Orthotopic Liver Transplantation for Hepatic Adenoma in a Patient with Portal Vein Agenesis

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Abstract: Congenital portal vein agenesis, known as the Abernathy malformation, was first described in 1793. It is associated with focal nodular hyperplasia and adenomas due to abnormal hepatic regeneration secondary to abnormal or absent flow to the liver. We report a case of a 25-year-old Caucasian female with a complicated medical history including idiopathic membranoproliferative glomerulonephritis, hypertension, hyperlipidemia, Sweet's syndrome, acute febrile neutrophilic dermatosis, who incidentally was diagnosed with multiple liver nodules, the largest 14 cm in diameter, arising at the junction of the left and right hepatic lobes. She was also noted to have a congenital absence of the portal vein. There was no evidence of cirrhosis or portal hypertension. Liver function tests and α- fetoprotein were within normal limits. A biopsy of the largest mass revealed hepatocellular adenoma. Because of the size, location, and multiplicity of the lesions, we elected to proceed with orthotopic liver transplantation. She subsequently underwent deceased donor liver transplantation using the piggyback technique. Despite dividing the portal vein shunt after completion of the caval anastomosis and minimizing the portal vein clamp time, her spleen spontaneously ruptured, for which splenectomy was performed. The patient did well postoperatively with good liver function.

INTRODUCTION

Hepatic adenoma is a benign tumor of the liver found in the background of an otherwise normal liver parenchyma. It is associated with contraceptive use, anabolic androgens, and glycogen storage disease. The estimated incidence of adenomas is 3 cases per 100,000 people per year with long-term contraceptive use [1]. It can be associated with fatal complications such as rupture leading to hemorrhage and malignant transformation. Because of the uncertainty of tumor behavior, the treatment is controversial and ranges from observation to resection and even liver transplantation in carefully selected cases. In this report we describe a patient with multiple liver lesions, the largest adenoma measuring 14 cm in diameter, associated with congenital vascular anomaly known as the Abernathy malformation or portal vein agenesis. Because of the size and location of the tumors in our patient, orthotopic liver transplantation was undertaken.

CASE HISTORY

Our patient is a 25-year-old Caucasian female with a complicated history of type I idiopathic membranoproliferative glomerulonephritis, hypertension, hyperlipidemia, anemia, hypothyroidism, Sweet's syndrome, and acute febrile neutrophilic dermatosis. She had experienced painful, subcutaneous erythematous nodules on the abdomen, nausea, vomiting, high fever, occasional left lower abdominal pain several times over a period of four years, which resulted in multiple admissions to an outside hospital. All symptoms essentially resolved spontaneously within 3 days. Her workup for abdominal pain included a CT scan of the abdomen and pelvis, which revealed an incidental finding of multiple masses in the liver and congenital agenesis of the portal vein. Biopsy of the liver masses was nondiagnostic, revealing benign liver tissue. She was referred to our hospital for further management of the liver masses.

On our evaluation she denied right upper quadrant abdominal pain or discomfort. There was no known family history of liver tumors. Her medications included valsartan (Diovan), lisinopril, furosemide (Lasix), and levothyroxine. She was never on oral contraceptives. On physical examination, she was a well-nourished and well-appearing young woman without scleral icterus. Her abdomen was nontender and without palpable masses. There were no psychoneurological changes. Laboratory investigations yielded the following results: CEA, alpha-fetoprotein, and CA 19-9 within normal ranges, AST 41 u/L, ALT 34 u/L, alkaline phosphatase 188 u/L, total bilirubin 0.5 mg/dL, INR 1.2, platelets 119, 000. Serologic tests for hepatitis B and C were negative. CT scan of the abdomen revealed multiple bilateral heterogenous, hypervascular masses in the liver, most compatible with either hepatic adenomas versus focal nodular hyperplasia. The largest lesion arose from the left lobe and measured 10 cm x12 cm x 7 cm. Portal vein was absent, with termination of the splenic and superior mesenteric veins directly into the inferior vena cava (IVC), Fig. (**1**). A very large hepatic artery was noted with conventional anatomy. Splenomegaly was present with spleen size of 16 cm. There was no evidence of portal hypertension or ascites. We proceeded with an open biopsy

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1874-4184/09

of the largest lesion, which was consistent with hepatic adenoma. Followup MR of the abdomen and pelvis again revealed numerous hepatic masses, with the largest centered in the region of the junction of the right and left hepatic lobes and increased in size to 14 cm in greatest dimension.

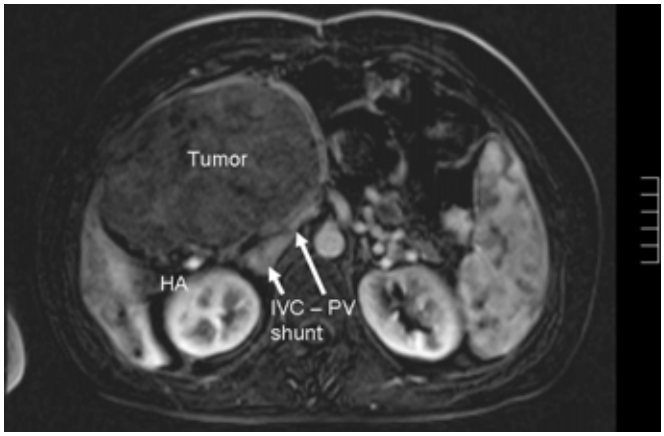

Fig. (1). Magnetic resonance imaging showed a large hepatic mass (tumor) and drainage of the portomesenteric vein (PV) into the inferior vena cava (IVC) constituting the congenital portacaval shunt. The hepatic artery (HA) was present at the hilum. No portal vein at the hilum was found.

The recommendation for treatment was liver transplantation due to the size, bilaterality, and multiplicity of tumors. The patient was listed for transplantation and was granted with exception a MELD score of 22 by the regional UNOS board. Orthotopic liver transplantation was performed using a deceased liver donor. During the operation, the liver was noted to be occupied by a large mass in the left lateral segment, Fig. (**2**). A prominent hepatic artery was noted. There was no evidence of portal vein at the hepatic hilum. Native hepatectomy was performed with total avascular approach sparing the native cava. The splenic and superior mesenteric veins joined together, i.e. congenital portal vein emptying into the suprarenal IVC, Fig. (**3**). The new liver allograft was implanted with the piggyback technique. The allograft suprahepatic cava was anastomosed to the recipient's hepatic venous ostium that was created with the right, middle, and left hepatic vein stumps. The recipient congenital portacaval connection was then divided with a vascular stapler at the portal vein and IVC junction.

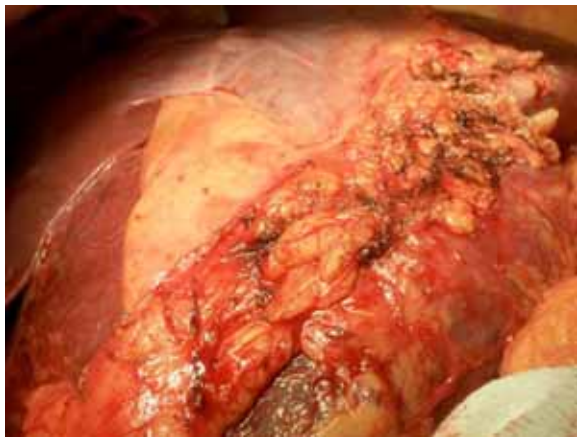

Fig. (2). Intraoperative demonstration of a large hepatic adenoma.

The graft portal vein was anastomosed to the recipient congenital portal vein in an end-to-end fashion. While the portal vein anastomosis was being completed, a sudden surge of venous blood from the left upper quadrant occurred. A splenic rupture was suspected. The portal vein anastomosis was promptly completed and the portal vein recirculation was carried out. Once the recirculation was established, the venous bleeding from the left upper quadrant subsided. The hepatic artery was reconstructed in an end-to-end fashion with loupe magnification. As we examined the spleen, a large splenic rupture beyond salvage at the splenic hilum was found. Splenectomy was performed. The pancreatic tail was preserved. The splenic bed was drained. The liver transplantation was completed with biliary duct-to-duct reconstruction. The patient's postoperative course was uncomplicated. The patient was discharged home on postoperative day 5 with good liver function. She was immunized in the past and now has to be followed carefully for any signs of infection.

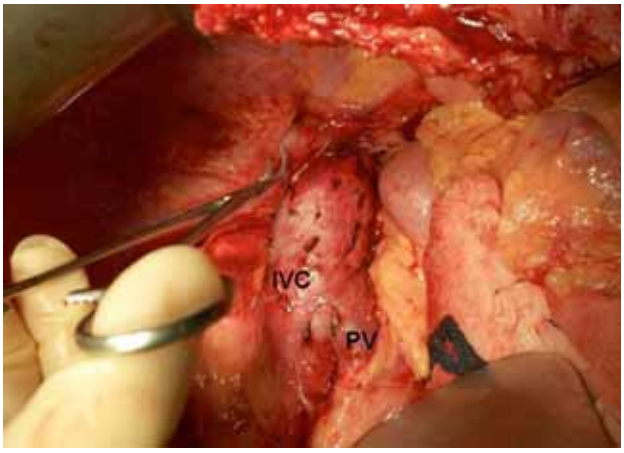

Fig. (3). Native hepatectomy completed with recipient cava (IVC) intact. The congenital portocaval shunt visualized with the portal vein (PV) draining directly into the cava.

The operation lasted 3 hours and 10 minutes from skin incision to closure. Warm ischemic time from removal of the allograft from the ice-cold UW solution for the suprahepatic caval anastomosis to portal vein recirculation was 28 minutes. Allograft cold ischemic time was 6 hours and 1 minute.

Fig. (4a). Hepatocellular adenoma (gross).

The explanted liver showed a large tan ovoid mass measuring 14.5 cm x 11.5 cm x 8.5 cm at the junction of the right and left hepatic lobes, Fig. (**4a**). The pathology was

consistent with hepatocellular adenoma, Fig. **(4b**). There was another adenoma in segment 8 measuring 4.0 cm. At least 10 other lesions consistent with focal nodular hyperplasia were noted in both lobes, the largest measuring 3.5 cm. There was no evidence of malignancy, parenchymal fibrosis, or inflammation. The intrahepatic portal vein branches showed obliterative smooth muscle hypertrophy, Fig. **(4c**).

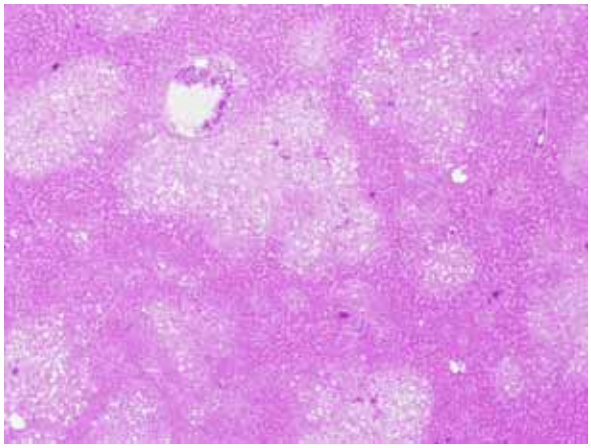

Fig. (4b). Hepatocellullar adenoma (microscopic, H&E stain).

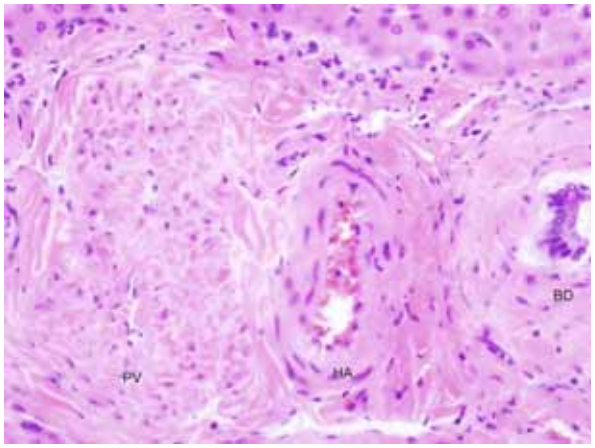

Fig. (4c). A portal tract showing portal vein (PV) smooth muscle hypertrophy and almost complete obliteration of the lumen (H&E stain, x 400).

DISCUSSION

Hepatic adenoma is a rare benign tumor of the liver. Although some patients present with abdominal pain, it is usually asymptomatic and diagnosed incidentally on imaging studies. Although most adenomas are solitary, in 20-30% of cases multiple adenomas can be found [2]. It is associated with the use of exogenous sex steroids including oral contraceptives and anabolic androgens [3, 4]. One of the complications of hepatic adenoma is intraperitoneal hemorrhage from rupture. Review of the literature reveals that approximately 30% of cases are complicated by hemorrhage [1, 5]. It has been suggested that adenomas greater than 5 cm in diameter should be resected as they are at increased risk of bleeding, though bleeding has also been reported with smaller lesions [6, 7]. The risk of malignant transformation to hepatocellular carcinoma is 5-10% [1, 5]. The natural history of tumor is uncertain, and thus the spectrum of treatment of hepatic adenomas range from careful observation with cessation of oral contraceptives to liver resection to orthotopic liver transplantation in unresectable cases [5, 8].

A recently recognized association is of hepatic adenomas and other lesions including focal nodular hyperplasia, hepatocellular carcinoma, and hepatoblastoma with a vascular abnormality known as portal vein agenesis. It has been postulated that it is likely due to abnormal hepatic development, function, and regeneration secondary to the lack of portal vein flow, hepatotrophic factors from the mesenteric flow, and enhanced arterial flow [9]. In 1793, Abernathy described a condition in which the flow from the gastrointestinal tract, pancreas, and spleen was diverted into a systemic circulation bypassing the liver [10]. The Abernathy malformation is subdivided into type I-end-to-side congenital portocaval shunt--in which the portal vein drains into the inferior vena cava, left renal vein, right atrium, iliac vein, azygos vein, or hepatic vein. It is further subclassified into type Ia--the splenic vein and superior mesenteric vein separately forming an anastomosis with the vena cava, and type Ib--the splenic vein joins the superior mesenteric vein before draining into the IVC. In type II malformation or side-to- side malformation, the shunt is not complete, and there is some flow through the liver [11, 12]. The Abernathy malformation is frequently associated with cardiac defects, skeletal deformities, biliary atresia, and portosystemic encephalopathy. The diagnosis is made usually in childhood, with most patients remaining asymptomatic with normal liver function and no evidence of portal venous hypertension or hepatic encephalopathy.

Orthotopic liver transplantation has been performed in patients with congenital portal vein agenesis. It has been described in children with hepatoblastoma [13], biliary atresia [11, 14-16], portopulmonary hypertension [17], portosystemic encephalopathy [18-20], and hepatic adenomatosis [21]. The first report of liver transplant in an adult was done for progressive portosystemic encephalopathy and was reported by Wojcicki *et al.* in 2004 [22]. Since then there have been other cases of liver transplantation described in adults [23].

Lack of collateral circulation should be taken into consideration when performing liver transplantation in patients with the Abernathy malformation. Patients with cirrhosis and portal hypertension have portal venous collaterals and can tolerate clamping of the portal vein without significant increase in portal venous pressure, while those who have normal liver parenchyma lack collaterals and have a significant increase in pressure while the portal vein is clamped. Mesenteric congestion with bowel swelling can rapidly occur [18]. Splenic rupture is another potential complication. It is important to minimize portal vein clamp time to avoid these complications. Using venovenous bypass is the approach taken at centers that routinely use this bypass. Alternatively, a portocaval shunt can be created using the recipient superior mesenteric vein or portal vein.

There are few reports in the literature describing spontaneous splenic rupture as a result of portal vein occlusion during liver resection [24-26]. To our knowledge, splenic rupture during liver transplantation has not yet been described in the literature. When performing the piggyback technique in patients who lack collateral circulation, the

exact upper limit of portal clamp time to avoid splenic rupture and other related complications is not known. At our center, we have performed more than 1800 cases of orthotopic deceased donor liver transplantations using only the piggyback technique. There have been 18 cases of acute liver failure (ALF). In one case, the anhepatic phase time with the portal vein clamped was 76 minutes and the spleen ruptured. This anhepatic time was much longer than the time in the remaining ALF cases without splenic rupture, which ranged from 44 to 62 minutes. In contrast, surprisingly, the case in this report had portal vein clamp time much less than 28 minutes.

Shinkai *et al.* [19] reported portal vein clamp time of about 20 minutes to reconstruct the portal vein in a 3-year-old boy with portosystemic encephalopathy secondary to portal vein agenesis. They described some mesenteric venous congestion with mild intestinal edema. Takeichi *et al.* [27] reported 17 minutes of portal vein clamp time without observing intestinal congestion in a 35-year-old woman who underwent living donor domino liver transplant for congenital portal vein agenesis-induced portosystemic encephalopathy. Nevertheless, the optimal time for portal vein clamping during liver transplantation in patients without cirrhosis remains to be defined.

In conclusion, the patient in this report represents a unique case in that the liver transplantation was performed in an adult with congenital portal vein agenesis. We believe that orthotopic liver transplantation using the piggyback procedure with complete clamping of the portal vein is possible if the portal vein reconstruction time is kept to a minimum. The surgeon needs to be cognitive of the potential for splenic rupture due to the lack of existing venous collaterals.

ACKNOWLEDGEMENT

The authors wish to thank Deason Foundation and Sandra/Eugene Davenport for their generous support to JHN for the clinical research in liver transplantation at Mayo Clinic Florida.

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Received: June 12, 2009 Revised: July 01, 2009 Accepted: July 06, 2009