Chapter 6

Biliary Fistulas

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Introduction

In the last decades the number of complex surgical interventions which involves intrahepatic and extrahepatic bile ducts increased, which is why bile leakage remains an important complication that prolongs hospitalization, requires maintaining drainage tubes for a longer period of time and require invasive methods of treatment and diagnosis. Bile leakage occurs in liver surgery, bile ducts surgery, after cholecystectomies, pancreatic surgery [1].

Definition and Classification

Literature does not establish a consensus for the definition of bile leakage. Many different definitions of bile leakage have been proposed [2-11]. Some studies define bile leakage as externalization of bile through drainage tubes or by determining the concentration of bile exteriorized through drainage tubes. Some studies compare levels of bilirubin exteriorized through drainage tubes with levels of serum bilirubin. The presence of bile collection detected at imaging investigations or some authors define detection of these collections at surgical re-interventions as bile leakage [9, 12]. According to International Study Group of Liver Surgery bile leakage definition [13] is: ”discharge of fluid with an increased bilirubin concentration via the intra-abdominal drains on or after postoperative day 3 or as the need for radiologic intervention and relaparatomy for biliary collections and bile peritonitis, respectively”.

Bile leakage can be classified in [14]:

- Central type, if the leaky bile ducts were confirmed to be in communication with the biliary tree by fistulography via the drainage catheter, endoscopic retrograde cholangiography, or percutaneous transhepatic cholangiography.

- Peripheral type, if the leaky bile ducts were not in communication with the biliary tree.

The International Study Group of Liver Surgery propose a classification of bile leakage by grading them by the impact of this complication on patient clinical management. According to this there are three types of bile leakage:

1. Bile leakage grade A: This type of bile leakage has a little impact on patient's general condition, and an intra-abdominal drain controls leakage adequately. The volume of drain fluid and the bilirubin concentration decreases daily. Not required additional diagnostic and treatment methods. A Grade A bile leakage requiring drainage for more than 1 week should be classified as Grade B bile leakage.

2. Bile leakage grade B: This type of bile leakage requires a change in patient’s treatment, but can be treated without relaparotomy. These patients present parameters suggestive of infection (fever, abdominal pain). The drains placed intraoperatively may not entirely drain the leakage, at imaging studies can be detected as intra-abdominal fluid collection. Patient with Grade B bile leakage may require antibiotic therapy, radiological and endoscopic drainage procedures. Postoperative hospital stay for these patients is prolonged, and a part from patients with bile leakage Grade B may be discharged with drains in situ to be treated in the outpatient setting.

3. Bile leakage Grade C: This group of patients require relaparotomy with suture/closure of leaking bile ducts, clearance of intra-abdominal collections, abdominal drainage supplementation. These patients present clinical manifestations of biliary peritonitis, which might be complicated by single or multiorgan failure. Imaging tests shows an intra-abdominal fluid collection, the postoperative course of the patients is prolonged and secondary postoperative complications may result [13].

Etiology

Etiology of bile leakage is varied; it can develop after a wide range of surgical interventions.

Bile leakage can occur in:

1. Hepatic resections for primary malignant and benign liver tumors, hepatic resection for metastases, liver transplantation and liver biopsy
2. Biliary-enteric anastomoses (after duodenopancreatectomy, bile ducts resections for biliary tumors, biliary reconstruction after iatrogenic injury, Roux-en-Y hepaticojejunostomy or choledocho-jejunostomy for unresectable pancreatic tumors) [15, 16]

Bile leakage can be detected, how we described above, by discharge of fluid with an increased bilirubin concentration via the intra-abdominal drains on or after postoperative day 3 or as the need for radiologic intervention and relaparatomy for biliary collections and bile peritonitis, respectively. Bile leaks often manifest within 1 week of surgery, however they may not manifest clinically for up to one month after intervention.

Intra-abdominal collections caused by bile leakage can be detected at CT and US, but both cannot distinguish between a bile leak and other postoperative collections. Hepatobiliary scintigraphy demonstrates physiologic biliary excretion and can help detect active bile leaks, both free intraperitoneal and contained intrahepatic leaks. A limitation of hepatobiliary scintigraphy is weak relation with biliary anatomy and spatial resolution. Recently, single photon emission computed tomography (SPECT)/CT has been used in combination with dynamic and planar hepatobiliary scintigraphy to enhance diagnostic and anatomic accuracy in the detection of bile leaks. Magnetic resonance cholangiopancreatography with hepatobiliary contrast agents can indicate the exact site of a bile leak and safely help distinguish between fluid collections of biliary and non-biliary origin. In fact, in a prospective study of patients who had undergone laparoscopic cholecystectomy, MR cholangiography with mangafodipir trisodium had a reported sensitivity of 95% and a specificity of 100% for the detection of bile leaks [17].

Magnetic resonance cholangiopancreatography with hepatobiliary contrast agents is useful in evaluation of biliary-enteric anastomoses, for which endoscopic evaluation is not possible because of altered anatomy. Endoscopic retrograde cholangiography has diagnostic and therapeutic role, sphincterotomy and temporary stent placement may be performed when nonsurgical management is desired. Endoscopic retrograde cholangiography is not the first line choice for diagnosis of a suspected bile leakage, because of invasive nature and its inability to detect extra-biliary bile leakage and also after endoscopic retrograde cholangiography may occur acute pancreatitis and bleeding [18].

A progress regarding biliary leakage diagnosis was the appearance of hepatocyte-specific contrast product (Primovist). The Primovist will be excreted biliary and it will show the biliary anatomy more accurate and a possible fistulas. Also accumulation of the Primovist into collection demonstrated it communication with the biliary tract. IRM with Primovist can describe more accurate the orientation and ramifications of a biliary fistula, comparing with MR cholangiography. His limitations are regarding hepatic insufficiency.

Bile leakage occurred in patients undergoing reconstruction for biliary injury represents a particular situation. This is because reconstruction is performed on a non-dilated biliary tree in the presence of inflammation, complex damage to the duct, associated vascular injury and diathermy injuries. The incidence of anastomotic bile leakage in patients undergoing reconstruction for biliary injury was 24% versus 2.8% for overall non-injury procedures. Risk factors for bile leakage are biliary reconstruction following injury and a high anastomosis, above the confluence. The biliary tree above the confluence is narrower and thinner, making anastomosis technically more difficult [16].

Most of bile's leakages occur after liver resection with or without biliary reconstruction. Bile leakage occurs in 3.6 to 12 % of patients undergoing a liver resection without biliary reconstruction and in 0.4% to 8% of patients undergoing a liver resection with biliary reconstruction [19]. The majority bile leakages after liver resection are of low clinical significance (Grade A). Certain studies assessed the risk factors linked with bile leakage after liver resections; these were the use of intra-operative drains and intra-operative blood loss greater than 500 ml [15]. The correlation between the type of hepatectomy and postoperative bile leakage has not yet been clearly defined. Lo et al. reported left-sided hepatectomy as an independent risk factor for the onset of postoperative bile leakage, because of the risk of damaging the right posterior biliary duct that drains into the left hepatic duct [6]. Hepatectomies in which the cut surface exposes the major Glisson's sheath and includes the hepatic hilum (central bisectionectomy, anterior sectionectomy, segmentectomy 1, and hepatectomy including segments 4, 5, and 8) are independent risk factors for bile leakage [20, 21]. Hepatectomies including segment 4 usually expose the major Glisson's sheath and hepatic hilum on the cut surface, with a high risk of damaging the bile duct wall [3]. In conclusion, complex hepatectomy and operating time are independent risk factors for postoperative bile leakage after liver resections [14].

Dokmak et al. reported that intraoperative bile leakage was risk factor of bile leakage [22]. Many methods have been described to prevent bile leakage after liver transection, including intraoperative cholangiography, air test by injecting air under ultrasonographic monitoring and bile leakage test. Bile leakage test consist in injecting a fat emulsion, indocyanine green or methylene blue through a catheter inserted in cystic duct into the common bile duct and the distal common bile duct is occluded [23]. Using this technique, some studies [24, 25] have identified intraoperatively additional potential bile leakage points in 19.7%-80.8% of the patients.

Clinical Presentation

Clinical manifestations of bile leaks may include unremitting abdominal tenderness, anorexia, fever, and general malaise. We can also have bile at the site of surgical wound. Clinical signs and symptoms of bile leaks are nonspecific and because of the late recognition of bile leaks that can increase morbidity and mortality rates. Imaging is crucial for establishing an early diagnosis and guiding the treatment algorithm [26].

Treatment

Conservative Treatment

Conservative treatment is the first choice in case of bile leakage grade A. This means that the drains placed intraoperative drain the biliary leak and the quantity of the bile leak is low. The drains must be followed daily and when the quantity decreases to less than 10 ml/day they can be removed. In case of increasing the quantity is requires interventional treatment.

Endoscopic Treatment

As opposed to the etiology of fistulae in other areas of the digestive tract and its annexes, biliary tract fistulae are often iatrogenic, resulting either from cholecystectomy or following liver transplantation. However, the management of biliary fistulae is similar regardless of cause, and consists of covering the parietal defect using stents.

The incidence of biliary fistulae in patients with liver transplantation can reach 25%. They may form at the site of anastomosis, at the level of the remaining cystic duct or at the site of T-tube implantation [27]. In patients with cholecystectomy the incidence of fistulae can reach 2.7% (Figure 1 and Figure 3) [28].

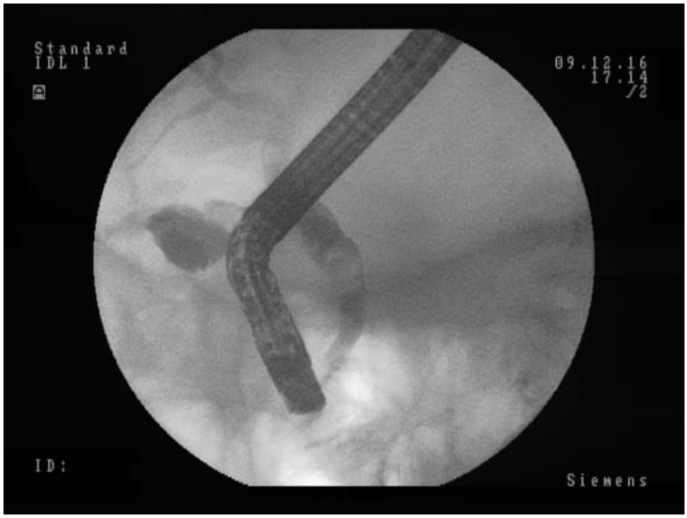

Figure 1. *Endoscopic cholangiography showing a dilated common bile duct with a stone and extravasation of contrast through the remnant cystic duct after cholecystectomy.*

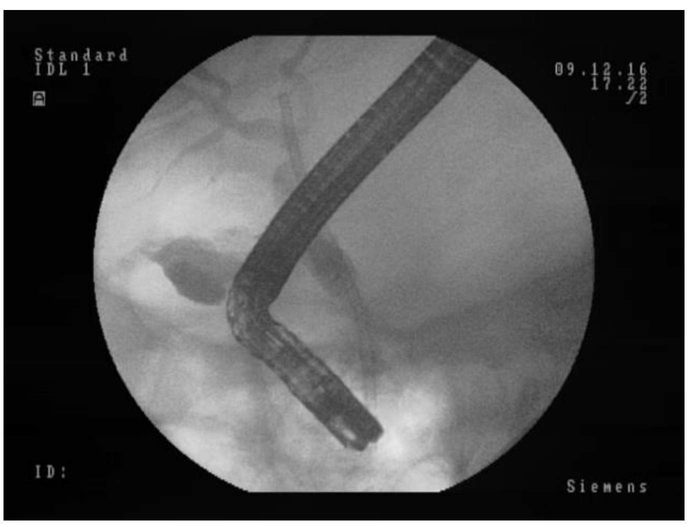

Figure 2. *Endoscopic cholangiography after removal of the stone and placement of a plastic stent inside the common bile duct.*

Figure 3. *Iatrogenic fistula after cholecystectomy. Arrow points to the extravasation of contrast from the biliary tree.*

Most patients with biliary fistulae can be treated endoscopically using ERCP. In patients with a low-flow fistula, some studies recommend performing only endoscopic biliary sphincterotomy [29]. Its purpose would be to abolish the muscular component of the papilla, thereby decreasing the pressure in the bile ducts and favoring preferential duodenal drainage. However, in most cases, it is preferred to cover the fistulous opening with one or more stents, thus preventing extravasation of bile in the subhepatic space (Figure 2 and Figure 4).

Figure 4. *Endoscopic cholangiography after stenting of the common bile duct.*

Plastic biliary stents are radiopaque stents made of polyethylene, polyurethane, or teflon, with a diameter and length that can vary from 5F to 12F and 1 to 18 cm, respectively (Figure 5). Plastic biliary stents are available in many configurations. Pigtail stents are coiled at one or both ends (Figure 5 and 6) (single or double pigtail). Side holes are placed along the curved pigtail ends. Flanged stents, which may be straight, angled, or curved, have a single flap proximally and distally with a side hole or 4 flaps proximally and distally without side holes [30].

Figure 5. *Angled biliary plastic stent.*

Figure 6. *Double pigtail biliary plastic stent.*

SEMS are made of different metal alloys ranging from 4 to 12 cm in length with diameters when expanded ranging from 6 to 10 mm. All SEMS are radiopaque. Most models have additional proximal and distal markers, with flared ends to prevent migration [30]. As in the case of digestive tract stents, biliary metallic stents can be fully covered, partially covered or uncovered (Figure 7).

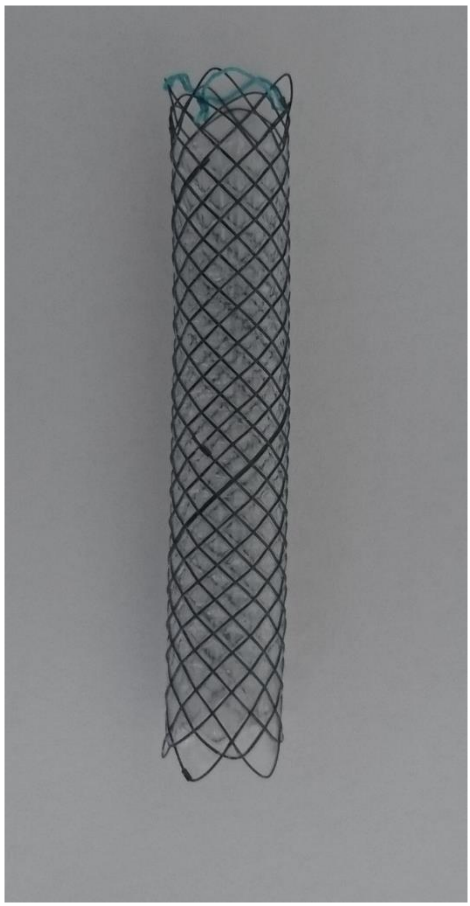

Figure 7. *Fully covered metallic biliary stent.*

Biliary stent placement, either plastic or metal, is performed under radiologic guidance. In both cases, the first step is endoscopically locating the papilla, followed by selective catheterization of the bile ducts. Endoscopic sphincterotomy is not necessary in all cases, multiple studies showing that stenting without sphincterotomy does not increase the incidence of postERCP pancreatitis [31]. After catheterization is performed the bile ducts are opacified using contrast, which allows for identification of site and size of the fistulous orifice.

If a plastic stent is chosen, a radiopaque guidewire is first advanced into the intrahepatic bile ducts. The stent is advanced over a catheter which acts as a pusher, which is itself placed over the guidewire. The length of the stent must be carefully chosen so that it exceeds the proximal end of the fistula, ensuring full coverage of the fistula. Once the stent has been properly advanced, the catheter and guidewire are withdrawn and the stent remains in place.

Metal stents are constrained by an outer sheath. After placement in the duct over the guidewire, the outer sheath is withdrawn, allowing the stent to expand. The guidewire is then removed.

Many studies have compared plastic and metal stents, but a more recent meta-analysis has shown no difference between SEMS and plastic stents with regard to technical or therapeutic success in draining the bile duct initially [32]. The main disadvantage of plastic stents over their metal counterpart is distal migration, which occurs in up to 10% of the cases, and can lead to bowel perforation. Stents can however migrate proximally as well, blocking biliary drainage and leading to cholangitis. Migration is less common in SEMS because of their larger diameter.

Plastic stent occlusion should be taken into consideration if the duration of the treatment will extend to more than 3 months. SEMS were found to have significantly less stent occlusion by 4 months and significantly reduced risk of recurrent biliary obstruction overall [32].

Postoperative bile leaks can be successfully treated with placement of a single plastic stent with or without sphincterotomy in 70% to 100% of patients [33-37]. Either plastic or metallic stents can be used as a first line therapy. Pigtail plastic stents, being coiled, have a lower migration rate than straight plastic stents. They also have side holes at both the proximal and distal ends, which theoretically allow for a better drainage. If metallic stents are chosen, only fully or partially covered stents may be used, as these may be subsequently removed. A few case series have been published which describe the successful use of metallic stents to treat large leaks where plastic stents failed [38]. Although symptom resolution is fast after stent placement, the actual healing of leak may take up to 6-10 weeks [39]. Consecutively, stent removal should not take place sooner than 2 months after placement.

In cases of leaks after liver transplantation, prolonged stenting is advised because healing may be delayed by immunosuppressors. If the leak is associated with a bile duct stricture, endoscopic dilatation using balloons or bougies can be attempted before stenting. Stents must be kept in place for 2 to 3 months, the aim being to ensure the proper healing of the leak. A recent study has found that using fully covered SEMS in patients with leaks after transplantation has resulted in a high bile duct stricture rate, therefore not recommending their use in managing these patients.

A common complication of stent placement is duodenal biliary reflux, with secondary bacterial colonization of the biliary tract and sludge/stone formation. Hence, after removal of the stent, the bile ducts have to be checked for sludge or stones and these have to be cleared.

Another complication of stents is related to their deployment too far inside the duodenum, or their migration, with subsequent impaction of the stent flanges in the duodenal wall and perforation. If stents migrate in the bowel they can also become stuck, mostly in the ileocecal valve, leading to bowel obstruction.

Interventional Imaging Treatment

Percutaneous Drainage

Needle aspiration is often required to definitively diagnose bile leaks, especially in case of bilomas and can also resolve the drainage by placement of a drain inside the collection. This procedure is usually performed utilizing an 18 to 22-gauge co-axial needle under CT or US guidance.

For the majority of the radiologists ultrasound is considered the preferred modality to guide diagnostic aspiration and drain placement due to the lack of radiation exposure, portability, flexibility to angle the probe and real time imaging capability. By using real time color with Doppler sonography it is easy to identify the vascular structures and alter the needle path to avoid traversing major vessels. In order to safely reach the target if no other reasonable window is identified, interventional radiologist can choose to traverse the liver.

Surgical Treatment

Surgical treatment is reserved for cases where endoscopic or interventional treatment can’t resolve the problem or when we have signs of general peritonitis, caused by biliary leakage. Surgical re-intervention is essential for a grade C bile leakage. Surgical procedures may include: suture closure of leaking bile ducts, clearance of intra-abdominal fluid collections, and (re-)construction of a bilioenteric anastomosis. Furthermore, additional drains for continuous postoperative lavage may be placed.

Conclusions

In conclusion bile leakage is an important complications that can occur and a quick diagnosis is important for establish the correct algorithm for it management that should be address in correlation with bile leakage grade.

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