Vascular Thrombosis in Acute Hepatic Allograft Rejection: Scintigraphic Appearance

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Hepatobiliary imaging with ^{99m}Tc diisopropyl iminodiacetic acid was employed serially in a patient with an hepatic allograft, in order to follow the function of the transplant. Initially improving liver uptake and biliary excretion was observed; however, 12 days postoperative with clinical deterioration the scintigrams revealed an absence of uptake ("phantom" liver), due to thrombosis of the hepatic artery related to acute rejection. Hepatobiliary imaging can be helpful in the study of hepatic allografts.

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The hepatobiliary images obtained in a case of acute liver transplant rejection are presented. In this context, the role of radionuclide scintigraphy in the postoperative evaluation of hepatic allograft recipients is discussed.

CASE REPORT

A 2½-yr-old female patient with known alpha-1-antitrypsin deficiency underwent orthotopic liver transplantation. She had been jaundiced since birth and her liver biopsies had shown progressive fibrosis. Preoperative liver function tests revealed a direct/total bilirubin of 5.3/17.5 mg/dl, SGOT 402 IU, SGPT 241 IU. Following a successful 6-hr transplant procedure, the patient had the first of three hepatobiliary scans using 800 μCi of technetium-99m (^{99m}Tc) disofenin. Ten initial images were obtained at 5-min intervals (250,000 counts per image). These were followed with static images at 1–4 hr postinjection as required. The initial study showed parenchymal activity but no visualization of the bile ducts or small bowel; significant renal excretion was noted (Figs. 1A,1B). On postoperative day (p.o.d.) 10, the patient's liver function test values had decreased markedly (direct/total bilirubin 1.28/2.72 mg/dl; SGOT 79 IU). A [^{99m}Tc]disofenin scan showed improved uptake of radionuclide as well as prompt biliary excretion with small bowel activity clearly visible (Fig. 2). Two days later, on p.o.d. 12, the patient became febrile and developed a leukocytosis. The liver function tests showed marked elevation (direct/total bilirubin 10.6/20.6 mg/dl, SGOT 5350 IU). Following clinical deterioration, the patient was transferred to the pediatric intensive care unit. The third hepatobiliary scintigraphic study demonstrated a remarkable absence of any uptake within the transplanted liver, which was surrounded by persistent blood-pool activity giving the appearance of a "phantom" liver (Fig. 3A,3B). The patient underwent an emergency laparotomy and thrombus was removed from the hepatic artery. Despite these measures, the patient died of metabolic complications and intractable cardiac arrhythmias. Postmortem histologic evaluation of the transplant revealed lymphocytic infiltration, immunoblasts, and necrosis compatible with acute allograft rejection.

DISCUSSION

Despite initial high mortality and morbidity, orthotopic liver transplantation has gained acceptance as the treatment of choice for many previously fatal, end-stage hepatic diseases (*1–3*). Surgical complications of the procedure include massive intraoperative hemorrhage, air embolus, and other difficulties secondary to the patient's preoperative clinical condition. While the liver is resistant to hyperacute rejection (*4*), acute and chronic rejection have been recognized in 10–15% of transplanted patients who have died and been autopsied (*1*). The role of rejection in graft failure can be inferred from the success of recent innovations in postoperative immunosuppression. The introduction of cyclosporin A, a selective T-lymphocyte inhibitor used in combination with steroids, has been associated with an increase in 1-yr

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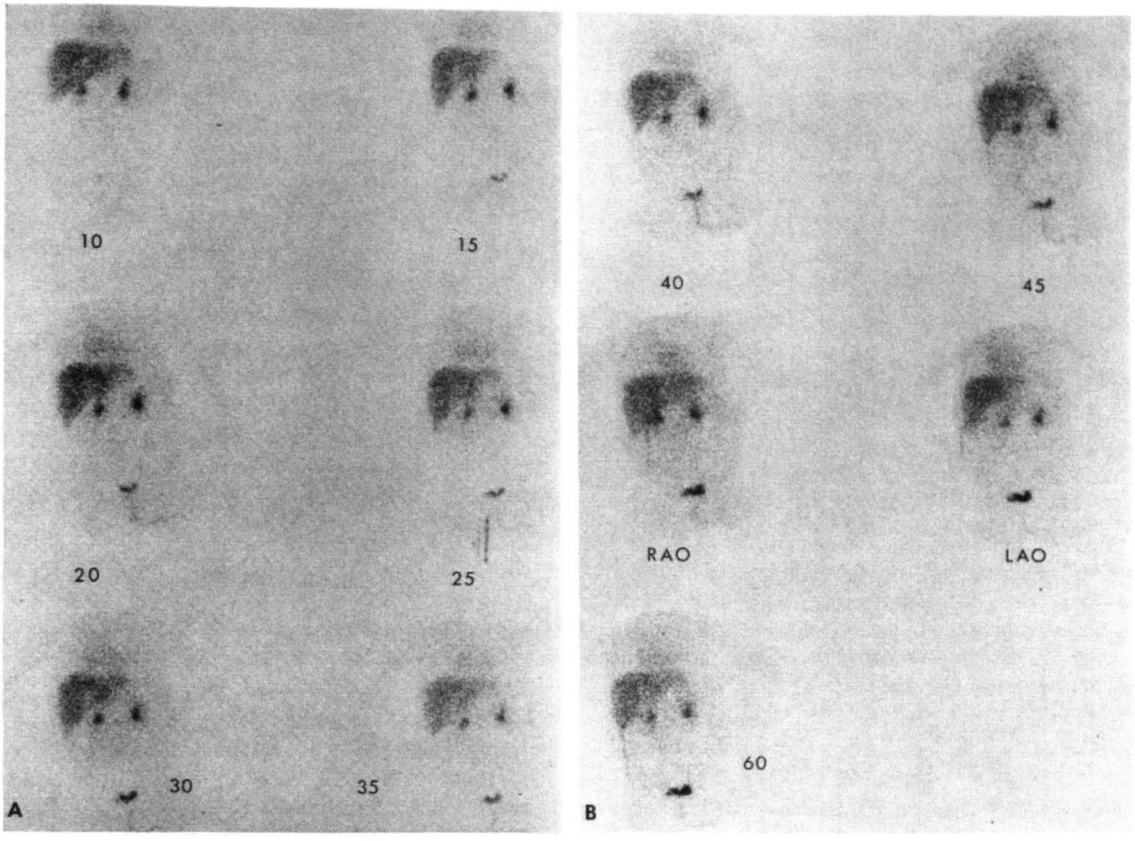

FIGURE 1
A,B: [^{99m}Tc]disofenin scan (800 μCi, 250,000 ct/image) on p.o.d. #1 shows activity within transplant but not in bile ducts or bowel. Findings persisted on delayed images. Intense renal excretion of radionuclide is apparent. (Note: all times are given in min)

survival, from 24 to 78% currently (*1*,*3*). Acute rejection may occur in the immediate postoperative period, or months later. Typical microscopic changes include lymphocytic and immunoblastic infiltrates, vascular thrombosis, and bile stasis (*4*). Early recognition of these events is important as they may be modified by increased immunosuppression.

Serial hepatobiliary imaging is clearly useful in the postoperative follow-up of liver transplant patients (*5*). Imaging with appropriate radionuclides provides a

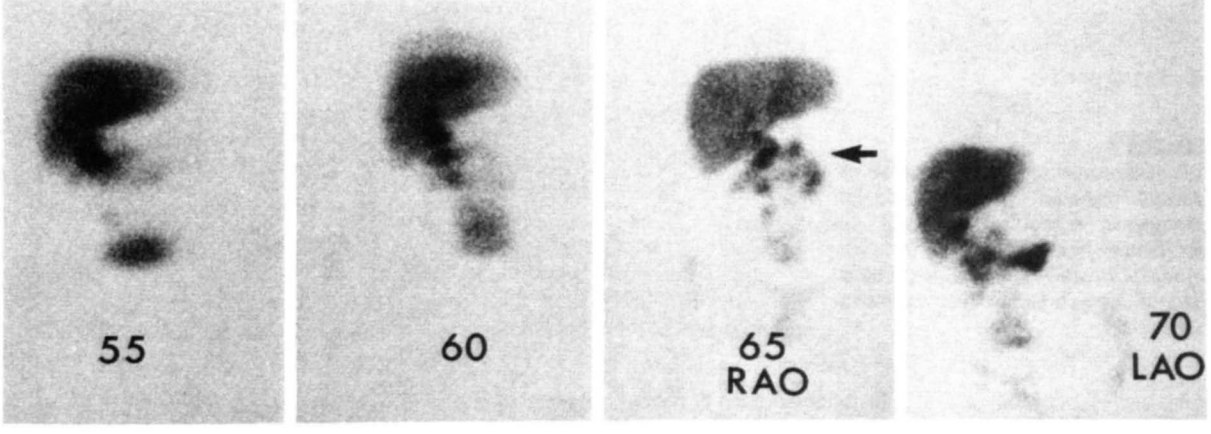

FIGURE 2
Scan obtained 8 days later now shows greater uptake of radionuclide by transplant, with prompt appearance of activity in bowel (arrow)

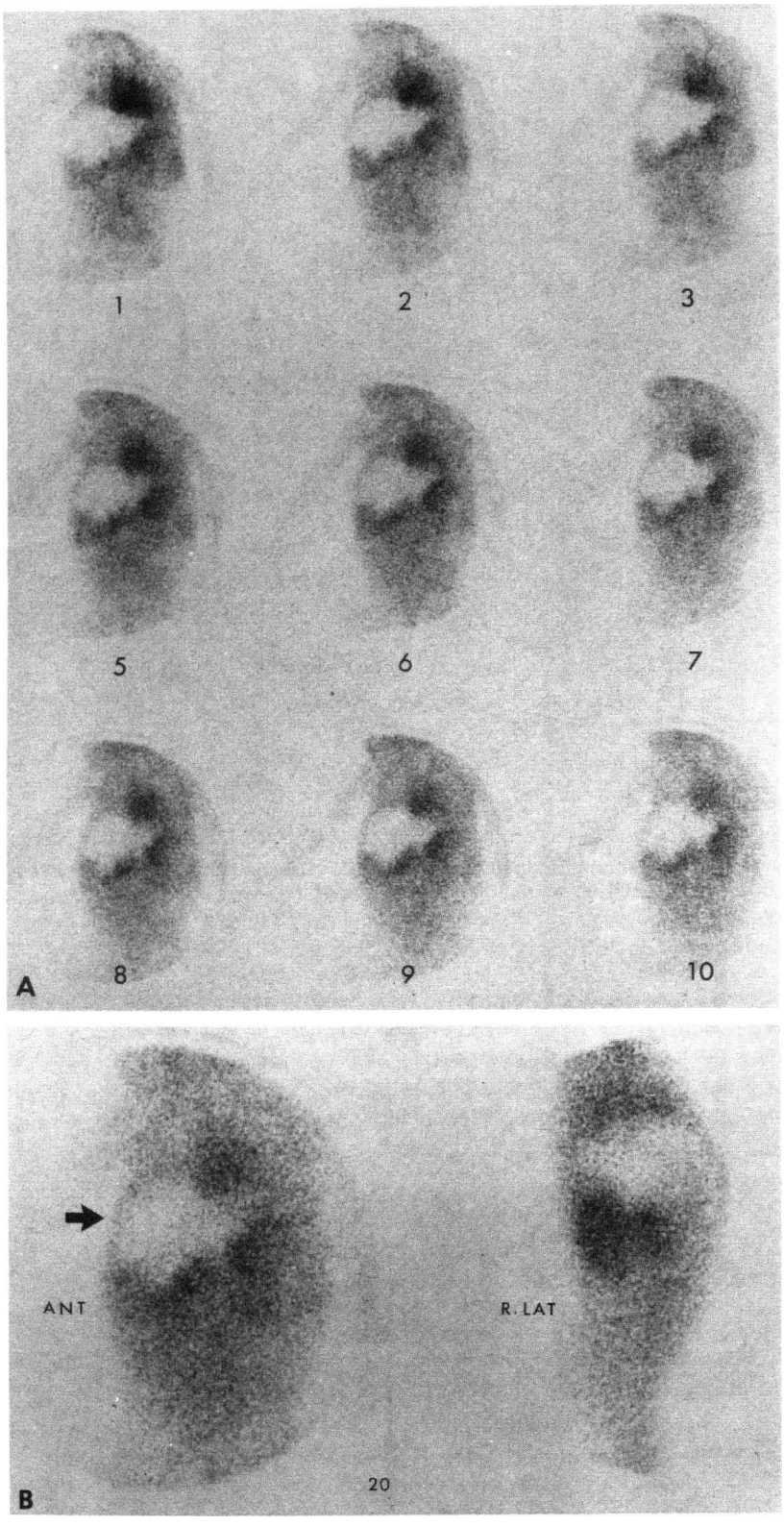

FIGURE 3
A,B: Disofenin study after onset of clinical rejection shows markedly photopenic transplant outlined by persistent blood-pool activity (arrow). Intensity of activity around transplant may be due to hyperemia or collateral circulation

measure of hepatocyte viability because active, membrane-bound carriers (anionic) are required for agent uptake and excretion (*6*). Bile duct reconstruction in liver transplantation has been a major source of morbidity (*2*). Direct visualization of the reconstructed biliary tree allows detection of anastomotic leaks and determines patency. Both iodine-131 (^{131}I) rose bengal and technetium-99m (^{99m}Tc) labeled iminodiacetic acid deriv-

atives (IDA) have been used to verify hepatic function and biliary integrity. The clinical application of the former has been limited by its high photon energy peak (364 keV) which is suboptimal for imaging with the Anger camera. In addition, its long half-life (8.4 days) and its significant beta emission result in a high patient radiation dose (52 rad/mCi) (*6*). Patient exposure is a particularly important parameter to consider given the young age of many liver transplant patients.

The newer [^{99m}Tc]IDA derivatives offer the advantages of a low patient dose (0.8 rad/mCi) and technetium's improved imaging characteristics. The efficacy of specific IDA analogs in imaging liver transplants has been studied. Klingensmith has shown [^{99m}Tc]diethyl IDA to be superior to ^{131}I rose bengal in all respects except relative renal excretion at high bilirubin levels (*7*). In another direct comparison, the diethyl IDA derivative also performed better than [^{99m}Tc]pyridoxylideneglutamate ([^{99m}Tc]PG) (*5*). More recently, the diisopropyl IDA derivative, [^{99m}Tc]disofenin, has demonstrated the best combination of imaging properties, especially when bilirubin levels are elevated as is often the case in transplant patients (*8*). Disofenin provides the highest liver-to-heart, blood-pool ratio and permits imaging at bilirubin levels as high as 30 mg/dl (*9*).

This case demonstrates that hepatobiliary imaging with [^{99m}Tc]disofenin can be a useful tool in studying hepatic allografts, correlating well with clinical and pathological events. The scintigraphic findings represent complete absence of perfusion caused by vascular thrombosis. This results when the cellular infiltrates of acute rejection lead to microvascular stasis in the liver parenchyma and in turn compromise flow in the larger vessels. Both hepatic arterial and mesenteric portal blood flow would be expected to be similarly affected by high vascular resistance within the transplant. Hence, acute allograft rejection may have a striking scintigraphic appearance in which the photopenic "phantom" liver is seen, surrounded by prolonged blood-pool activity.

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