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LETTER TO THE EDITOR

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Hepatic artery thrombosis as a complication of amputation neuroma of the liver graft hilum

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Sir: Nachtwey et al. [2] recently reported a case of hilar traumatic neuroma causing compression and secondary thrombosis of the hepatic artery. They cite our study and our finding of frequent development of hilar amputation neuromas larger than 1 cm in diameter in liver grafts (prevalence of 27.9 % when systematically searched for in a series of 93 lost grafts) [1]. Only one of our cases was symptomatic (extrahepatic cholestasis caused by a neuroma obstructing the main bile duct), but neuromas developed more frequently in liver grafts in this series after long intervals post-transplantation. These observations suggest that further symptomatic cases can be expected, with an increasing number of patients surviving for longer periods of time after liver transplantation.

Eight months after the publication of our work, we retransplanted a patient who lost his liver graft due to ischemic cholangitis secondary to thrombosis of the hepatic artery; the thrombus was found encased in a hilar traumatic neuroma. Our previous experience prompts us to present this new case and to comment on some observations from the work of Nachtwey et al. [2].

A 38-year-old male with alcoholic liver cirrhosis (Child-Pugh grade C) underwent orthotopic liver transplantation with an ABO-identical graft. An arterial anastomosis was created at the celiac artery bifurcation, both in the recipient and in the graft. Bile duct reconstruction was a duct-to-duct anastomosis without a T tube. Immunosuppression consisted of cyclosporin, azathioprine, and steroids. One episode of acute cellular rejection on the 11th postoperative day was treated with steroid boluses, and liver dysfunction resolved. The patient was discharged on postoperative day 28.

After a year and a half, the patient presented with a mild alteration in liver function tests: aspartate aminotransferase (AST) was 119 IU/l; alanine aminotransferase (ALT) 220 IU/l, bilirubin (Bil) 2.9 mg/dl, alkaline phosphatase (AP) 464 IU/l, and gamma-glutamyl transpeptidase (GGT) 2461 UI/l. He was eventually diagnosed as having biliary intrahepatic stenoses and cholangiectasis, most likely caused by post-ischemic cholangitis due to irregular dilatations of the intrahepatic bile ducts with deposition of biliary sludge, as shown by ultrasound and percutaneous transhepatic cholangiography. Stenosis of the biliary anastomosis was also observed and surgery was indicated. The biliary confluence was stenosed and both donor and recipient bile ducts were dilated with mucosal necrosis. Arterial bleeding was found at the ends of both bile ducts when the anastomosis was resected. Choledochojejunostomy to a Roux-en-Y limb was performed. The liver hilum was fibrotic and dissection of the hepatic vessels was not considered necessary. Histological examination of the resected specimen showed pigmented coagulative necrosis of the wall of the stenotic perianastomotic biliary ducts surrounded by inflammatory tissue. The patient showed some improvement in liver function tests, with only mild cholestasis (AST 45 IU/l; ALT 46 IU/l, Bil 3.7 mg/dl, AP 731 IU/l, and GGT 197 IU/l). Resolution of the dilatation of the main bile duct, persistence of hyperechogenic material in the intrahepatic biliary tract, and absence of arterial flow were observed by echo-Doppler.

One year later, the patient developed jaundice, bouts of cholangitis, and progressive alterations in liver function tests (AST 765 IU/l, ALT 556 IU/l, Bil 24.3 mg/dl, AP 297 IU/l, and GGT, 556 IU/l). He was listed for retransplantation, which was performed 1 month later. The patient is now doing well and has normal liver function tests after 2 years of follow-up.

The patient's resected graft showed a consistent fibrous hilar neuroma, 3 cm in diameter, surrounding and compressing the hepatic artery, which was occluded (Fig. 1). Transversal serial sections of the artery showed an irregular diameter in the entire intraneuroma segment. Sections of the cholestatic liver graft parenchyma showed biliary sludge in intrahepatic cholangiectasis that alternated with fibrous

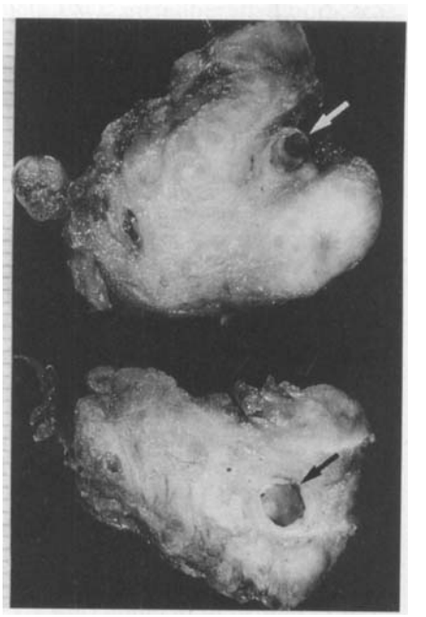

Fig. 1 Two serial sections of the traumatic neuroma. Note the thrombotic occlusion and the different diameter of the hepatic artery (*arrows*) in each section

stenoses of the intrahepatic bile ducts. No parenchymatous infarcts were seen. Microscopically abundant proliferating nerve bundles, immunohistochemically positive for S-100 protein, intermixed with collagen fibers were seen in the tissue surrounding the artery. A recent thrombus with only some peripheral organization was obliterating the lumen. Some calcic deposition was seen in the media of the hepatic artery but neither infiltrating bundles of nerve fibers nor dense subintimal fibrosis was seen in the wall.

This case and the Natchwey et al. case share some interesting features, other than the traumatic neuroma. Both of them initiated a liver dysfunction in which the cholestatic alterations in liver function tests were the most severe, although their main pathology was ultimately due to poor blood perfusion of the whole graft. Moreover, their patient, like ours, had stenosis of the biliary tract probably caused by ischemia. This kind of biliary complication has been described after early and late thrombotic occlusion of the hepatic artery [3, 4].The arterial lumen was probably progressively compressed by the neuromatous proliferation before total thrombotic obstructions were established in these cases. The reduced flow in the hepatic artery could have been responsible for the selective ischemic injury of the biliary tract [3, 4] and for the secondary cholestatic profile of the liver function tests.

Natchwey et al. speculate about the origin of the neuroma. It is obvious that cutting nerves without taking surgical precautions to avoid traumatic neuroma (as happens in liver transplant surgery) will increase the likelihood of developing these neuromatous proliferations. More than one-half of our neuroma cases showed surgical threads inside their mass. This finding suggests that neuroma will be most frequent in nerves that have been the most surgically manipulated. Moreover, the risk of developing neuromatous proliferations may be increased if additional surgery in the hilum, such as biliary reconstructions, have to be performed.

With regard to the possible pathogenetic relationship between neuroma and temporary chylous leakage, which were observed simultaneously in the Nachtwey et al. patient, we did not find any such association among our 27 cases of amputation hilar neuromas. The only case of chylous ascitis we found in the files of 486 transplant recipients was controlled with diet and parenteral nutrition. The graft survived and no traumatic hilar neuroma was identified during any of the routine examinations.

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