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Cholangiographic Findings in Hepatic Artery Occlusion After Liver Transplantation

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Because the hepatic artery provides the only blood supply to the biliary tree of a liver allograft, posttransplantation arterial occlusion may result in a biliary complication. Cholangiograms were reviewed retrospectively in 31 transplant patients who had proved complete or partial occlusions of the hepatic artery (thrombosis in 29 and marked stenosis in two). Cholangiograms were abnormal in 26 (84%). The most common abnormality, seen in 16 patients, was nonanastomotic contrast leakage from the donor intra- or extrahepatic bile ducts. Strictures of the donor biliary tree occurred in 14 patients, four of whom also had a nonanastomotic bile leak. In 12 of the 14, the strictures were nonanastomotic. Other findings included poor filling of the intrahepatic bile ducts, generalized donor ductal dilatation and irregularity, and intraductal filling defects. Sixteen (89%) of 18 transplants with nonanastomotic contrast leakage had occlusions of the hepatic artery. Of 21 transplants with nonanastomotic strictures, 12 (57%) had occlusions of the hepatic artery. Only two (10%) of 20 transplants with biliary anastomotic strictures had arterial occlusion.

We conclude that liver transplant recipients who exhibit nonanastomotic contrast leakage or nonanastomotic strictures on cholangiography should be evaluated for occlusion of the hepatic artery as the probable cause.

Occlusion of the hepatic artery (thrombosis or stenosis) is an important cause of morbidity and mortality after liver transplantation. Thrombosis of the hepatic artery is the most common and most serious vascular complication after transplantation [1]. It is usually a devastating event that requires retransplantation for survival in most cases [2, 3]. Mortality is 73% without retransplantation and 27% if retransplantation is performed [2]. Stenosis of the hepatic artery anastomosis may require surgical revision or balloon angioplasty. Prompt recognition that occlusion of the hepatic artery is the cause of a poor postoperative course is important to patient survival.

Because the blood supply of the allograft biliary tree is entirely dependent on the hepatic artery, occlusion (thrombosis or stenosis) may result in a biliary complication. Often, the clinical signs of occlusion of the hepatic artery are nonspecific. If the patient has signs of a possible biliary complication, cholangiography may be performed before the diagnosis of occlusion of the hepatic artery is known. In this paper we review the cholangiographic findings in 31 liver transplant patients who had complete or partial occlusions of the hepatic artery. The cholangiographic abnormalities presented are those that should alert the radiologist and surgeon to occlusion of the hepatic artery as the cause of an abnormal postoperative course.

Materials and Methods

During the 6-year period ending January 1, 1987, 742 patients (278 children and 464 adults) received 968 orthotopic liver transplants. We studied all patients with proved partial or complete occlusions of the hepatic artery who also had postoperative cholangiography. Seventy-two (7.4%) of the transplants (in 46 children and 26 adults) had thromboses of the

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hepatic artery documented by angiography, surgery (retransplantation), or autopsy. Another eight transplants had angiographically proved stenoses of the hepatic artery anastomoses. Cholangiography was performed only in those patients with suspected biliary complications. Thirty-one patients (29 with thromboses and two with marked stenoses) underwent transhepatic or T-tube cholangiography after transplantation. Retrospective review of these cholangiograms forms the basis of this study.

These cholangiograms were compared with a group of 75 transhepatic cholangiograms performed during the study period of liver transplants that had no occlusions of the hepatic artery.

Results

Cholangiograms were abnormal in 26 (84%) of the 31 cases with occlusions of the hepatic artery. Major abnormalities were nonanastomotic contrast leakage and biliary strictures. Biliary strictures were classified as either anastomotic or nonanastomotic (Table 1). Nonspecific findings, such as narrowing and poor filling of peripheral intrahepatic ducts, were seen in three patients. Two patients had normal cholangiograms.

TABLE 1: Prevalence of Hepatic Artery Occlusion in Liver Transplants with Nonanastomotic Bile Leakage and Biliary Strictures

Cholangiographic Findings	Hepatic Artery Occlusion (%)
Nonanastomotic contrast leakage (N = 18)	16 (89)
Nonanastomotic strictures (N = 21)	12 (57)
Isolated anastomotic strictures (N = 20)	2 (10)

Note.— N = number of transplant patients.

Contrast Leakage

Nonanastomotic contrast leakage from the donor intra- or extrahepatic bile ducts was seen in 16 patients (nine children and seven adults) who had occlusions of the hepatic artery (sensitivity, 52%). The bile leaks were hilar or intrahepatic in 15 of the 16 cases. Eight of these were seen as focal collections of contrast material within the hilum and parahilar area (Fig. 1). Four patients had intrahepatic bilomas; three of these also had bilomas in the hilar area (Fig. 2). Diffuse leakage from the central intrahepatic bile ducts was observed in two patients (Fig. 3). In addition to bilomas, one patient also had irregularity, dilatation, and intraluminal filling defects in the entire donor biliary tree (Fig. 4). An extrahepatic nonanastomotic bile leak was seen in one patient (Fig. 5). Poor filling of the intrahepatic ducts (Figs. 2 and 3) and intraluminal filling defects (Figs. 1 and 4) accompanied bile leakage in six and four cases, respectively.

Nonanastomotic intrahepatic contrast leakage was observed in two cases in the group of patients with patent hepatic arteries (specificity, 97%).

The mean interval between the diagnosis of occlusion of the hepatic artery and the demonstration of contrast leakage was 36 days (range, 0–130). In four of the 16 cases, the cholangiographic diagnosis of nonanastomotic bile leak was the initial finding that prompted angiographic evaluation. In the remaining 12 cases, the diagnosis of occlusion of the hepatic artery was known before the cholangiograms were obtained.

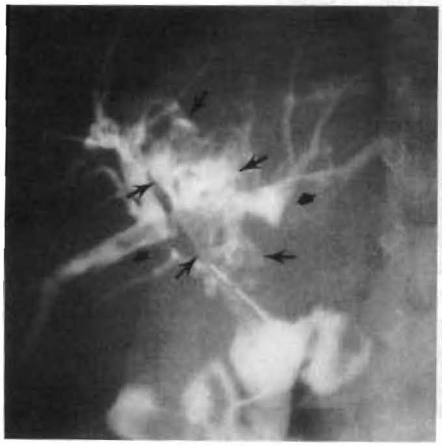

Fig. 1.—Hilar and parahilar biloma. Transhepatic cholangiogram shows contrast leakage into a central biloma cavity (*long arrows*) and filling defects within main right and left hepatic ducts (*short arrows*). Main left hepatic duct cannot be identified. Histologic examination of the hepatectomy specimen after retransplantation showed an infected central biloma cavity with necrosis of main left hepatic duct. Filling defects in right and left hepatic ducts probably represent necrotic debris and biliary sludge.

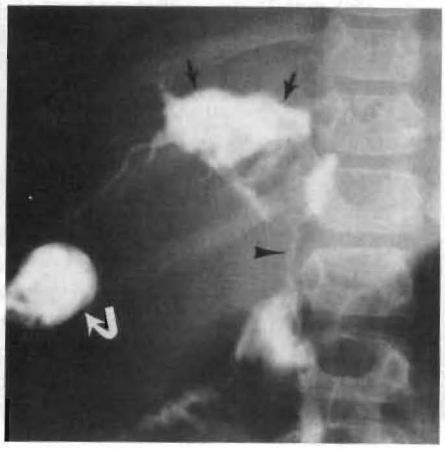

Fig. 2.—Intrahepatic and hilar bilomas. After percutaneous drainage of a peripheral intrahepatic biloma (*curved arrow*), a central hilar biloma (*straight arrows*) is seen to fill via a small right hepatic bile duct. Filling of intrahepatic biliary tree is poor, and main right and left hepatic ducts cannot be identified. Filling of common duct (*arrowhead*) and a Roux limb of jejunum is seen. Histologic examination of hepatectomy specimen after retransplantation showed necrosis of hilar structures with a bile abscess cavity.

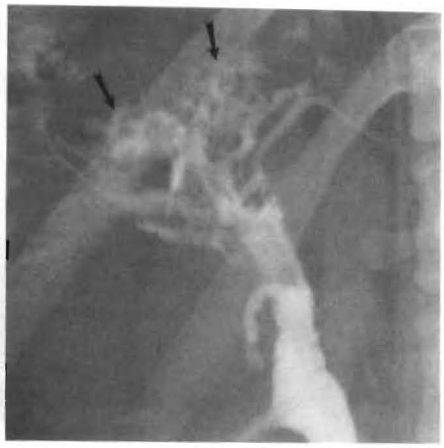

Fig. 3.—Diffuse bile leak. T-tube cholangiogram shows extensive contrast leakage (*arrows*) from central hepatic bile ducts. Ductal irregularity and poor filling of peripheral intrahepatic bile ducts are evident. Histologic examination of hepatectomy specimen after retransplantation showed bile duct necrosis with multiple hepatic infarcts and abscesses. (Reproduced with permission from Campbell and Zajko [4].)

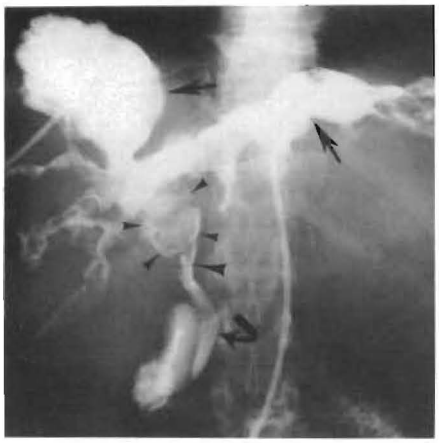

Fig. 4.—Necrosis of entire donor biliary tree. Sinogram 6 weeks after percutaneous drainage of fluid collections in right and left hepatic lobes (*straight arrows*) shows communication with biliary tree. Generalized ductal irregularity and dilatation with diffuse intraluminal filling defects are seen. Note hilar biloma cavity (*small arrowheads*) that replaces donor common duct. Recipient common bile duct (*curved arrow*) below biliary anastomosis (*large arrowhead*) is normal. Histologic examination of the hepatectomy specimen after retransplantation showed bile duct necrosis with purulent and necrotic material filling donor biliary tree.

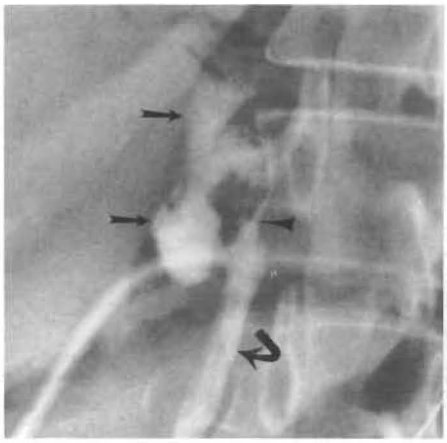

Fig. 5.—Nonanastomotic extrahepatic bile leak. T-tube cholangiogram shows contrast leakage (*straight arrows*) above choledochocholedochostomy (*arrowhead*) with no filling of donor biliary tree. Recipient common bile duct (*curved arrow*) is normal. Donor common duct was completely necrotic at laparotomy.

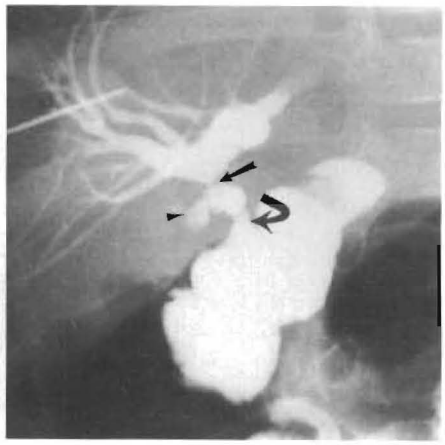

Fig. 6.—Nonanastomotic biliary stricture. Transhepatic cholangiogram shows partial biliary obstruction due to a severe stricture in common hepatic bile duct (*straight arrow*). Note that choledochojejunostomy anastomosis (*curved arrow*) is patent. Remnant (*arrowhead*) of donor cystic duct is also filled.

Biliary Strictures

Biliary strictures occurred in 14 patients (eight children and six adults) who had occlusions of the hepatic artery. Nonanastomotic strictures occurred in 12 of the 14 patients (sensitivity, 39%), three of whom also had bilomas. None of these strictures occurred at the previous site of a T-tube insertion. In two of the 12, choledochojejunostomy stricture was also present. In seven patients, the stricture developed in the common hepatic duct (Fig. 6); in four of these seven, the stricture extended into the bifurcation and involved both the main right and left hepatic ducts. Intrahepatic strictures of secondary and tertiary branches occurred in the other five patients. One of the five patients had a single stricture (Fig. 7A) that progressed to complete obstruction within 16 days (Fig. 7B). This patient also had an intrahepatic biloma. Multiple intrahepatic strictures developed in the other four patients (Fig. 8).

Isolated anastomotic strictures at a Roux-en-Y choledochojejunostomy were observed in two of the 14 patients, one of whom also had a biloma.

If two children in whom biliary stricture was discovered at 12 and 20 months after occlusions of the hepatic artery are excluded, the mean interval between the diagnosis of arterial occlusion and the cholangiographic demonstration of biliary stricture was 62 days (range, 1–154).

Five of the 14 patients presented with suspected biliary obstruction. The cholangiographic diagnosis of nonanastomotic biliary stricture prompted angiographic evaluation. In the remaining nine patients, the diagnosis of occlusion of the hepatic artery was known before the cholangiograms were obtained.

In the group of patients with patent hepatic arteries, nonanastomotic biliary strictures were observed in nine cases (specificity, 88%). Anastomotic strictures occurred in 18 cases.

Discussion

The arterial blood supply to the biliary tree is complex. The hepatic artery is the major blood supply to the hilar and portal tract structures [5, 6]. The intrahepatic biliary tree (above the common hepatic duct bifurcation) is supplied mainly by hepatic arterial branches [6–8]. The extrahepatic bile duct receives its blood supply from several sources, most commonly the retroduodenal branch of the gastroduodenal artery, the retroportal artery from the celiac axis or superior mesenteric artery, and the descending branches of the right hepatic artery [7].

At donor hepatectomy, the retroportal artery and the branches from the gastroduodenal artery are severed. This leaves the hepatic artery to provide the entire blood supply to the donor biliary system after transplantation. Arterial occlusion due to thrombosis or stenosis of the hepatic artery therefore may lead to ischemia and cause donor intra- or extrahepatic bile duct complications.

Biliary complications will not develop clinically in all transplant patients who have occlusion of the hepatic artery. In most transplant patients who have occlusion, the diagnosis

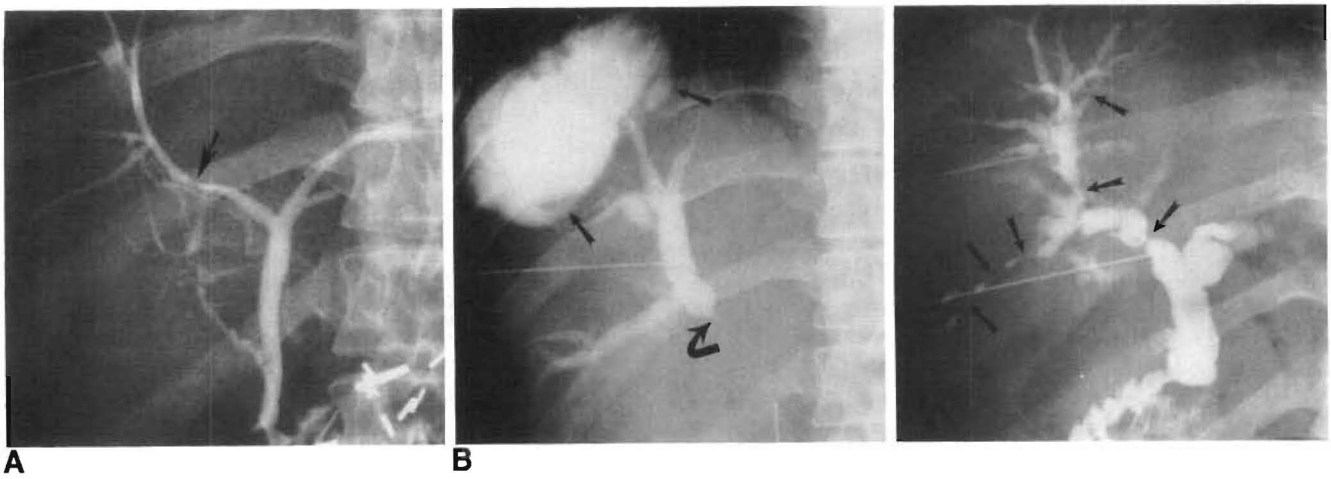

Fig. 7.—Intrahepatic biliary stricture.
A, Transhepatic cholangiogram shows stricture of right hepatic duct (*arrow*).
B, Transhepatic cholangiogram 16 days later shows complete obstruction of previously strictured right hepatic duct (*curved arrow*). Contrast leakage occurred from obstructed duct and filled a peripheral intrahepatic biloma cavity (*straight arrows*) that had been drained percutaneously earlier the same day.

Fig. 8.—Transhepatic cholangiogram shows multiple intrahepatic biliary strictures (*arrows*). Histologic examination of liver at autopsy showed arterial occlusion due to severe chronic rejection, with multiple bile duct infarcts and strictures.

is made early. Most of these patients undergo retransplantation for liver failure or hepatic necrosis before biliary complications develop.

The three main clinical presentations of posttransplantation thrombosis of the hepatic artery are fulminant hepatic necrosis, bile leak, and relapsing bacteremia [2]. Sonography often is performed in these settings to evaluate patency of the hepatic artery (by means of pulsed Doppler examinations) [9] and to evaluate for possible biliary abnormalities, especially if a bile leak or obstruction is suspected. Duplex Doppler sonography is an excellent screening test for detection of thrombosis of the hepatic artery [9]. However, we have observed a high false-negative rate with sonography for suspected biliary complications in transplant patients (Zajko AB, unpublished data). In the immunosuppressed liver transplant recipient, serious biliary complications are associated with a high mortality if not diagnosed and treated promptly. For this reason, cholangiography may be the first procedure performed in transplant patients who have suspected biliary complications.

In transplant patients, the indications for cholangiography are not absolute. The most common indication is suspected biliary obstruction. Other common indications include unexplained elevation of liver enzyme levels or fever and suspected biloma on noninvasive imaging [10, 11]. Bilomas usually appear as parahilar fluid collections on CT and sonography. Because of their high association with thrombosis of the hepatic artery, occasionally these findings have led directly to angiographic evaluation. A complete analysis of noninvasive imaging in posttransplantation thrombosis of the hepatic artery, including duplex sonography and CT, is currently underway and will be the subject of a separate report.

Bile leakage is the most common complication after transplantation in patients with biliary anastomosis via choledochocholedochostomy [12]. Most bile leaks occur at the T-tube choledochotomy and, if small, may close spontaneously [10]. Leaks occurring at the choledochocholedochostomy or choledochojejunostomy sites generally require revision of the anastomosis [12]. The demonstration of nonanastomotic contrast leakage on cholangiography strongly suggests that occlusion of the hepatic artery has occurred. Of 18 transplants with nonanastomotic contrast leakage seen on cholangiography, 16 (89%) had occlusion of the hepatic artery (Table 1). Retransplantation usually is required for survival. Two patients with patent hepatic arteries had intrahepatic contrast leakage into liver abscesses that communicated with the biliary tree [11].

Nonanastomotic leaks may occur from the extra- or intrahepatic donor biliary tree (Figs. 1–5). Tzakis et al. [2] reported their findings in seven transplant patients with extrahepatic bile leaks and thromboses of the hepatic artery; all had donor common duct necrosis at laparotomy (Fig. 5). If thrombosis of the hepatic artery results in necrosis of intrahepatic bile ducts, a hilar or intrahepatic biloma may develop (Figs. 1, 2, and 4). These bilomas frequently become secondarily infected. We have performed percutaneous drainage in most cases until such time as a suitable donor liver was available for retransplantation [11]. Bile duct necrosis [13] and cysts [14, 15] also have been reported to occur in nontransplant patients after occlusion of the hepatic artery by embolization.

Two patients had diffuse bile leakage from the central intrahepatic bile ducts (Fig. 3). This finding may represent the earliest cholangiographic change in bile duct ischemia and necrosis before formation of a frank biloma. In the first patient, the amount of leakage was small and was overlooked at first. A central biloma eventually formed, which was drained percutaneously. The patient required retransplantation after several months. In the second patient, the sole indication for the

cholangiogram (Fig. 3) was elevation of liver enzyme levels. On demonstration of the nonanastomotic bile leak, angiography was performed, which showed thrombosis of the hepatic artery. The patient underwent retransplantation 3 days later.

Biliary stricture is the most common cause of biliary obstruction after transplantation [11]. Biliary strictures can be classified as anastomotic or nonanastomotic. Most anastomotic strictures can be explained on the basis of scar formation with retraction and narrowing, although ischemia also may be a factor [7, 16]. Of 20 liver transplants with isolated anastomotic strictures, only two (10%) had occlusions of the hepatic artery (Table 1).

Most nonanastomotic strictures in the liver transplant biliary tree probably are due to ischemia. Of 21 transplants with nonanastomotic strictures, 12 (57%) had occlusions of the hepatic artery (Table 1). In patients without transplants, bile duct strictures have been shown to occur after peripheral hepatic artery embolization [17]. These strictures result from occlusion of the end arterial supply of the bile duct, the peribiliary vascular plexus. Strictures have not been reported to occur after more proximal occlusion of the hepatic artery. With proximal occlusions in patients without transplants, collateral arterial inflow develops rapidly and protects the liver [14]. However, in liver allografts, thrombosis of the hepatic artery effectively produces complete dearterialization of the liver because all potential extrahepatic collateral pathways have been severed.

Extrahepatic hepatopetal arterial collaterals have been shown in approximately 30% of children with liver transplants who have thromboses of the hepatic artery [1]. These collaterals probably are responsible for allograft survival in most of these children. Arterial collaterals also have been documented in several children in the current study. We have not observed these collaterals in adults who have transplants. In patients without transplants, hepatopetal collaterals develop rapidly after arterial occlusion and prevent ischemic injury. However, in liver allografts, these collaterals probably require a longer time to develop because they must arise de novo. Therefore, they may not be effective in preventing hepatic ischemic injury in all cases.

We speculate that posttransplantation nonanastomotic biliary leaks and strictures may represent a spectrum of ischemic injury from occlusion of the hepatic artery. Biliary strictures may develop after less severe ischemic disease, which allows the bile duct to heal with fibrosis and ductal stenosis. Bile leaks, on the other hand, result from duct necrosis, probably due to severe ischemia. Among other possible unknown factors, collateral circulation may have a role in preventing severe ischemic injury in some cases.

Ischemic injury also may occur during organ harvesting [18, 19] or result from chronic rejection. Severe chronic rejection can produce vascular compromise and ischemia by causing progressive narrowing and eventual occlusion of intrahepatic arteries [5]. Of the 21 transplants with nonanastomotic biliary strictures diagnosed by cholangiography, nine did not have occlusions of the hepatic artery. The cause of strictures in these patients is uncertain. Potential causes include harvesting injury, recurrent sclerosing cholangitis, ascending cholangitis, cytomegalovirus infection, and cholangiocarcinoma.

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