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Liver retransplantation for alcoholic cirrhosis recurring within a 21-month period

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Sirs: Orthotopic liver transplantation (OLT) increases the 2-year survival of patients with severe alcoholic cirrhosis, as shown by a case-control study comparing survival in transplant recipients with control patients matched for age, severity of cirrhosis, and bleeding history [7]. Survival of transplant recipients with end-stage alcoholic liver disease seems to be equal to that of patients with end-stage liver disease from other causes, with an overall 1-year survival rate of 70 %–90 % [4]. The incidence of recidivism is considered the only important parameter for outcome of alcoholism in patients who undergo OLT for alcoholic liver disease. This rate may depend on the quality of the follow-up, with values around 31 %–40 % [5] in OLT units with a close follow-up, which contributes to a more accurate detection of drinking episodes. Underlying the problem of predicting and preventing recidivism is the major issue of whether any level of drinking after transplantation damages the liver [8]. Thus far, no one has been able to answer this question. Recently, Baddour et al. reported cirrhosis in 4 out of 23 alcohol-abusing recipients developing from day 177 to day 711 postoperatively [1]. We report here on a 21-month progressive, histologic evolution to severe cirrhosis requiring retransplantation in a nonabstinent woman.

A 45-year-old white female underwent transplantation for alcoholic cirrhosis in March 1992. She had had two episodes of decompensated liver disease in 1990 with edema, ascites, jaundice, and altered liver function tests: bilirubin 43 μmol/l (normal values < 17 μmol/l), ASAT 184 IU/l, ALAT 61 IU/l (normal values < 50I U/l), and prothrombin time and factor V 45 % and 58 %, respectively. She had esophageal and cardial varices for which she was put on therapy (propranolol) to prevent a first bleeding. The patient had been used to drinking 80 g of alcohol daily for the past 15 years. At the time of transplantation, in spite of abstinence for more than 15 months and diuretics, she was still mildly ascitic. She was overweight (74 kg, height 1.60 m). Her ASAT, ALAT, and AP were normal, GGT 67 IU/l (normal values < 50 IU/l), bilirubin 30 μmo/l, albumin 29 g/l, prothrombin time and factor V 65 % and 69 %, respectively, platelet count 218 000/mm^3, and mean corpuscular volume 97.5 fl. Her Child Pugh classification was 7. All viral and immunological tests were negative. The explanted liver (1500 g) showed micronodular cirrhosis with less than 25 % steatotic hepatocytes. She received triple immunotherapy and left the hospital 1 month later with normal liver function tests.

In May 1992, liver function tests were abnormal. Arteriography revealed an anastomotic stenosis of the hepatic artery and this was dilated. However, this did not improve the liver function tests. Because the liver biopsy showed signs of acute cellular rejection, the patient received three boluses of steroids. Still, the biological abnormalities did not return to normal. During the follow-up, liver function tests remained abnormal, particularly ASAT (two to six times the normal level), which were more increased than ALAT. Bilirubin level increased as well as mean corpuscular volume (to 113 fl in November 1994), and prothrombin time dropped. She had several liver biopsies which, as early as month 7, showed steatohepatitis with severe activity, fibrosis, and steatosis (60 %) . At month 21 post-OLT, cirrhosis was confirmed. The patient had two serious episodes of decompensated liver cirrhosis with ascites and jaundice, a rise in transaminases, and a fall in prothrombin time (34 %), from which she recovered after a few weeks in the hospital.

Although the patient always denied that she drank alcohol, her alcohol level was found to be elevated when tested twice (0.6 and 2 g/l, respectively). All virologic and autoimmune markers remained negative. There was no radiological or pathological evidence of vascular disorders or rejection.

The patient underwent retransplantation in March 1995 after 3 months of abstinence. Her weight was 78 kg and she has gained 15 kg in the last 12 months. The graft was cirrhotic and micronodular with moderate activity and little steatosis. Ten months after transplantation she is well and abstinent.

This is, to our knowledge, the first reported case of retransplantation for alcoholic cirrhosis. The reasons for the recurrence of alcohol-related liver cirrhosis in this patient were clear. The first transplantation was performed for alcoholic cirrhosis that was not associated with any other liver disease, particularly viral-related. Although the patient denied having had any alcohol, her blood alcohol level was elevated on at least two occasions, and her blood chemistry and liver histology [3] were fully compatible with alcoholic liver disease. Liver function tests and clinical signs improved during her hospitalizations. Furthermore, there was no evidence of nonalco-

holic steatohepatitis, although she was slightly overweight with rather large weight variations in-between the two transplantations.

There are only two reports (in abstract form) in the literature showing the influence of recidivism on liver histology [1, 6]. In the first one, among 23 individuals who survived after OLT and were known to have resumed alcohol abuse, 22 of 23 had steatosis, 20 of 23 central sclerosis, 12 of 23 pericellular fibrosis, 22 of 23 Mallory's hyaline, and 4 of 23 cirrhosis from 177 to 711 days post-OLT [1]. In the other report, alcohol recidivism was asserted in ten patients with a mean alcohol intake of 69 g/day (range 40–110 g/day). Steatosis was found in all patients (> 50 % in eight patients and < 50 % in two). None had fibrosis or cirrhosis [6].

In general, there has been slowly increasing evidence that perivenular fibrosis [3] and, more recently, mixed macro/microvesicular steatosis at the fatty liver stage [9] indicate individuals at high risk of progression to cirrhosis if they continue to drink. Both histologic abnormalities were already present in our patient at month 7 post-OLT.

If, at present, we cannot give a definitive answer to the crucial question of whether any level of drinking after transplantation actually damages the graft [8], we can at least add a word of caution. Of the various risk factors that may play a role in the occurrence of cirrhosis, [2] alcohol intake is probably the key factor. We do not know, in this case, the amount of alcohol that was consumed per day. However, given our patient's previous habit and the probablitiy that she was a destructive, post-transplant drinker, we can assume that she drank at least 80 g daily. Gender may be an additional factor to consider. It is also possible, although less likely in this case, that obesity, combined with fluctuations in weight gain, favored the development of cirrhosis. Indeed, there was no major steatosis in the native liver or the explant, suggesting that alcohol – and not obesity – was responsible for it.

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