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Complications of Biliary Tract in Liver Transplantation

Giuliano Testa, M.D., Massimo Malagò, M.D., Christoph E. Broelsch, M.D., Ph.D.

Department of General Surgery and Transplantation, University Hospital Essen, Hufelandstr. 55, D-45122 Essen, Germany

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Abstract. Bile duct leaks and stenosis, although greatly reduced in their incidence, still play a major role in early and late graft loss. Their pathogenesis is multifactorial, being related to graft quality, ischemia time, arterial blood flow, and, of course, technical mishaps. The diagnosis and treatment of biliary complications is nowadays a joint effort among surgeons, interventional radiologists, and gastroenterologists. The correct algorithm in obtaining a fast diagnosis and the correct therapeutic approach are necessary to save the graft, avoid retransplantation or recipient death. Although this may seem to be a simple and basic concept, it assumes tremendous importance in liver transplantation in which the differential diagnosis between biliary and arterial complications or graft rejection and malfunctioning is often a difficult one.

Biliary reconstruction after orthotopic liver transplantation has been an issue of intense discussion since the establishment of a standardized technique of liver replacement. With a reported complication rate as high as 40% [1, 2], biliary anastomosis was the leading cause of surgical complications. There was no consensus among transplant surgeons regarding the type of anastomosis to perform [3, 4] until the last decade during which two types of biliary reconstruction, the choledocho-choledocotomy (CC) and the hepaticojejunostomy (HJ) on a Roux-en-Y loop, have become almost universally accepted. A better understanding of how blood is supplied to the bile duct [5–7], improved suturing material, and the exploitation of the learning curve have contributed to better results, although the complication rate for biliary anastomosis is still around 15% [8, 9]. Biliary leaks, biliary stricture, ampullary dysfunction, and biliary obstruction are now the most common causes of biliary complications after orthotopic liver transplant. It is of paramount importance to entertain the possibility of a biliary complication in the differential diagnosis of a malfunctioning graft. A delay in the proper diagnostic and therapeutic approach may result in the death of the patient.

The diagnosis and treatment of biliary complications after liver transplant have changed in the past decade and a nonoperative initial approach has become more common [10, 11]. We remain of the opinion that procedures such as endoscopic retrograde cholangio-pancreatography (ERCP), percutaneous transhepatic cholangiography (PTC), and percutaneous drainage are indispensable tools for the diagnosis and often for the treatment of biliary complications but a correct surgical strategy needs to be designed when these procedures fail.

Correspondence to: G. Testa, M.D., Universitätsklinik Essen, Klinik für Allgemein-und Transplantationschirurgie, Hufelandstr. 55, D-45122 Essen, Germany, e-mail: giuliano.testa@uni-essen.de

Biliary Leaks

Biliary leaks have been reported with a similar incidence after CC or HJ [8]. Early leaks (within 4 weeks of the transplant) usually occur at the anastomotic site and are more often caused by a technical mishap. In a minority of the cases, the cause of the leak is due to poor vascular supply to the anastomotic site. These leaks can be diagnosed at the routine T-tube cholangiogram before becoming symptomatic. Unless associated with a major disruption of the anastomosis, leaks are managed conservatively by keeping the T-tube open and repeating the contrast study after 1 or 2 weeks. The formation of a biloma is the usual consequence of a biliary leak in the absence of an intra-abdominal drain. Abdominal discomfort or pain, nausea, fever, and at times a persistent elevation of alkaline phosphatase and gamma glutamil transferase (GGT) [12] are usually associated with the leak and the formation of the biloma. When a biliary drain is in place, the diagnosis of the biliary leak is straightforward and an ultrasound or a computed tomography (CT) scan completes the examination to confirm the presence of the biloma. Doppler ultrasound is performed to exclude the possibility of an arterial problem. When no drain is in place, an ultrasound can suggest the presence of a biliary leak [13], but a definitive diagnosis must be obtained with a contrast study. The initial management should be nonoperative. ERCP is the preferred contrast study, since it also allows stenting of the bile duct while the biloma is drained percutaneously under ultrasound guidance. Antibiotic treatment should be established. After successful conservative management, the biliary system should be studied in 4 weeks, and the stent removed in the absence of any pathological findings. An episode of cholangitis or an increase in the cholestatic parameters in a patient treated conservatively should always raise the suspicion of stent dislodgment or obstruction and, therefore, call for a contrast study.

When the anastomotic defect is too wide or the conservative treatment fails, operative intervention is necessary. Primary repair has been suggested in the very early postoperative period and

when technically feasible [9]. In our opinion, this should be performed only in ideal situations, in the absence of tension between the two ends of the bile ducts, in the absence of infected tissues, and without concerns regarding the blood flow to the bile ducts. In all other scenarios, the construction of an HJ on a Roux-en-Y loop remains the best solution and allows wide debridement of the donor bile duct to remove necrotic or infected tissue. The conversion to an HJ is also mandatory when a disruption of the CC is associated with thrombosis of the hepatic artery. In this situation or whenever there are concerns regarding the biliodigestive anastomosis, a transanastomotic catheter should be placed.

The diagnosis of a leak occurring after a primary HJ in which no trans-anastomotic catheter was placed in surgery can be obtained with a cholescintigraphy [9, 14] and in selected cases with PTC [15, 16]. When PTC is feasible, conservative treatment is established with an internal-external drain that can be changed with an internal stent before the patient is discharged. In all other cases, operative treatment with primary repair or refashioning of the anastomosis, following the same guidelines mentioned above, is necessary.

Bile leaks that occur more than 1 month after the transplant are usually a complication of the T-tube removal and have been reported with an incidence as high as 31% of all leaks [8]. A leak at the T-tube site is suspected when the T-tube is removed and the patient complains of abdominal discomfort or pain. Most of the times, the symptoms are short lived and disappear spontaneously or with pain medications. It is useful to reinsert a small feeding tube in the drain tract to prevent the accumulation of bile. When the symptoms do not subside, an ERCP is indicated to place a transanastomotic drain; Short-term antibiotic therapy is also needed. Laparotomy and primary repair is indicated only when the conservative management and ERCP fail. The likelihood of complications caused by T-tubes and the great reliability in terms of diagnosis and treatment offered by ERCP have made many transplant centers, including ours, less inclined to routinely use T-tubes. At present, we restrict the use of T-tubes for those grafts in which a delayed function is expected, and the production and the evaluation of bile remains, together with the laboratory findings, a good parameter of liver function.

Biliary Strictures

Biliary strictures have been reported with an incidence between 3% and 6%, and at least in two large series, more often after choledochojejunostomy than after choledochotomy [8, 9]. They may occur at the anastomotic site or above or below the anastomosis. Early stenoses (within 1 month of the transplant) are usually caused by a surgical mistake. The strictures occurring at a later time are very often the effect of poor blood supply to the bile duct due to either an excessive dissection of the periductal tissues, a nonsufficient trimming to well-perfused biliary tissue at both sites of the anastomosis, or to a newly occurred arterial problem.

An elevation of alkaline phosphatase, GGT, and bilirubin values is usually associated with the presence of a biliary stricture. An episode of cholangitis may also occur, and may be complicated by the formation of intrahepatic abscesses when an arterial problem is the cause of the biliary stricture.

When the only clinical presentation is the elevation of the liver biochemistries, a biopsy is performed to check for rejection. If no signs of rejection are revealed, the next step is to check for cholestasis. An ultrasound may fail to show biliary dilatation in the early posttransplant period [9, 17] but is otherwise an excellent diagnostic tool [13]. Cholangioscintigraphy is also a useful screening test especially when an HJ was performed at the time of the transplant [14]. Although invasive and not free of complications, ERCP and PTC are a good combination for diagnosis and therapy in this scenario.

A contrast study is performed to confirm a diagnosis of biliary stricture and to determine the location, extension, and at the same time treat the stricture. Even if anastomotic strictures seem to respond well to balloon dilatation and short-term (3 months) stenting [10, 18], the recurrence rate is very high (30–40%) and several reinterventions may be necessary. In this setting, it is probably best to attempt nonsurgical intervention first, but if this fails do not hesitate to adopt surgical treatment.

Nonanastomotic strictures and multiple strictures may be the consequence of ischemia and tend to respond very poorly to a nonsurgical treatment. In these cases, a surgical revision is almost invariably needed. If a CC was performed, this must be changed to a Roux-en-Y HJ. If the latter was performed, it needs to be redone. In both cases, it is necessary to trim the bile duct of the graft to an area that is well vascularized. A preoperatively placed stent can be helpful in guiding the surgical dissection and can be used to stent the new anastomosis.

Multiple intrahepatic biliary strictures, also reported as type 2 lesions [19], have been associated with prolonged ischemia time prior to transplantation, with ABO incompatible grafts, and with hepatic artery problems [20]. In these cases, the overall outcome is not good, and retransplantation is needed. In these cases, PTC and the placement of internal-external stents still play a role and may be extremely useful in relieving jaundice, ameliorating the conditions of the patients, and allowing better clinical conditions at the time of the retransplant.

Ampullary Dysfunction

Ampullary dysfunction or diskinesia occurs in 2% to 5% of patients with a CC and represents about 20% of biliary complications after orthotopic liver transplantation [8, 9]. The etiology of the dysfunction of the sphincter of Oddi is unknown but a logical hypothesis is that the dissection performed at the time of the recipient hepatectomy causes destruction of the natural blood supply and innervation leading to a permanent alteration of the motility of the ampulla. This pathology manifests itself with a slow increase of cholestatic parameters and bilirubin, which in 75% of the patients occurs between 1 and 12 months of the transplant. The diagnosis is suspected when an intrahepatic and extrahepatic biliary tract dilation is seen by ultrasound and confirmed by ERCP. ERCP is the test of choice because it allows the performance of a sphincterectomy at the time of diagnosis. Although sphincterectomy is not successful in all cases [10, 21], it remains, in our opinion, the best initial approach. However, in case of failure, a conversion to an HJ is needed.

Sludge and Stone Formation

Intrahepatic biliary obstruction can be caused by the formation of sludge and stones, or by multiple strictures. Most of the time strictures are the only real pathology complicated by recurrent clinical and subclinical episodes of cholangitis leading to the

formation of sludge and then stones. Multiple intrahepatic strictures are mainly related to either ischemia caused by hepatic artery problems [21, 22] or prolonged cold ischemia time prior to transplantation [23]. The incidence of the latter has greatly diminished, thanks to proper flushing of the bile duct with University of Wisconsin (UW) solution and keeping the ischemia time within 8 hours. Intrahepatic strictures can remain clinically silent for a long time or can manifest as graft dysfunction with increasing alkaline phosphatase and GGT and eventually bilirubin. Episodes of cholangitis may also occur. The diagnosis is best made by ERCP or PTC. PTC in particular has been successful in improving graft functioning by clearing the sludge and in combination with dye laser in fragmenting the stones [24]. Unfortunately, the long-term success of intrahepatic biliary strictures percutaneous dilatation is uncertain [25], requires multiple sessions, and the placement of temporary stents.

Chenodesossicholic acid may play a role in making the bile more fluid, therefore, delaying new sludge formation and prolonging the efficacy of percutaneous treatment. When these medical and noninterventional treatments fail or when the intrahepatic strictures are related to an arterial problem the only other option is retransplantation.

Adult-to-Adult Living Related Liver Transplantation

A new chapter on biliary complications after liver transplantation has been opened with the growing success of adult-to-adult living-related liver transplantation using the right lobe, segments 5, 6, 7, 8. Biliary leaks and stenosis have been reported with an incidence as high as 30%. [26, 27] Such a high incidence is due to the difficulties in defining the dissection plane around the right hepatic duct, aiming on one side at avoiding injury to the donor biliary system and on the other side at obtaining only one duct for the anastomosis in the recipient. Increased experience in performing the donor hepatectomy has allowed a drop to less than 15% in biliary complications. Whether in the presence of a single donor hepatic duct to anastomize a direct duct-to-duct anastomosis with the recipient choledocus or an HJ is the better solution or whether stenting these anastomosis really plays a role in decreasing the complication rate are still open questions.

Conclusions

In conclusion, biliary complications after orthotopic liver transplantation even if greatly decreased in incidence still constitute a problem that at times can lead to the loss of the graft. Proper management of the graft prior to implantation and accurate surgical technique are the best tools to avoid posttransplant complications. Early diagnosis of any biliary complication and correct intervention can in many cases assure complete and definitive treatment.

Résumé

Bien que l'incidence soit grandement diminuée, les fuites et la sténose biliaires jouent un rôle majeur dans le rejet de greffon précoce et retardé. Leur pathogenèse est multifactorielle, en rapport avec la qualité du greffon, le temps d'ischémie, le débit artériel et bien sûr, les complications techniques. Le diagnostic et le traitement des complications biliaires sont actuellement le résultat d'un effort combiné des chirurgiens, des radiologues interventionistes et de gastro-entérologues. L'algorithme le plus adapté pour obtenir un diagnostic rapide et une approche thérapeutique correcte sont les seules chances pour récupérer le greffon et pour éviter la retransplantation ou le décès du receveur. Même si ce concept peut paratre simple et basique, il prend une importance formidable dans la transplantation du foie où le diagnostic différentiel entre complications biliaires et artérielles du rejet et un mauvais fonctionnement est souvent difficile.

Resumen

La fuga anastomótica y la estenosis de la vía biliar, aunque con una incidencia notoriamente disminuida, juega un papel importante en la pérdida tanto precoz como tardía, de un trasplante hepático. Su patogénesis es multifactorial, y se relaciona con la calidad del injerto, el tiempo de isquemia, el flujo sanguíneo arterial y, por supuesto, factores de orden técnico. El diagnóstico y el tratamiento de las complicaciones biliares es actualmente un esfuerzo conjunto de los cirujanos con los radiólogos intervensionistas y los gastroenterólogos. Un algoritmo correcto para diagnóstico precoz y abordaje terapéutico constituye la única posibilidad de salvamento del trasplante y de prevenir un re-trasplante o la muerte del paciente. Aunque esto pudiera parecer un concepto simple y fundamental, realmente es algo que reviste enorme importancia en el trasplante hepático, donde el diagnóstico diferencial entre complicaciones biliares y arteriales, o rechazo, o malfunción del trasplante es frecuentemente difícil.

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