Case Study in the Management of Patients with Hepatocellular Carcinoma

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This 50-year-old married man with three children has a history of chronic hepatitis C that progressed to cirrhosis. Risk factors for hepatitis C were intravenous drug use in the 1960's and multiple transfusions given for trauma in 1975. Cirrhosis had been complicated by bleeding esophageal varices in 2001 but treatment with endoscopic banding was effective. Furthermore he developed ascites and hepatic encephalopathy. A computed tomography (CT) scan in November 2001 demonstrated a 6x6.5x7cm mass lesion in segment 7 of the liver. The mass increased in size to 11.2x9.2x5.8cm on a repeat CT scan two months later (Figure 1). Serum alpha-fetoprotein (AFP) was above 16,000ng/mL.

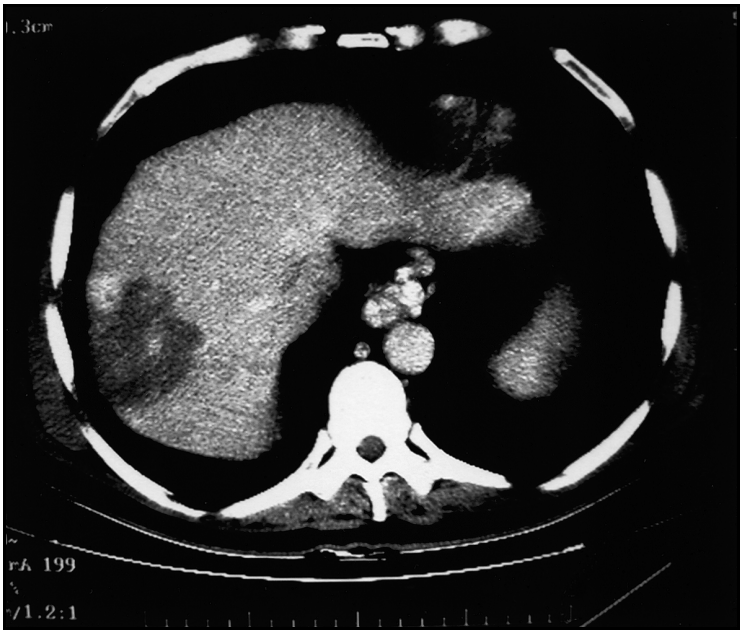

Figure 1: CT scan demonstrating mass in right hepatic lobe.

What therapy would you recommend?

Chemoembolization was undertaken with mitomycin, adriamycin and carboplatinum in February of 2002. By late July 2002 the CT scan showed an area of decreased enhancement 3-4cm in diameter in segment 7 associated with a dramatic drop in serial AFP values.

Would you recommend liver transplantation at this point?

An orthotopic liver transplant was performed in August of 2002. The explant showed advanced cirrhosis without any histologic evidence of residual hepatocellular carcinoma (Figure 2, Figure 3).

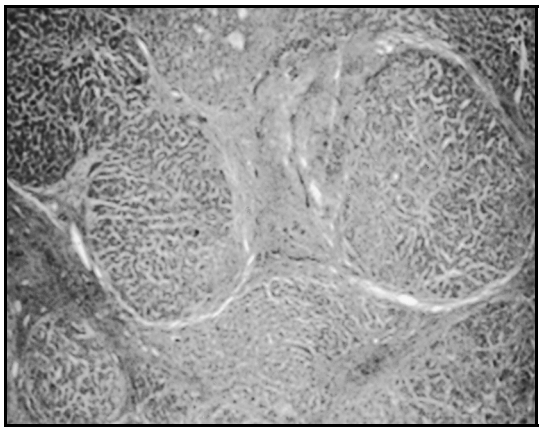

Figure 2: Liver biopsy showing presence of cirrhosis.

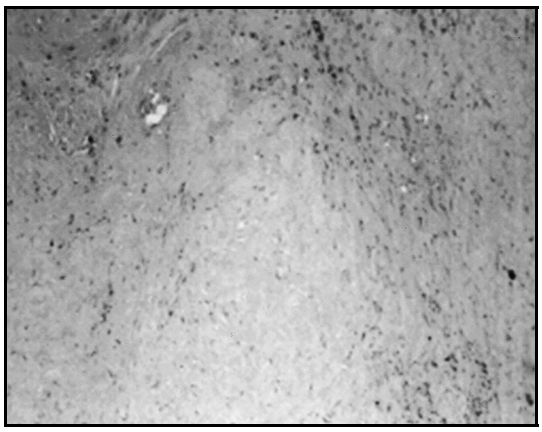

Figure 3: Liver tissue from site chemoembolization.

Would you treat the patient with chemotherapy post-liver transplant?

The decision was made not to treat the patient with chemotherapy. Five months post transplant he was maintained on tacrolimus 7mg b.i.d. and medrol 16mg q.d. after several episodes of acute rejection. He was generally feeling fine but had developed diabetes and was started on insulin. Laboratory values included total bilirubin 1.2mg/dL, alanine aminotransferase (ALT) 32U/L, aspartate aminotransferase (AST) 42U/L, alkaline phosphate 102U/L. hepatitis C virus (HCV) RNA >500,000IU/mL. Liver biopsy was consistent with chronic hepatitis C (Grade 3) and mild rejection.

Would you treat this patient with pegylated interferon and ribavirin?

Treatment was not started until 6 months later when he became increasingly icteric and developed diarrhea. A repeat liver biopsy suggested recurrent hepatitis C and mild rejection. At that time the total bilirubin was 21.5mg/dl, AST 417U/L, ALT 218UL, alkaline phosphate 267U/L, albumin 2.7g/dL, creatinine 0.8mg/dL, AFP 14.3. He was treated with pegylated interferon-alpha-2a, 90µg weekly and ribavirin 200mg b.i.d. He continued to deteriorate and a repeat liver biopsy one month later was consistent with fibrosing cholestatic hepatitis and without significant rejection. He succumbed 1.5 years post liver transplantation. There was never any evidence of recurrent hepatocellular carcinoma.

CASE DISCUSSION

This patient presented with a hepatocellular carcinoma more than 5cm in diameter that grew to 11cm in diameter. Liver transplantation was contraindicated at that stage. However he underwent chemoembolization, which literally eradicated the hepatocellular carcinoma which was absent in the explant. Hepatic artery chemoembolization for hepatocellular carcinoma in patients listed for transplantation is beneficial but must be considered in relation to the risk of chemoembolization induced deterioration. The latter was a transient problem in this patient prior to transplantation. The impact of the Model for End Stage Liver Disease (MELD) for patients with hepatocellular carcinoma has significantly improved the probability of

a timely orthotopic liver transplant. Recurrence of hepatocellular carcinoma after a liver transplant develops in approximately 20% of patients with a median of one year. Recurrence of hepatocellular carcinoma significantly shortens post transplant survival but as many as 20% of these patients survive for at least 5 years compared to 65% in patients without recurrent hepatocellular carcinoma. Recurrence of hepatitis C is inevitable in almost 100% of patients with endstage liver disease secondary to chronic hepatitis C who undergo liver transplantation. Unfortunately current antiviral therapy for hepatitis C is contraindicated in patients with decompensated cirrhosis. Furthermore there is no antiviral regimen comparable to that used in decompensated cirrhosis secondary to hepatitis B prior to liver transplantation, e.g. nucleoside analogs and hepatitis B immunoglobulin. The development of protease and polymerase inhibitors for HCV is in a relatively early stage and thus far no high titer anti-HCV preparation has been shown to successfully prevent hepatitis C. Although the use of pegylated interferon and ribavirin post liver transplant is being assessed, efficacy is limited and the side-effect profile is high in this immunosuppressed group. As many as 40% of post transplant patients with recurrent hepatitis C develop cirrhosis within 5 years after transplantation. Retransplantation of patients with fibrosing cholestatic hepatitis as in the present case has been shown to be ineffective as has antiviral therapy. Retransplantation of recurrent hepatitis C patients who have progressed to cirrhosis has been associated with relatively poor survival rates but these patients would do better if they were retransplanted with MELD scores less than 16 and with livers from donors who are under 60 years old.

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