Liver Failure and the Need for Transplantation in 6 Patients With Hepatoportal Sclerosis

E.C. Ataide, I.N. dos Santos, D.L. Martins, T.S. Pereira, J.R. de Souza Almeida, R.S.B. Stucchi, C.A.F. Escanhoela, and I.d.F.S.F. Boin

ABSTRACT

Hepatoportal sclerosis (HPS), first reported by Mikkelsen et al in 1965, is a pathologic condition that does not cause cirrhotic portal hypertension. The primary hepatic lesion in HPS is found in portal vein branches with preserved synthetic function. Rarely do patients with HPS need liver transplantation. The aim of this study was to describe the clinical and pathologic features of 6 HPS cases who underwent liver transplantation (OLT). From 2000 to 2008, 6 OLT candidates were diagnosed with HPS: 3 displayed bleeding varices and 4 ascites. Child-Pugh evaluation was class B ($n = 4$) or C ($n = 2$). The Model for End-stage Liver Disease scores were 18 ($n = 2$), 20 ($n = 3$), and 22 ($n = 1$). Cirrhosis resulted from presumed diagnoses of alcohol $n = (1)$, autoimmune $n = (2)$ or cryptogenic cirrhosis $n = (3)$. On histologic examination, there was marked phlebosclerosis in all cases, including nonocclusive portal vein thrombosis ($n = 3$), intense portal fibrosis ($n = 1$), moderate portal fibrosis ($n = 5$), and uniform moderate sinusoidal dilatation without megasinusoid formation, but with ductal biliary proliferation and ductal biliary fibrosis in all cases. Cholestasis was observed in 1 and incomplete septal cirrhosis in 4 cases. None of the subjects showed histological features of the presumed underlying liver disease. The overall survival of this group was no different from that of other OLT patients. HPS causing hepatic failure may require liver transplantation. Fhlebosclerosis andportal fibrosis may contribute to the loss of hepatic synthesis leading to the need for hepatic transplant. Significant portal fibrosis and phlebosclerosis can contribute to hepatic parenchymal and posterior synthetic loss.

HEPATOPORTAL SCLEROSIS (HPS) is a term suggest by Mikelsen et al.[1] to describe fibrous intimal thickening of the portal vein or its branches in patients with noncirrhotic portal hypertension. They described 17 cases without extrahepatic portal venous obstruction, 13 with portal obliteration, and 6 with incomplete portal vein obstruction.[1] Other nearly synonumous terms are often used in Japan and Indian are idiopathic portal hypertension and noncirrhotic portal fibrosis, respectively.[2,3]

Usually the major presenting clinical symptoms are those of portal hypertension with hepatic synthetic function almost always well preserved and hepatic encephalopathy rare.[4] Uncommonly patients with HPS require liver transplantation (OLT), Usually this procedure has been performed in HPS patients on the presumption that they had cirrhosis.[5–7] The aim of this study was to describe the clinical and pathologic aspects their of 6 patients undergoing OLT who were diagnosed as displaying HPS based on examination of their explanted livers.

MATERIALS AND METHODS

The 6 patients diagnosed as having HPS were transplanted between 2000 and 2008. The diagnosis of HPS was based on both gross and microscopic examinations of explanted native livers. The information obtained from each case included presumed cause of liver disease; presence of varices or of variceal bleeding, of ascites, and/or of encephalopathy; albumin, bilirubin international normalyzed ratio (INR) and creatinine concentrations at the time of

From the Unit of Liver Transplantation (E.C.A., J.R.d.S.A., R.S.B.S., C.A.F.E., I.d.F.S.F.B.), State University of Campinas (I.N.d.S., D.L,M., T.S.P.), Campinas, Brazil.

Address reprint requests to Eliane Cristina de Ataide, Rua Zerillo Pereira Lopes 651 casa 37, Alto Taquaral, Campinas, São Paulo, Brazil CEP: 13087-757. E-mail: elainebataide@yahoo.com.br

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OLT. We calculated Child class Model for End Stage Liver Disease (MELD) and score.

Representative hematoxylin-eosin (HE) stained sections from the right and left lobes as well as portahepatis were supplemented with Trichome's Perls, and Gomori's stained, to identify phlebosclerosis, sinusoidal dilatation, megasinusoid formation, biliary ductal proliferation, or fibrosis as well as cholestasis and incomplete septal cirrhosis.

RESULTS

Over an 8-year period (2000–2008) 6 OLT patients diagnosed with HPS included 3 men and 3 women of age range 28–57 years (mean = 42). The presumed causes of cirrhosis were: alcohol (n = 1), autoimmune (n = 2) or cryptogenic (n = 3).

The duration of symptoms ranged from 18 months to 5 years (mean = 2.5). The clinical presentations including an history of bleeding varice (n = 3), ascites (n = 4), and for mild to moderate encephalopathy (n = 2). Four patients were (n = 3) Child class and 2 Child class C. The MELD score was 18 (n = 2), 20 (n = 3), and 22 (n = 1). The mean of creatinine level was 1.4 mg/dL, the mean INR was 1.5 and mean bilirubin was 3.5 mg/dL. All of the patients displayed serum albumin concentratins abover than 3g/dL.

All explanted livers showed vague nodularity and rough surfaces. Their weights were 800 g (n = 1), 850 g (n = 1), 930 g (n = 1), 963 g (n = 1), 1000 g (n = 1), and 1050 g (n = 1).

On histologic examination, there was marked phlebosclerosis in all cases accompanied by nonocclusive portal vein thrombosis (n = 3), intense portal fibrosis (n = 1), and moderate portal fibrosis (n = 5). All subjects displayed moderate sinusoidal dilatation but none showed megasinusoid formation. Biliary ductal proliferation and fibrosis were observed in all cases. Cholestasis was noted in one and incomplete septal cirrhosis in 4 cases. None showed histologic features of the presumed underlying liver disease (Fig. 1).

DISCUSSION

Although the etiology of the HPS is unknown,[8] several theories have been proposed: recurrent digestive tract infections, exposure to toxins such as arsenic, treatment with drugs such as azathioprine, autoimmune disease, or a multifactorial origin.[8] After the first report of HPS by Mikkelsen et al in 1965,[1] various terms had been given to this entity: obliterative portal venopathy, idiopatic portal hypertension, nodular regenerative hyperplasia, and incomplete septal cirrhosis.[2,3,9,10] In patients with this diagnosis, the major symptoms relate to portal hypertension with rare reports citing the need for OLT.[11,12,13]

In 2008 Geramizadeh et al reported of 3 patients undergoing OLT whose explant assessment showed hepatoportal sclerosis. In this study, variceal bleeding and ascites were the most common presenting symptoms, albumin levels were normal, and bilirubin ranged around 2.0 to 3.0 mg/dL. No patient displayed encephalopathy.[11,12] In 2007, Fiel et al evaluated 8 patients undergoing OLT whose explants demonstrated the presence of HPS. Their presenting clinical major symptoms despite prior shunt procedures were bleeding varices (n = 7), with concomitant ascites (n = 5), and hepatic encephalopathy (n = 2). Six patients were Child clas C and 2 Class B.[12,13]

In our series, 6 patients were diagnosed with hepatoportal sclerosis upon examination of the liver explant after

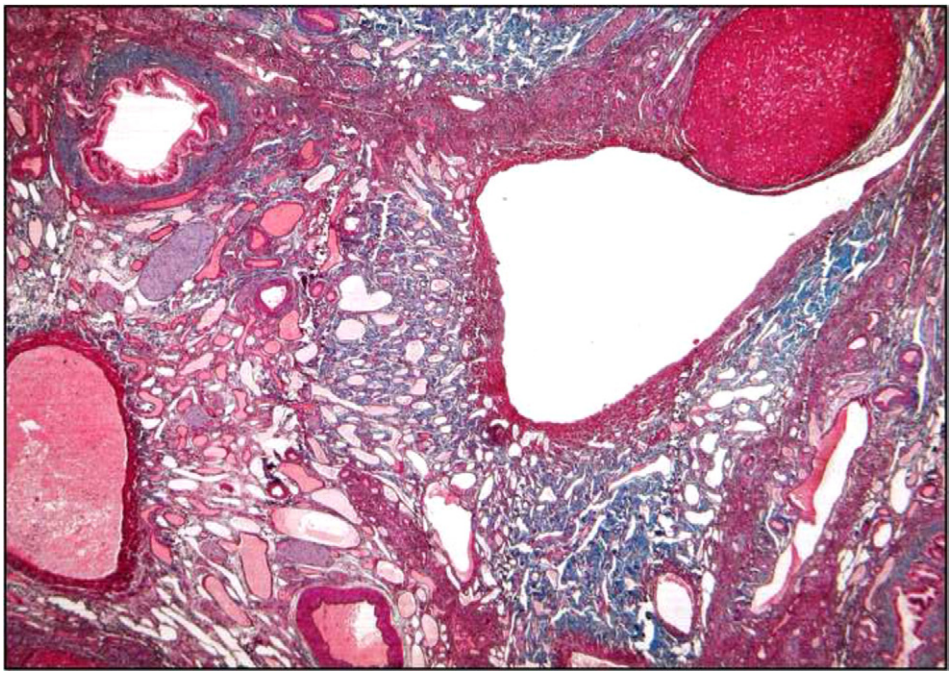

Fig 1. Intense portal angiomatoid proliferation associated portal venous branch compression seen on Masson coloration.

hepatic transplantation. Among these patients 3 had variceal bleeding and 4 ascites. The subjects were classified as Child class B ($n = 4$) or Class C ($n = 2$). MELD score was 18 ($n = 2$), 20 ($n = 3$) or 22 ($n = 1$). The mean creatinine level was 1.4 mg/dL; the INR 1.5; and bilirubin 3.5 mg/dL. All of the patients displayed serum albumin concentratinos above 3 g/dL. The elevated creatinine levels were observed among patients with ascites generally following introduction of high-doses diuretic therapy.

Encephalopathy was present in patients with higher MELD scores probably due to the intrahepatic shunts seen in more advanced cases. They also showed lower weights of their explanted livers. Other findings such as albumin and INR did not change significantly as previously described in the literature as cases compatible with EH generally show liver functions close to normal values.[4,12,13]

The overall survival of these patients who underwent orthotopic liver tranplantation (OLT) for hepatoportal sclerosis (HPS) was similar to the that of subjects undergoing transplantation for other conventional causes, in our institution: 91% in 1 year, 84% in 2 years and 67% in 5 years.

In summary, we have demonstrated that patients with HPS display, hepatic synthetic dysfunction especially when there is a small liver volume. Liver synthetic compromise concurrent with portal hypertensive complications may necessitate OLT for advanced HPS.

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