Case report

Case 1

An 82-year-old woman was referred to our hospital for the treatment of cholangiocarcinoma of the hepatic hilum. The right hepatic lobe and extrahepatic bile duct were resected, and left hepatic duct was anastomosed with the elevated jejunum. The postoperative clinical course was uneventful, but bile continued to flow from the peritoneal drainage tube at a rate of 30-130 mL/day. Computed tomography (CT) performed 16 days after surgery showed residual liver tissue of the anterosuperior segment (S8) behind the middle hepatic vein (**Fig. 1a**). The isolated biliary tree in S8 was also opacified on fistulography via the drainage tube performed 30 days after surgery (**Fig. 1b**). Bile leakage continued; therefore, we decided to attempt intrahepatic biliary ablation with ethanol. Informed consent was obtained from
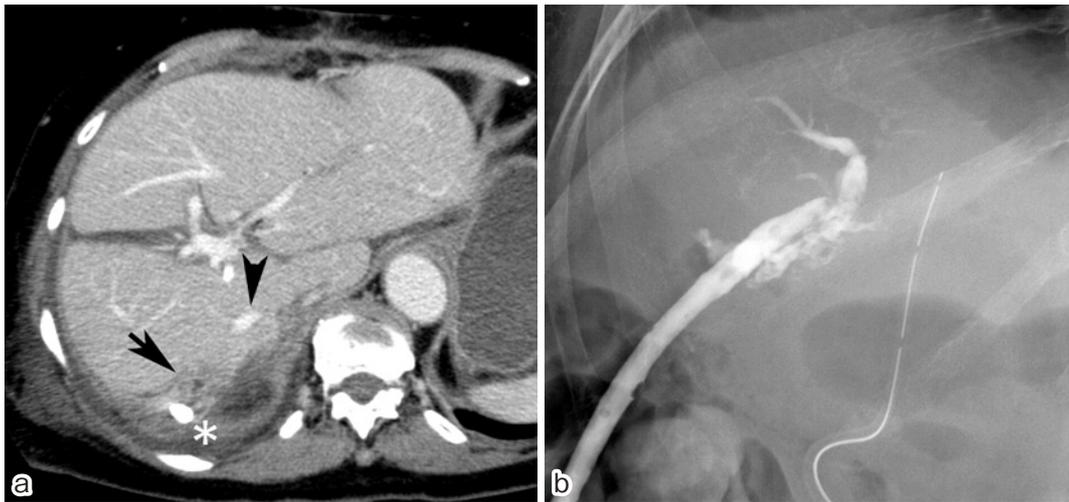
Figure 1.

a. Contrast-enhanced computed tomography performed 16 days after surgery shows residual liver tissue of the anterosuperior segment (S8) (arrow) behind the middle hepatic vein (arrowhead). The asterisk indicates the peritoneal drainage catheter.

b. Fistulography via the drainage tube performed 30 days after surgery demonstrates the isolated bile duct in the liver remnant through the fistula. The other drainage catheter placed in the left hepatic duct is also seen.
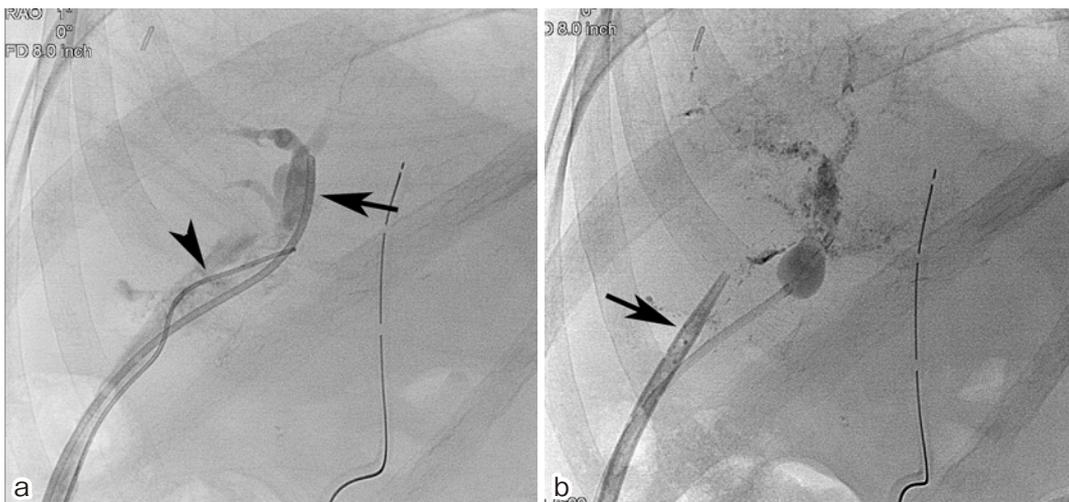
Figure 2.

a. On day 43 after surgery, intrahepatic biliary ablation was performed. First, a 5-F J-shaped angiographic catheter was inserted into the fistula (arrow). The arrowhead indicates the safety wire.

b. A 5.2-F balloon catheter was advanced into the bile duct, and a mixture of ethanol and iodized oil at a 10:1 ratio was injected twice into the bile duct under balloon occlusion for 20 minutes. Subsequently, the mixture was injected under balloon occlusion overnight. A 10.2-F drainage catheter was also placed in the fistula side-by-side (arrow).

the patient.

Intrahepatic biliary ablation was performed 43 days after surgery (**Fig. 2**). After the insertion of a 0.035-inch guidewire (Coons interventional guidewire, Cook, Bloomington, IN, USA) via the drainage tube, the tube was exchanged to a 9-F sheath (Medikit, Tokyo, Japan). The guidewire was left in place as a safety wire, and a 5-F J-shaped angiographic catheter (Terumo, Tokyo, Japan) was

inserted into the fistula using another 0.035-inch hydrophilic guidewire (Radifocus, Terumo) through the sheath. The angiographic catheter was navigated into the isolated bile duct with the hydrophilic guidewire and then the catheter was exchanged to a 5.2-F occlusion balloon catheter (9 mm in diameter) (Selecon MP catheter II, Terumo Clinical Supply, Kakamigahara, Japan) over the guidewire. Ethanol and iodized oil (Lipiodol 480, Guerbet Japan, Tokyo, Japan) were

Figure 3.
a. Unenhanced computed tomography performed 12 days after intrahepatic biliary ablation shows iodized oil accumulation in the liver remnant.
b. Contrast-enhanced computed tomography performed 11 months after surgery shows atrophy of the liver remnant.

mixed at a 10:1 ratio to render the mixture radiopaque, and the mixture was slowly injected under balloon occlusion until all branches of the isolated bile duct were opacified. Thus, 2 mL of the mixture was injected into the bile duct, and the catheter was clamped for 20 minutes. After aspiration of the mixture, 1.4 mL of the mixture was re-injected for 20 minutes. Subsequently, the hydrophilic guidewire was advanced into the catheter, and both the catheter and sheath were withdrawn. The balloon catheter was re-advanced into the bile duct over the hydrophilic guidewire, and a 10.2-F drainage catheter (Ultrathane, Cook) was placed in the fistula side-by-side using the safety wire to prevent the dislodgement of the balloon catheter by pushing it to the fistula wall and drain the fluid retained in the fistula. Subsequently, 1.4 mL of the mixture was injected through the balloon catheter under balloon occlusion overnight. The balloon catheter was withdrawn on the next day, and bile leakage was found to have markedly decreased after the procedure. A low-grade fever (37.5℃) was recorded the day after the procedure without any treatment. Fistulography performed 48 days after surgery showed the disappearance of the bile duct. The drainage catheter was withdrawn 55 days after surgery, and the patient was discharged after 63 postoperative days. The clinical course after intrahepatic biliary ablation was uneventful (**Fig. 3**); however, the tumor recurred 9 months after surgery, and the patient died from tumor progression 14 months postoperatively without recurrence of bile leakage.

Case 2

A 69-year-old man was referred to our hospital for the treatment of carcinoma of the pancreatic head, and we performed subtotal stomach-preserving pancreaticoduodenectomy. The patient's postoperative course was uneventful, but bile continued to flow from the peritoneal drainage tube at a rate of 20-60 mL/day. On CT performed 7 days after surgery, the presence of an accessory hepatic duct was suspected (**Fig. 4a**). Retrospectively, gadoxetate disodium-enhanced magnetic resonance imaging performed before surgery also showed that the bile duct of the anteroinferior liver segment (B5) directly communicated with the common hepatic duct (**Fig. 4b**). Fistulography through the drainage tube performed 18 days after surgery depicted the accessory hepatic duct (**Fig. 5a**). We selected percutaneous intervention to stop bile leakage, and informed consent was obtained from the patient.

On day 21 after surgery, percutaneous transhepatic biliary drainage (PTBD) of B5 was performed under sonographic guidance. Cholangiography showed extravasation of the contrast material at the hepatic hilum, and a 7.2-F drainage catheter (Medico's Hirata, Osaka, Japan) was left in place at B5 (**Fig. 5b**). Bile leakage continued at a rate of 40-210 mL/day through the PTBD catheter. First, we planned the puncture of the elevated jejunum via B5 using a hand-made metal canula and 21-G needle (Hakko, Chikuma, Japan); however, we considered that puncture of the jejunum through B5 might be impossible because of difficulty in controlling the puncture direction. Therefore, intrahepatic biliary ablation was performed via the PTBD route 29 days after surgery. The drainage catheter was exchanged with a 7-F sheath (Terumo) over a 0.035-inch guidewire (Cook), and a 1.7-F-tip microballoon catheter (5 mm in diameter) (Logos, Piolax, Yokohama, Japan) was navigated into the bile duct using a 0.016-inch microwire (Meister, Asahi Intecc, Seto, Japan). The balloon was inflated to occlude the bile leak and 2 mL of a mixture of ethanol and iodized oil at a 10:1 ratio was injected for 10 minutes through the side arm of the 7-F sheath. After aspiration of the mixture, 3 mL of
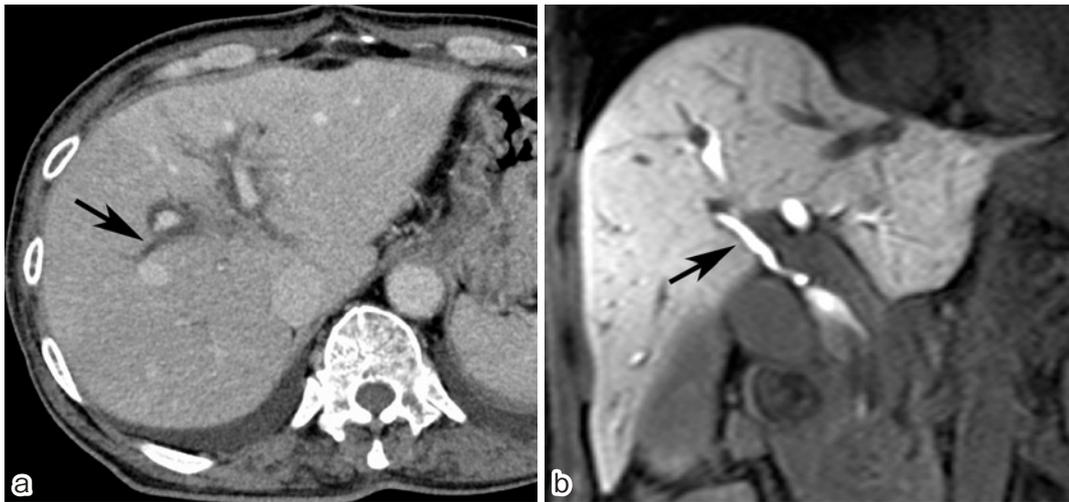
Figure 4.
a. Contrast-enhanced computed tomography performed 7 days after surgery shows that the bile duct in the anteroinferior liver segment (B5) is slightly dilated (arrow).
b. Coronal gadoxetate disodium-enhanced magnetic resonance imaging performed before surgery shows that B5 (arrow) directly communicates with the common hepatic duct.
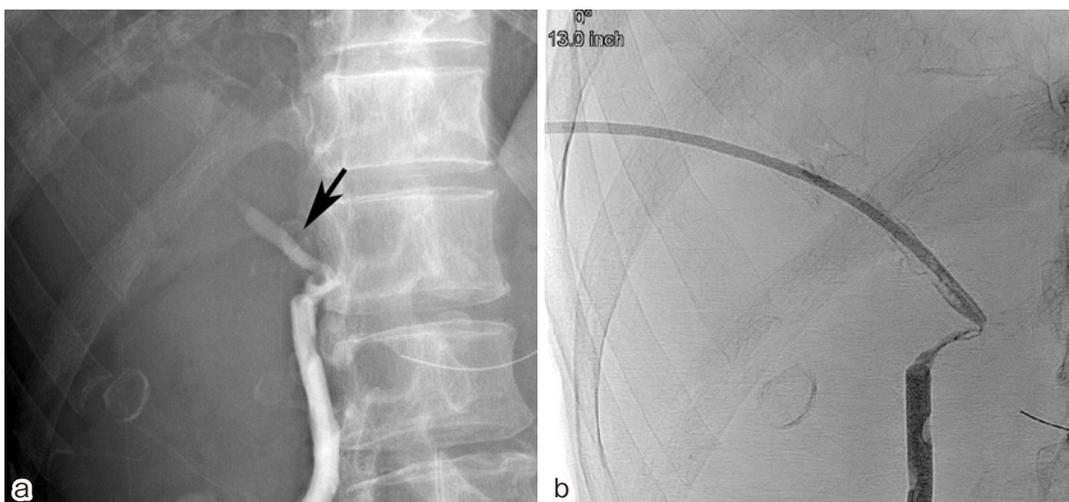
Figure 5.
a. Fistulography through the drainage tube performed 18 days after surgery depicts the disrupted accessory hepatic duct (arrow).
b. On day 21 after surgery, percutaneous transhepatic biliary drainage of B5 was performed under sonographic guidance, and extravasation of the contrast material at the hepatic hilum was confirmed.

the mixture was re-injected for 10 minutes to distribute it into the distal biliary branches. However, a small amount of the mixture overflowed along the sheath (**Fig. 6a**). Therefore, after aspiration of the mixture, the microballoon catheter was advanced into the distal biliary duct beyond the sheath while turning back at the hepatic hilum and 1 mL of the mixture was injected through the microballoon catheter under balloon occlusion for 10 minutes (**Fig. 6b**). After removal of the mixture, the microballoon catheter was withdrawn, and sheath was exchanged with a 7.2-F drainage catheter (Medico's Hirata). No complications occurred during or after the procedure. Bile leakage resolved the day after biliary ablation, and the drainage tube and PTBD catheter were removed 37 days after surgery. The clinical course after intrahepatic biliary ablation was uneventful, and the patient was discharged after 45 postoperative days; however, the tumor recurred 14 months after surgery, and the patient died from tumor progression 16 months postoperatively without recurrence of bile leakage (**Fig. 7**).
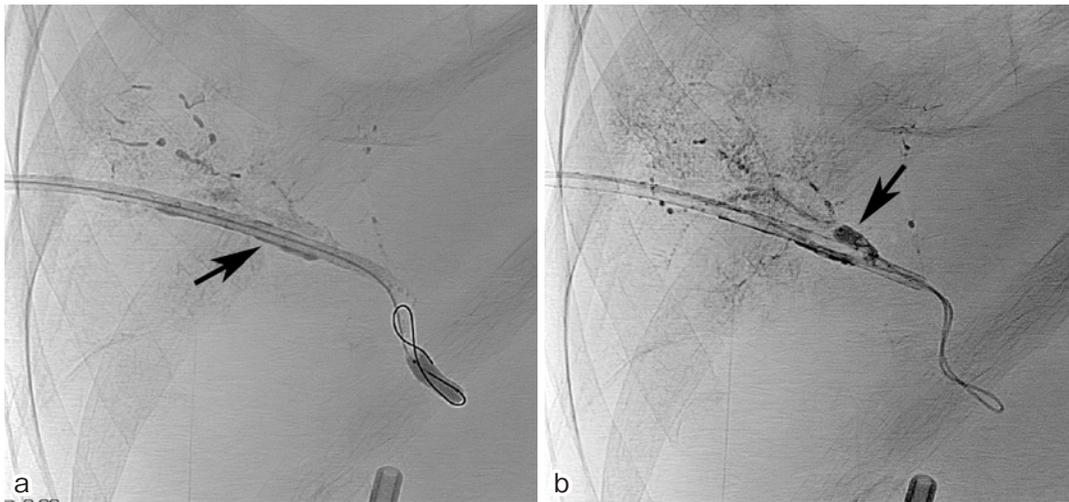
Figure 6.
a. On day 29 after surgery, intrahepatic biliary ablation was performed. First, the fistula was occluded with a microballoon catheter, and a mixture of ethanol and iodized oil at a 10:1 ratio was injected twice through the side arm of the 7-F sheath. However, a small amount of the mixture overflowed through the sheath (arrow).
b. Therefore, the microballoon catheter was advanced into the distal biliary duct beyond the sheath while turning back at the hepatic hilum and a mixture of ethanol and iodized oil was injected through the microballoon catheter under balloon occlusion. The arrow indicates the balloon.
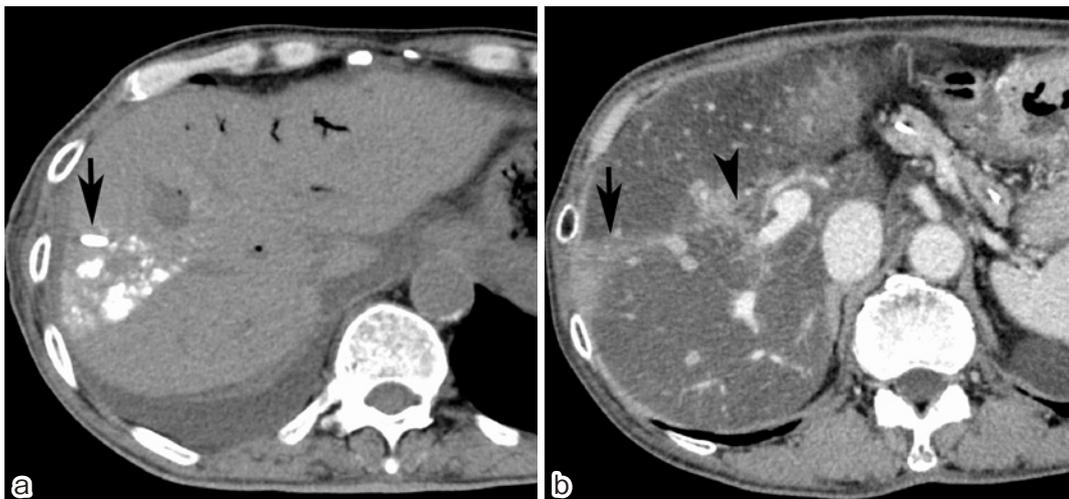
Figure 7.
a. Unenhanced computed tomography performed 5 days after intrahepatic biliary ablation shows iodized oil accumulation in liver segment 5 (S5). The arrow indicates the percutaneous transhepatic biliary drainage catheter.
b. Contrast-enhanced computed tomography performed 1 year after surgery shows shrinkage of S5 (arrow) and B5 (arrowhead). Marked fatty infiltration in the liver is also seen.

Discussion

The cause of an intraoperative bile duct injury can be anatomical, inflammatory, or technical [3]. Among these causes, an accessory hepatic duct, defined as an intrahepatic bile duct that directly joins the main extrahepatic bile duct, exhibits an incidence rate of 2%-10.8% [6, 7] and is a sig-

nificant risk factor for intraoperative bile duct injury [6]. Therefore, making a precise preoperative diagnosis is required to prevent intraoperative bile duct injuries, although we missed it on preoperative imaging in case 2.

Failure or delay in early recognition or inappropriate management of bile duct injury leads to catastrophic consequences. Surgical, endoscopic, or percutaneous interventions should be promptly performed according to the type of bile

duct injury and patient condition [2]. Reoperation after hepatic resection is associated with a high mortality rate of 39.3% [8], and a wait-and-see approach, with a success rate of 69-94%, usually requires a long treatment duration [5]; therefore, percutaneous interventions, such as placement of a drainage catheter and intrahepatic biliary ablation, are first-line treatments for an intraoperative disrupted bile duct.

Absolute ethanol has generally been used as an injected agent percutaneously or angiographically to treat various tumors or vascular lesions owing to its highly destructive properties, leading to cell death through cell membrane lysis and protein denaturation [9]. Ethanol also destroys the biliary epithelium and surrounding liver parenchyma when it is injected into the biliary tree. As a result, bile leakage can be stopped; however, repeated ethanol injections are usually required. In previous reports, 1-4 ethanol injections were administered in one session, and 4-19 sessions were performed at 1-3-day intervals [4, 5]. We continuously injected ethanol thrice, and bile leakage could be stopped in a single session. We consider that the therapeutic effects of ethanol may be influenced by the liver volume drained by the disrupted bile duct. In patients with a larger liver volume, more frequent ethanol injections may be required, and occasionally, bile leakage cannot be controlled with ethanol injections alone. In such a case, combination with portal vein embolization is the next step to stop bile leakage [10].

There are no standard techniques for intrahepatic biliary ablation. It is clear that a balloon catheter should be used to prevent outflow of ethanol. In a report by Ito et al. [5], however, ethanol was also injected through a 21-gauge needle after a percutaneous direct puncture of the target bile duct in three of 31 patients when a drainage catheter could not be advanced into it. The inflation time of the balloon has not been standardized and varies from 5 minutes to 24 hours [4, 5]. We performed overnight inflation in case 1; however, it remains uncertain whether or not this is effective. Moreover, the optimal volume of ethanol for efficacious and safe ablation is unknown. The quantity of ethanol filling into the entire branches of the isolated bile duct is generally considered the optimal volume. Since ethanol is not radiopaque, it is impossible to observe its distribution directly. Therefore, a test injection of the contrast material is required to determine the optimal ethanol volume [4, 5]. We mixed iodized oil with ethanol to render the mixture radiopaque. As a result, distribution of ethanol could be monitored under fluoroscopy, and the endpoint of the ethanol injection could be easily determined. As for the approach route, we performed PTBD in case 2. However, it might be unnecessary if intrahepatic biliary ablation was initially planned because the microballoon catheter might be successfully advanced into the disrupted accessory hepatic duct through the fistula. Therefore, further studies are required to establish an appropriate standard technique for intrahepatic biliary ablation.

The side effects of intrahepatic biliary ablation are usually mild. We experienced no severe complications, except for a low-grade fever in one patient. In a report of a large cohort [5], transient fever developed in 27 of 31 patients, mild pain in 13, flushing in two, and liver abscess in two. An ethanol injection into the intraoperative disrupted bile duct may not cause severe pain, although a preoperative ethanol injection into the portal vein or hepatic artery usually causes severe pain. Although the exact reason is unknown, it is speculated that denervation of the autonomic nerve in hepatobiliary resection with skeletonization of the hepatoduodenal ligament is a possible cause [5]. However, the use of excessive volume of ethanol may cause a liver abscess; therefore, we believe that adding a small amount of iodized oil into ethanol is helpful not only to control the injection volume of ethanol under fluoroscopy but also to prevent complications.

In conclusion, we encountered two cases of refractory bile leakage due to an intraoperative bile duct injury treated successfully with intrahepatic biliary ablation with a mixture of ethanol and iodized oil. This technique is effective in select patients with refractory bile leakage after surgery.

References

1. Kajiwara T, Midorikawa Y, Yamazaki S, Higaki T, Nakayama H, Moriguchi M, et al. Clinical score to predict the risk of bile leakage after liver resection. BMC Surgery 2016; 16: 30.
2. Cohen JT, Charpentier KP, Beard RE. An update on iatrogenic biliary injuries: identification, classification, and management. Surg Clin North Am 2019; 99: 283-299.
3. Gad EH, Ayoup E, Kamel Y, Zakareya T, Abbsay M, Nada A, et al. Surgical management of laparoscopic cholecystectomy (LC) related major bile duct injuries; predictors of short-and long-term outcomes in a tertiary Egyptian center- a retrospective cohort study. Ann Med Surg (Lond) 2018; 36: 219-230.
4. Kyokane T, Isomasa S, Kuroyanagi Y, Kobayashi S, Suzuki K, Miyata K, et al. A case of major bile leak after laparoscopic cholecystectomy successfully treated by biliary ablation with absolute ethanol. Jpn J Gastroenterol Surg 2006; 39: 1498-1504.
5. Ito A, Ebara T, Yokoyama Y, Igami T, Mizuno T, Yamaguchi J, et al. Ethanol ablation for refractory bile leakage after complex hepatectomy. Br J Surg 2018; 105: 1036-1043.
6. Noji T, Nakamura F, Nakamura T, Kato K, Suzuki O, Ambo Y, et al. ENBD tube placement prior to laparoscopic cholecystectomy may reduce the rate of complications in cases with predictably complicating biliary anomalies. J Gastroenterol 2011; 46: 73-77.
7. Hirao K, Miyazaki A, Fujimoto T, Isomoto I, Hayashi K. Evaluation of aberrant bile ducts before laparoscopic cholecystectomy: Helical CT cholangiography versus MR cholangiography. AJR Am J Roentgenol 2000; 175: 713-720.
8. Lo CM, Fan ST, Liu CL, Lai EC, Wong J. Biliary complications after hepatic resection: risk factors, management, and outcome. Arch Surg 1998; 133: 156-161.
9. Yamamoto H, Hayakawa N, Nagino M, Kamiya J, Nimura Y. Percutaneous transheptic cholangioscopic ethanol injection for intrabiliary tumor thrombi due to hepatocellular carcinoma. Endoscopy 1999; 31: 204-206.
10. Yamakado K, Nakatsuka A, Iwata M, Kondo A, Isaji S, Uemoto S, et al. Refractory biliary leak from intrahepatic biliary-enteric anastomosis treated by selective portal vein embolization. J Vasc

Interv Radiol 2002; 13: 1279-1281.