pendent risk factor for tumor recurrence after LDLT (P=0.012; Table 1).

It is important to clarify when patients with HCC should be listed as candidates for LDLT. Actually, 47 of 68 patients underwent more than two pretransplant treatments. The times of pretransplant treatment, the interval between the first treatment and LDLT, and the interval between the last pretransplant treatment and LDLT did not affect the outcome. We could not find a correlation between the kind of pretransplant treatment and the outcome, because most patients in this study had undergone more than two kinds of pretransplant treatment before LDLT to treat primary and recurrent HCC. Moreover, there was no evidence concerning how prior hepatic resection, especially major resection, might affect the outcome of LDLT in this study, probably due to the relatively small number of cases. On the basis of the results, we propose that HCC can be treated with any treatment modality as long as the patients' liver can tolerate it (*7*). Especially, HCC patients with hepatitis C might not be good candidates for LDLT at initial diagnosis because of high recurrence rate of hepatitis C after LDLT.

The up-to-seven criteria might be able to predict patient survival even after LDLT (*4*). However, the absence of microscopic vascular invasion was crucial to use as a criterion, and surrogate markers to predict microscopic vascular invasion are necessary. DCP more than 300 mAU/mL was an independent risk factor for tumor recurrence after LDLT. DCP level is significantly correlated with pathologic vascular invasion (*8*) or intrahepatic metastasis, or both (*5*).

In conclusion, the kind, times, and interval of pretransplant treatment did not affect the outcome of LDLT, but its indications should be carefully considered for patients with HCC who have had pretransplant treatment associated with DCP more than 300 mAU/mL to prevent tumor recurrence.

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Acute Amiodarone Hepatotoxicity After Liver Transplantation

A 64-year-old white male with end-stage liver disease, secondary to nonalcoholic steatohepatitis and hepatocellular carcinoma, underwent an orthotopic liver transplant (OLT) from a 21-year-old donation-after-cardiac-death donor. Postoperatively, he had primary nonfunction of the allograft manifested by increased hepatic biochemical markers, acute renal failure, increasing lactate level, increasing coagulopathy, and hemodynamic instability. Two days later, he underwent a second OLT and was started on triple-drug immunosuppression regimen as per institutional protocol consisting of tacrolimus, mycophenolate mofetil, and prednisone. He was also started on posttransplant infectious prophylaxis with valganciclovir, sulfamethoxazole-trimethoprim, and mycamine. One day after his second transplant, he experienced atrial fibrillation as detected by telemetry and confirmed on electrocardiography. Consequently, he was started on intravenous amiodarone with a bolus dose of 150 mg followed by a continuous infusion at a rate of 1 mg/min. Esmolol was added on postoperative day (POD) 5 at a rate of 50 μg/kg/min to control the heart rate.

On POD 7, his liver transaminase levels started to increase (Fig. 1A). Alanine aminotransferase (ALT) values increased from 688 to 2028 U/L, aspartate aminotransferase (AST) from 375 to 932 U/L, alkaline phosphatase from 66 to 104 U/L, and bilirubin (BILI) from 6.5 to 13.4 mg/dL. Doppler ultrasound was performed to exclude hepatic artery thrombosis, which showed a patent hepatic artery, portal vein, and hepatic veins with normal blood flow. Endoscopic retrograde cholangiogram did not show any biliary obstruction. In addition, a liver biopsy was performed, which showed canalicular cholestasis, increased mitotic activity, and numerous apoptotic hepatocytes, especially around the central veins; there were no features of acute cellular rejection (Fig. 1B–D). Considering these findings, a likelihood of a drug-related hepatotoxicity was examined. On reviewing his medications, amiodarone was the only drug that is known to cause hepatotoxicity and was stopped after 11 days of therapy. He was then started on metoprolol 100 mg orally twice daily for atrial fibrillation. After withdrawal of ami-

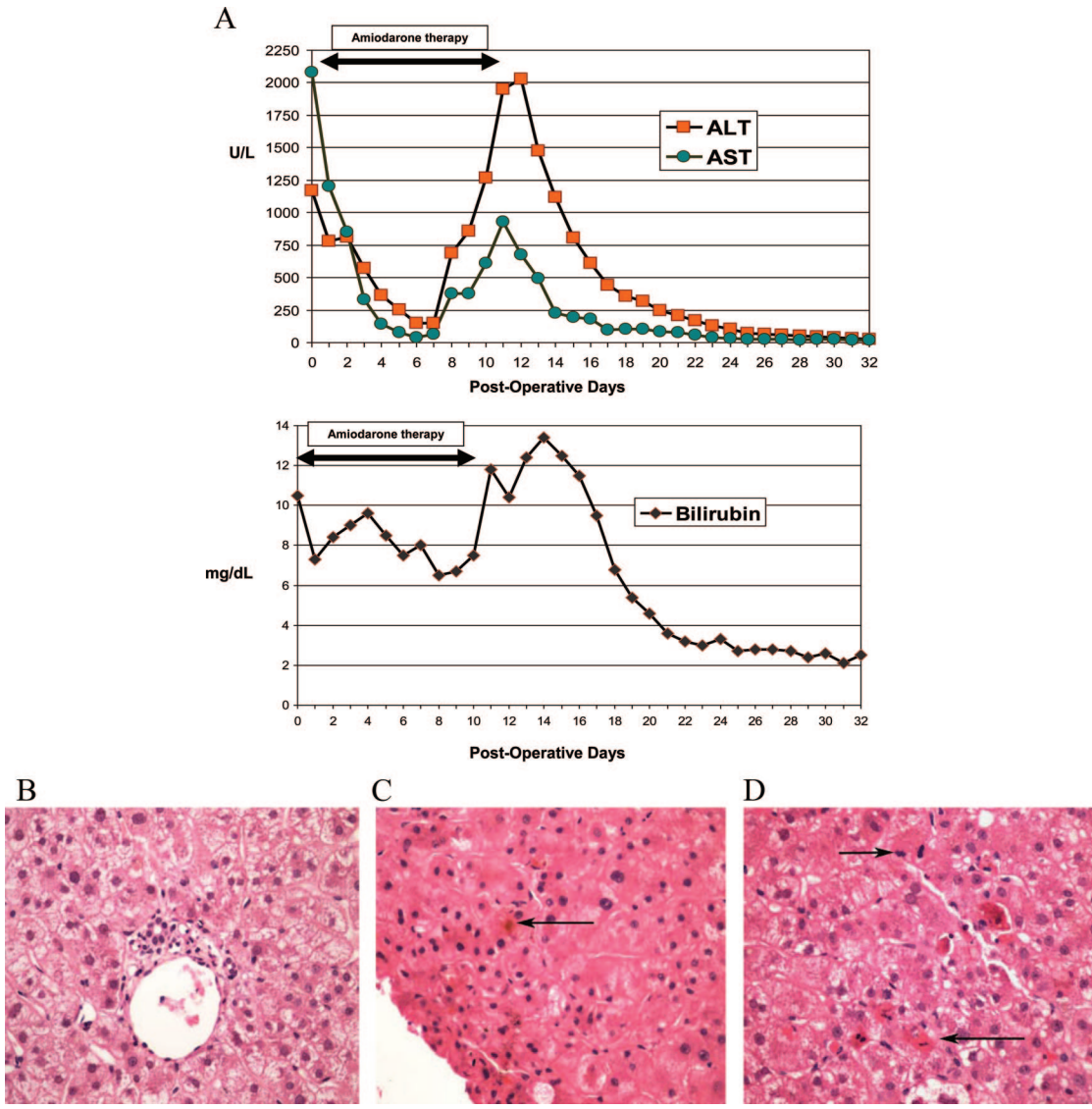

FIGURE 1. (A) Hepatic biochemical markers over postoperative days with duration of amiodarone therapy; (*upper*) alanine aminotransferase (ALT) and aspartate aminotransferase (AST, units per liter); (*lower*) bilirubin (milligram per deciliter). (B) Portal area with no evidence of rejection; (C) cholestasis (*arrow*); (D) increased mitoses (*upper arrow*) and apoptotic bodies (*lower arrow*).

odarone, his liver functions gradually normalized over the next 2 weeks (Fig. 1A). He was discharged on POD 25 having nearly normal hepatic function with ALT 72 U/L, AST 27 U/L, and BILI 2.7 mg/dL. At his most recent follow-up, he is 3.5 months posttransplant; doing well; and has a normal hepatic function with ALT 20 U/L, AST 17 U/L, and BILI 0.8 mg/dL.

DISCUSSION

Amiodarone is becoming the drug of choice in the treatment of atrial fibrillation, particularly in the postsurgical setting (*1*,*2*). However, it is associated with many adverse effects including hepatotoxicity. Amiodarone-induced hepatotoxicity usually occurs with chronic use of oral amiodarone with a reported incidence of approximately 24% to 26%; this is frequently transient and asymptomatic increase of transaminases, which returns to a normal level after dose reduction or withdrawal (*3*,*4*). Symptomatic and potentially fatal liver injury has also been reported during intravenous amiodarone treatment (*3*–*7*).

Amiodarone-induced hepatotoxicity has been not described in liver transplantation. Its presentation can mimic the more frequent causes of post-OLT hepatic dysfunction including ischemic-reperfusion hepatic injury, hepatic artery thrombosis, rejection, or biliary obstruction and will lead to diagnostic confusion. Our patient developed signs of acute hepatic injury during intravenous amiodarone treatment within therapeutic dosages, and his liver functions normalized gradually after withdrawal of amiodarone. Considering the prevalence of perioperative cardiac arrhythmias after OLT and use of amiodarone to treat them, it may be prudent to say that amiodarone-induced hepatotoxicity is frequent and remained undiagnosed, most likely because of its short-term use and the fact that hepatotoxicity is reversible.

In conclusion, we recommend that clinicians should anticipate this potential adverse effect of amiodarone and consider in differential diagnosis of he-

patic dysfunction whenever used. Fortunately, hepatotoxicity is reversible after withdrawal of amiodarone.

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