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Radiographic Features of Liver Allograft Rejection

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Abstract. The radiographic features of 19 transplanted patients with failure of the liver allograft were evaluated. These features were: poor filling, stretching, attenuation of intrahepatic biliary ducts documented by T-tube cholangiogram, attenuation of branches of the hepatic artery seen on angiogram as well as a decrease of blood flow through the liver seen on angiogram and nuclear medicine dynamic scintigram. These findings were secondary to swelling of the transplanted liver and were not specific for rejection; they may also be present in hepatic infarction or infection.

Key words: Liver transplant, rejection – Cholangiography, postoperative.

Failure of the allograft is still a significant risk in all liver transplants. Rejection is the most common cause of early failure, followed by vascular thrombosis, biliary complications, and other nonspecific surgical complications. Early recognition is essential because aggressive treatment, including retransplantation, has proven very useful.

This paper assesses the usefulness of T-tube cholangiography as a noninvasive diagnostic method in the evaluation of these patients. It outlines the radiographic spectrum of findings of liver allograft failure based on our experience with 19 cases from a group of 210 liver transplants, and makes a comparative histologic study of these damaged grafts.

Material and Methods

The medical records of 210 patients receiving their first liver orthotopic transplant at the Presbyterian University Hospital and Children's Hospital of Pittsburgh between March, 1981, and March, 1984, were evaluated for presence of liver rejection or failure. The following criteria were established for this study: histologic evaluation of the failed graft, intraoperative cholangiogram (used as a baseline) available, and 1 follow-up cholangiogram during 20 days prior to removal of the damaged graft. Nineteen patients fulfilled these criteria.

For the purpose of the study, the patients were classified into 2 groups. Group I contained 11 patients, 7 women and 4 men (ranging from 23 to 46 years): rejection was the reason for graft failure. Group II contained 8 patients, 6 women and 2 men (ranging from 20 to 52 years): the cause of failure was other than rejection.

In addition to cholangiography, other radiographic studies were available. Technetium (^{99m}Tc) liver blood flow was available in 4 cases in group I and 5 cases in group II. Celiac axis arteriography was available in 3 patients. Ultrasound (US) was performed in all the patients; however, only 2 studies were positive for parenchymal abnormalities. All these studies were completed within 10 days of the last cholangiogram.

Results

The major cause of graft failure was rejection (11 cases), followed by cytomegalovirus hepatitis (3 cases), hepatic artery thrombosis (2 cases), *Aspergillus* abscesses (2 cases), and extrahepatic cholestasis (1 case).

The most consistent findings were seen through the T-tube cholangiogram as generalized stretching and narrowing of the intrahepatic bile ducts (Fig. 1). These findings were seen in 5 patients in group I (45%) and 2 in group II (25%).

Decreased blood supply to the liver was also noted through nuclear medicine ^{99m}Tc dynamic scintigram in 3 of the 4 cases studied in group I and 2 of the 5 cases available in group II. Vascular compromise was also detected by arteriographic studies in 1 case from each group. The findings consisted of poor or delayed arterial filling and delayed venous opacification (Fig. 2).

Although the hepatic ultrasound study was normal in all patients of group I, abnormal liver

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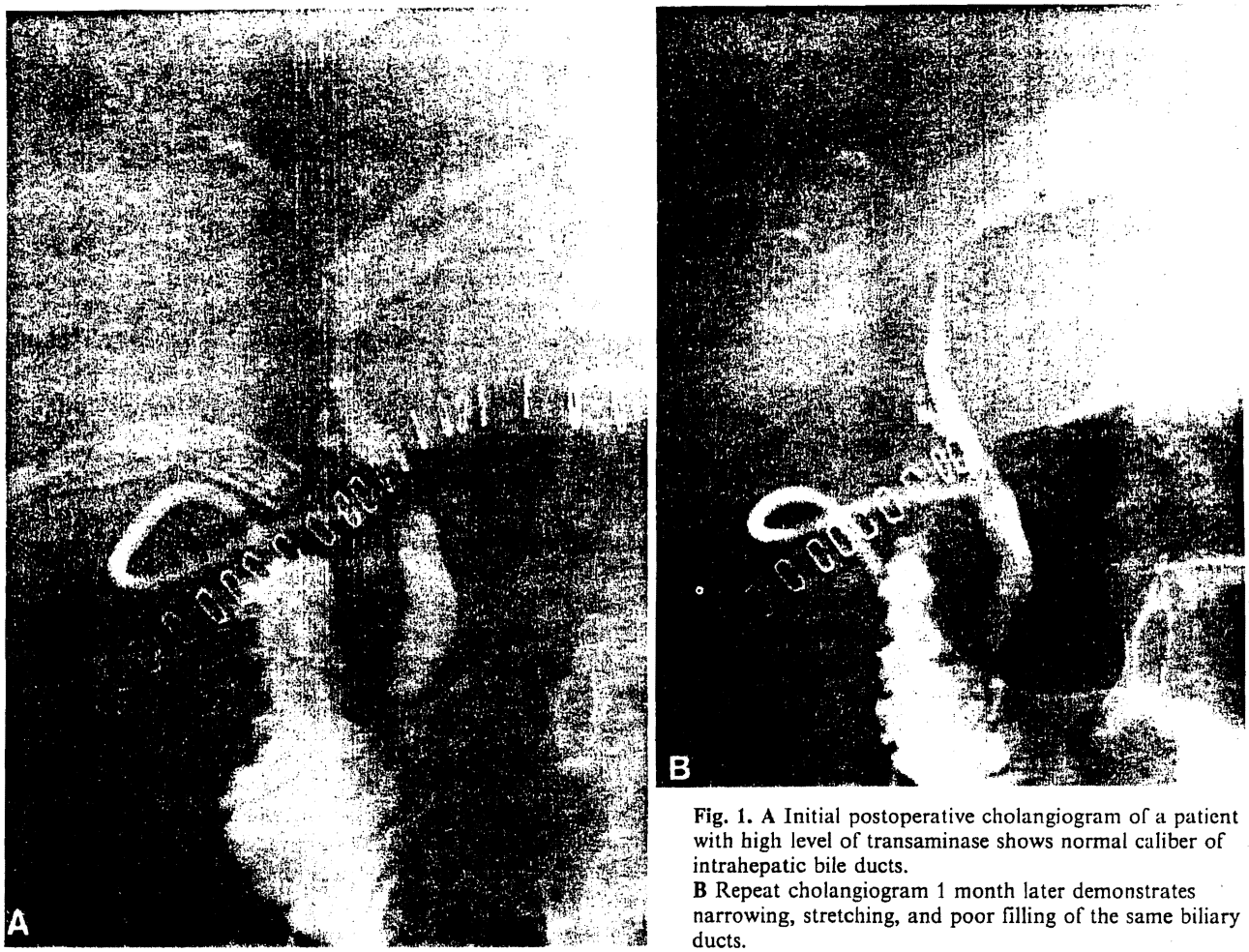

Fig. 1. A Initial postoperative cholangiogram of a patient with high level of transaminase shows normal caliber of intrahepatic bile ducts.
B Repeat cholangiogram 1 month later demonstrates narrowing, stretching, and poor filling of the same biliary ducts.

echoes representing infarctions were noted in 2 patients of group II (Fig. 3).

Discussion

In the last several years, the life expectancy of patients undergoing liver transplantation has increased due to: better initial selection of candidates for the procedure, refinements in organ procurement and surgical grafting techniques, the introduction of cyclosporine, and improvements in the postoperative management of such patients [1]. As a result of these improvements, orthotopic liver transplantation has become a practical, albeit sophisticated, mode of therapy for patients with otherwise terminal liver disease [2].

Following successful engraftment, preservation of the patient's life depends on the prompt and adequate function of the graft. If complications occur, early diagnosis and appropriate treatment are essential for a successful outcome. Consequently, liver ischemia, infarction, hepatic arterial and/or portal vein thrombosis, biliary tract stenosis or obstruction, leakage at the site of the biliary anastomosis, graft infection, and, above all, rejection are conditions to be aware of when clinical deterioration occurs. Unfortunately, fever and changes in hepatic liver injury tests are nonspecific signs of the graft injury [1, 3].

In the past, errors in the operative technique during the performance of hepatic transplantation had been the major cause of posttransplantation morbidity and mortality [4]. At the present time, rejection is the most common cause of graft failure.

Graft function, following our transplantation, is checked daily by the use of several biochemical parameters of hepatic injury (according to a standard protocol). When any abnormality is recognized, the first steps we take are to exclude biliary obstruction by means of cholangiogram and graft vascular thrombosis by sonogram and/or angiogram. Needle biopsies of the graft have not been included in the protocol follow-up of graft function. Nevertheless, liver biopsies have been per-

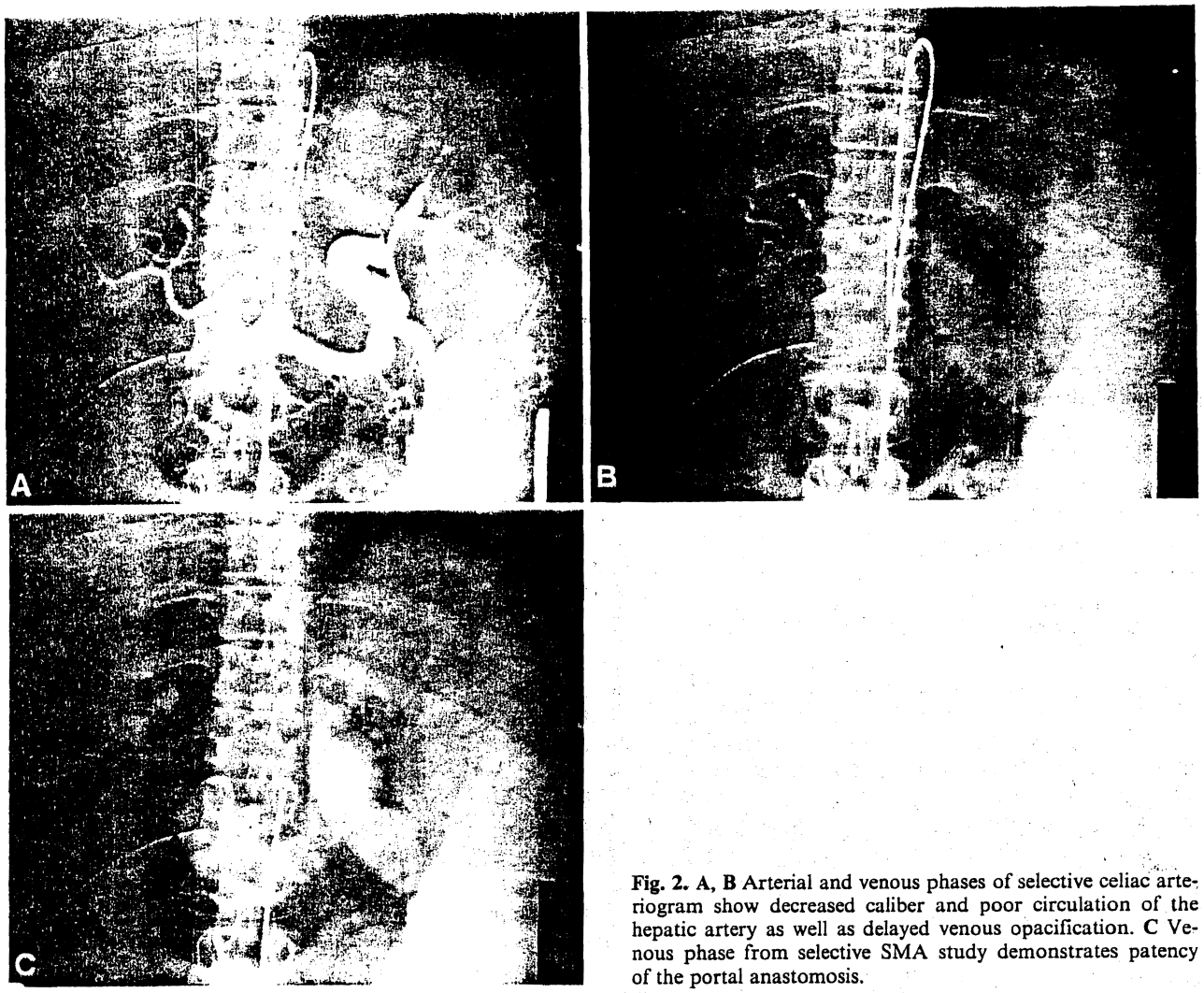

Fig. 2. A, B Arterial and venous phases of selective celiac arteriogram show decreased caliber and poor circulation of the hepatic artery as well as delayed venous opacification. **C** Venous phase from selective SMA study demonstrates patency of the portal anastomosis.

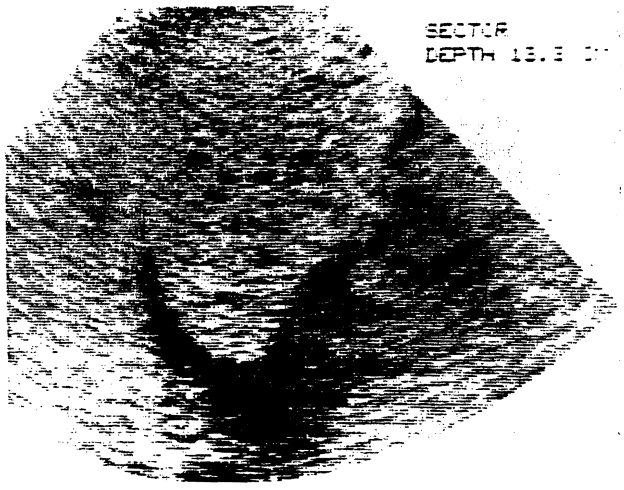

Fig. 3. Sonogram of transplanted liver in oblique plane reveals an abnormal area with increased echogenicity in the center of the liver. Pathologic specimen demonstrated a sequential infarction.

formed when indicated clinically in selected patients. As a result, the less invasive techniques of cholangiography and ultrasonography have been the pivotal studies used (most of the time) in the evaluation of altered liver function after transplantation.

According to histologic reports, the criteria for rejection are, in acute rejection, portal and/or lobular inflammatory infiltrates, disruption of the limiting plate, and bile duct cell injury with occasional portal and central venous thickening; and in chronic rejection, a vascular injury of medium-sized hilar arteries, showing subendothelial foam cells, fibrinoid necrosis, and intimal hyperplasia, as well as extensive periportal fibrosis and disappearance of bile ductules.

In some patients with clinical diagnosis of liver graft rejection, poor filling, stretching, and mild attenuation of the intrahepatic biliary tree have

been observed. In some of these patients, the cholangiographic findings have returned to normal after successful treatment of presumed rejection. As a result of this observation, it has been speculated that these intrahepatic biliary tract changes might be due to the lymphocytic infiltration occurring in the portal tracts during the rejection process [5]. To test this hypothesis, we selected patients (following liver transplantation and graft loss) whose allografts were available for later pathologic examination and who had undergone sufficient diagnostic imaging studies. Consequently, the pathologic findings present in each lost graft could be related to the diagnostic imaging information available in the same patient.

Stretching and attenuation of the intrahepatic biliary ducts were observed in only 5 of the 11 patients in whom rejection was the main cause of graft loss. Unfortunately, this radiologic sign was seen also in 2 of the 8 patients in whom a cause other than rejection was the major reason for graft loss. Based upon these data, stretching of the intrahepatic biliary ducts as a sign of rejection had a low sensitivity (45%), a low specificity of 75%, a positive predictive value of 71%, and a negative predictive value of 50%. It is apparent from these data that the radiologic finding of stretched intrahepatic biliary ducts is of no real use in an individual case in which an elevation in serum bilirubin and/or liver enzyme levels occurs after liver transplantation.

These cholangiographic findings along with slowed down hepatic blood flow, occasionally seen also in such cases by isotopic scanning and/or angiogram, are perhaps due to the presence of increased intrahepatic pressure, secondary to hepatic swelling, as well as rejection. Unfortunately, hepatic swelling can be produced by a variety of different pathologic processes. In 2 of our patients this was due to cytomegalovirus hepatitis and massive hepatic infarction secondary to thrombosis of the hepatic artery. These patients had stretching and poor filling of the intrahepatic biliary ducts and diminution of hepatic blood flow, but no histologic evidence of rejection. Thus, decreased liver flow, determined by isotopic technique and/or angiography, and stretching and poor filling of the intrahepatic biliary tree, demonstrated by cholangiography, may be due not only to allograft rejection but also to other causes such as ischemic liver injury secondary to vascular thrombosis or stenosis and various postoperative viral infections of the grafted organ.

In summary, we have not found any radiologic procedure, including ultrasonography and nuclear medicine imaging, to be particularly diagnostic of hepatic allograft rejection. Nevertheless, these studies are vital in evaluating biliary obstruction and hepatic vascular complications when they occur in liver transplant recipients. As a result of these findings, we believe there is no reliable noninvasive diagnostic study for the detection of liver graft rejection presently and thus rejection of the allograft can only be established by histologic examination of the transplanted liver.

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