Hepatic Venous Outflow Obstruction in Autosomal Dominant Polycystic Kidney Disease¹

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ABSTRACT
To discuss the clinical presentation, diagnosis, and treatment of hepatic venous outflow obstruction as a complication of polycystic liver disease, four cases diagnosed and treated at our institution have been reviewed and the information from six previously published case reports has been summarized. Eight of the 10 patients were women. All presented with severe ascites. Nine had polycystic kidneys. Three had moderate-to-advanced renal insufficiency, four were on hemodialysis, and one had a renal allograft. Possible predisposing factors were identified in seven patients; the most common was recent abdominal surgery, which, in three cases, was a bilateral nephrectomy. All patients had extrinsic compression of the hepatic veins and the inferior vena cava by hepatic cysts, and four had proven superimposed thrombosis of the inferior vena cava and/or hepatic veins. In the patients seen in this institution, magnetic resonance imaging was helpful in determining the level of obstruction in the inferior vena cava and the patency of the hepatic and portal veins. The outcome was worse in the patients with thrombosis; one recovered after a portocaval shunt, and the remaining three patients died. On the other hand, five of the six patients without thrombosis recovered after alcohol sclerosis of a large dominant cyst (one patient) or after hepatic resection and cyst fenestration (four patients). Hepatic venous outflow obstruction probably has been underrecognized as a cause of portal hypertension, ascites, and liver dysfunction in polycystic liver disease. The diagnosis can be reliably established with current imaging techniques, especially magnetic resonance imaging. The treatment is aimed at decompressing the congested liver by relieving the obstruction of the intrahepatic inferior vena cava and, in the case of thrombosis of the hepatic veins, by a portosystemic shunt.

Key Words: Polycystic liver disease, inferior vena cava compression, Budd-Chiari syndrome, hepatic resection, portosystemic shunt

Polycystic liver disease (PLD) is a disorder characterized by multiple cystic lesions of the liver parenchyma (1–4) that develop by progressive dilation of biliary microhamartomas (5–7). The vast majority of patients with PLD have associated autosomal dominant polycystic kidney disease (ADPKD). Although patients with PLD often remain asymptomatic, a small proportion may develop symptoms, usually from large dominant cysts or massive organ enlargement by extensive cystic disease. In either case, the symptoms may be caused by abdominal distention or by the extrinsic compression of structures such as the bile ducts (8–12). The hepatic cysts by themselves never cause hepatic failure. In fact, quantitative assessments of hepatic parenchymal and cystic volumes in patients with severe PLD indicate that parenchymal volumes are preserved (13). Hepatic metabolic tests are essentially normal (14). Congenital hepatic fibrosis with portal hypertension has been observed in a small number of families, but its transmission in these families does not occur in an autosomal dominant pattern, suggesting the coexistence of modifying alleles or genes (15–17).

The purpose of this report is to describe the development of hepatic venous outflow obstruction (HVVO) in PLD and the value of magnetic resonance imaging (MRI) in making the diagnosis of this complication. Only a few case reports of HVVO complicating PLD have been published (18–22). Because we have recognized this complication with increasing frequency in our practice, we believe that the description of these cases will increase the awareness of physicians caring for patients with ADPKD and will help in the recognition of this syndrome.

PATIENTS AND METHODS

Between July 1985 and February 1994, 37 patients with severe, symptomatic PLD were evaluated at the Mayo Clinic and treated by either liver resection and cyst fenestration (36 patients) or by a side-to-side portocaval shunt (1 patient). Preoperatively, four patients had severe ascites, marked
narrowing of the intrahepatic inferior vena cava (IVC) demonstrated by MRI or inferior vena cavogram, and HVOO. Cases from the literature were identified through a Medline search of English, French, Spanish, and German language articles.

CASE REPORTS

Patient 1

A 53-year-old white woman with ADPKD and moderately severe renal insufficiency was referred to the Mayo Clinic in January 1992 for the treatment of severe PLD and ascites. She had noted a gradual increase in abdominal girth over several years and progressive ascites over 6 to 12 months associated with fatigue, exertional dyspnea, and emaciation. She had not been pregnant and was postmenopausal without any estrogen supplementation. Examination confirmed massive hepatomegaly with tense ascites associated with umbilical herniation and uterine prolapse. Liver function tests were entirely normal (Table 1) except for slight prolongation of the prothrombin time to 13.7 s, which was corrected with vitamin K supplementation. Computed tomography (CT) and ultrasound scans of the abdomen confirmed massive polycystic disease of the liver and kidneys with ascites. The massive PLD distorted the liver and vascular planes to such a degree that Doppler evaluation of the portal and hepatic veins did not provide any valuable information. MRI examination of the liver demonstrated a patent main and right portal system and patent hepatic veins but narrowing of the IVC near its confluence with the hepatic veins, probably from extrinsic compression (Figure 1). The patient underwent an extended left hepatectomy and partial excision and fenestration of several cysts in the right lobe and the interlobar plane. After the surgery, the IVC was found to be patent and wider than on the preoperative MRI examination (Figure 2), the patient's symptoms improved, and her ascites resolved (Figure 3). The liver function tests all remained in the normal range.

Patient 2

A 61-year-old white man with ADPKD and ESRD on hemodialysis since 1988 was referred to the Mayo Clinic in December 1993 for the treatment of severe PLD and ascites. He had undergone bilateral nephrectomy in July 1993 in preparation for renal transplantation. Two months after this procedure, he developed progressive ascites with symptoms of early satiety, abdominal distention, heartburn, and orthopnea.

TABLE 1. Laboratory parameters at the time of diagnosis of HVOO

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Alkaline Phosphatase (U/L)</th>
<th>Aspartate Aminotransferase (U/L)</th>
<th>Bilirubin (mg/dL)</th>
<th>Prothrombin Time (s)</th>
<th>Albumin (g/dL)</th>
<th>Cholesterol (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>155</td>
<td>13</td>
<td>0.3</td>
<td>13.7</td>
<td>3.4</td>
<td>134</td>
</tr>
<tr>
<td>2</td>
<td>315</td>
<td>12</td>
<td>0.6</td>
<td>10.8</td>
<td>4.3</td>
<td>145</td>
</tr>
<tr>
<td>3</td>
<td>139</td>
<td>14</td>
<td>0.4</td>
<td>9.9</td>
<td>2.2</td>
<td>130</td>
</tr>
<tr>
<td>4</td>
<td>2,731</td>
<td>105</td>
<td>5.3</td>
<td>11.0</td>
<td>2.6</td>
<td>—</td>
</tr>
<tr>
<td>Normal Range</td>
<td>84–309</td>
<td>12–31</td>
<td>0.1–1.1</td>
<td>8.4–12.0</td>
<td>3.5–5.0</td>
<td>—</td>
</tr>
</tbody>
</table>
HVOO in ADPKD

Multiple large-volume paracenteses were required for symptomatic relief. Examination confirmed the presence of a large polycystic liver with tense ascites and an umbilical hernia. His liver tests were normal except for a minimal elevation of the serum alkaline phosphatase (Table 1). MRI of the abdomen demonstrated marked narrowing of the intrahepatic IVC, probably by extrinsic compression (Figure 1). The portal and hepatic veins were distorted but patent. The patient underwent surgery to relieve HVOO by resection of segments II to IV of the left lobe of the liver and partial excision and fenestration of multiple cysts in the remaining liver parenchyma. After surgery, the IVC was found to be patent and wider than on the preoperative MRI examination (Figure 4). His postoperative course was complicated by a biliary fistula, which required drainage for 7 wk. His abdominal girth and ascites resolved after surgery.

Patient 3

A 58-year-old white woman on hemodialysis for ESRD from ADPKD was referred to the Mayo Clinic in May 1993 for the treatment of severe PLD and ascites. The presence of liver cysts was diagnosed in 1980, and she had developed progressive ascites requiring multiple paracenteses since December 1991. She had symptoms of abdominal discomfort, fatigue, and lower extremity edema and pain but had maintained her appetite. She had three prior pregnancies and was postmenopausal for 8 yr. She had not received any estrogen supplementation. Examination confirmed the presence of hepatomegaly, marked ascites, and emaciation with lower extremity and sacral edema. Liver tests were all normal (Table 1). A CT scan of the abdomen confirmed the presence of ascites and cystic disease of the liver, pancreas, and kidneys. MRI examination of the liver demonstrated a patent portal vein with antegrade flow but marked narrowing of the intrahepatic IVC at the level of its confluence with the hepatic veins, probably by extrinsic compression (Figure 1). The patient underwent surgery to resect the left
A 73-year-old white woman with ADPKD and autosomal PLD presented to the Mayo Clinic in 1984 because of a family history of ADPKD, epigastric fullness, intermittent right flank pain, and gross hematuria. She developed progressive renal failure requiring hemodialysis in 1990. She underwent bilateral nephroureterectomy in March 1990 because of persistent gross hematuria. In January 1993, she had a cadaveric transplant, after which she was maintained on a standard triple immunosuppressive regimen consisting of cyclosporine, azathioprine, and prednisone. Her renal allograft function gradually improved over several weeks, with a drop in the serum creatinine to a baseline of 1.1 mg/dL. Her liver tests were entirely normal in 1984 and remained in this range, with the exception of a transient slight elevation of alkaline phosphatase to 492 U/L (normal range, 119 to 309 U/L) in March 1990 before transplantation. In the first 6 months posttransplant, however, there was a progressive and asymptomatic rise of alkaline phosphatase to over 2,000 U/L, with a total bilirubin of 3.9 mg/dL (normal, 0.1 to 1.1 mg/dL) and a direct bilirubin of 2.1 mg/dL (normal, 0 to 0.3 mg/dL). The serum aminotransferases also rose over the first 4 wk posttransplant to two- to threefold that of normal.

In June 1993, she noted progressive abdominal bloating, abdominal pain, low-grade fever, and fatigue. Ascites was noted on examination, and cultures of blood and abdominal fluid were negative. A liver biopsy was nondiagnostic but showed possible fibrosis around hepatic venules. An endoscopic retrograde cholangiopancreatography demonstrated mild ductal abnormalities compatible with extrinsic compression by PLD. An abdominal CT showed enlargement of the caudate lobe and IVC narrowing in the upper intrahepatic portion (Figure 5). An inferior vena cavogram and hepatic venogram were performed (Figure 5) and demonstrated irregularity of the intrahepatic IVC wall, compatible with thrombus and marked stenosis of two right hepatic veins at the caval junction. The patient underwent a side-to-side portocaval shunt and was noted intraoperatively to have an elevated portal pressure exceeding 26 mm Hg, which fell to 17 mm Hg after the procedure. She made an uneventful postoperative recovery, except for a transient episode of mild encephalopathy with a blood ammonia level of 90 mg/dL associated with fever of undetermined origin. This resolved completely with empiric antibiotic therapy. Her ascites and symptoms of abdominal distention improved. Six months later, alkaline phosphatase and bilirubin levels had dropped to 719 U/L and 1.5 mg/dL, respectively, and aminotransferases were normal.

DISCUSSION

Six previous cases of HVOO complicating PLD have been reported (18–22). The clinical features of those patients and those of the four patients in this report are summarized in Table 2. Eight of the 10 patients were women, and all but one had coexisting polycystic kidney disease. Severe ascites was the presenting feature in every case. Three patients had moderate-to-advanced renal insufficiency, four patients were on hemodialysis, and one had received a renal allograft. Possible predisposing factors were identified in seven patients. Three patients had a recent history of bilateral nephrectomy. The development of HVOO after bilateral nephrectomy has been attributed to the possible hemodynamic effect of spatial changes caused by the removal of large polycystic kidneys (21). All of the patients had extrinsic compression of the intrahepatic IVC and hepatic veins by cysts, and four had a superimposed thrombosis of the IVC and/or hepatic veins. One of the four patients with a superimposed thrombosis had thrombocytosis and an elevated plasma fibrinogen level. In addition, these four patients may have had a hypercoagulable state associated with abdominal surgery and, in one case, the administration of cyclosporine (23,24). The outcome in these
HVOO in ADPKD

Figure 5. CT scans of the abdomen (A to C) in Patient 4, demonstrating marked extrinsic compression of the intrahepatic IVC (A, arrow), ascites (A, arrowhead), and mild dilation of intrahepatic bile ducts. Inferior vena cavogram (D) and hepatic venograms (E and F) demonstrating an irregularity along the right wall of the IVC related to old thrombus (D, arrows), a marked stenosis of a right-sided hepatic vein secondary to old thrombus (E, arrow), and a stenotic area of the superior right hepatic vein at the junction with the cava with a 10 mm Hg pressure gradient (F, arrow).

patients was worse than that of the patients without thrombosis. One patient treated by a portocaval shunt recovered, with the disappearance of the ascites, whereas the remaining three patients died. Five of the six patients without proven thrombotic occlusion of the hepatic veins were initially treated with alcohol sclerosis (one patient), surgical fenestration (one patient), or combined hepatic resection and cyst fenestration (three patients). These five patients had resolution of HVOO, although the patient treated by surgical fenestration required a partial hepatic resection because of recurrence of the ascites.

HVOO is an uncommon condition characterized by hepatomegaly, abdominal pain, and ascites (25-28). Causes of HVOO include hepatic vein thrombosis (Budd-Chiari syndrome), cardiac disease (constrictive pericarditis), congenital webs of the IVC, and veno-occlusive disease (29). Hepatic vein thrombosis is associated with hypercoagulable states such as pregnancy, use of oral contraceptives, polycythemia vera, paroxysmal nocturnal hemoglobinuria, and myeloproliferative disorders. PLD is not commonly recognized as a cause of HVOO, although it was listed by Wang et al. (27) as a cause of Budd-Chiari syndrome in 1 of their 100 patients.

The presentation of HVOO can be insidious, usually in patients with an idiopathic membranous obstruction of the IVC, or acute, usually in patients with thrombotic occlusions. Both types of presentations are possible in patients with PLD, as seen in our patients and in the review of the literature. The most common manifestation of HVOO is ascites (25-28). Ascites was seen in all of our patients, as well as in those from the literature. Hepatomegaly and abdominal pain are also very common but are less likely to suggest the diagnosis of hepatic outflow obstruction in the presence of massive PLD. Dilated thoracoabdominal collateral veins are very common and may be helpful in the diagnosis. Standard liver tests may be normal or nonspecific and are therefore of limited value. Liver biopsy shows centrilobular congestion in acute cases, but this may be less prominent in chronic cases (26) and probably explains the nondiagnostic appearance of the liver biopsy in our Patient 4.

HVOO has likely been underrecognized (28). Patients with intractable ascites and HVOO may be incorrectly diagnosed as having cirrhosis if a liver biopsy is not performed. It is possible that some of the patients with fatal hepatic polycystic disease or portal hypertension of undetermined cause in patients with PLD (30-32) might have had HVOO. The diagnosis of HVOO can be reliably established with current noninvasive imaging techniques. Most patients with severe PLD have a CT scan of the abdomen. If HVOO is suspected, MRI should be performed for further evaluation. MRI with spin echo and gradient echo images is particularly useful in establishing the patency and direction of flow in the IVC and hepatic and portal veins and in detecting abnormal collateral veins. Because of the markedly distorted anatomy of the polycystic liver, this information is of great assistance in the planning of treatment or at the time of surgery. If thrombosis in the IVC or hepatic veins is suspected by CT or MRI, IVC and hepatic vein catheterization, measurements of pressure gradients, inferior vena cavogram, and hepatic venograms should be performed.

HVOO is often fatal and requires aggressive surgical decompression of the congested liver (25-28). The damage to the liver results primarily from the marked increase in venous pressure. In the absence of hepatic vein thrombosis, the treatment should be directed at...
<table>
<thead>
<tr>
<th>Author</th>
<th>Age (yr)/ Gender</th>
<th>PKD Renal Function</th>
<th>Predisposing Factor</th>
<th>Methods of Diagnosis</th>
<th>Thrombosis</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>Yaqoob et al., 1990 (18)</td>
<td>49/M</td>
<td>Yes 7.1°</td>
<td>None</td>
<td>CT</td>
<td>No</td>
<td>Recovery after alcohol sclerosis</td>
</tr>
<tr>
<td>Bhupalan et al., 1992 (19)</td>
<td>47/F</td>
<td>Yes Normal</td>
<td>Hysterectomy, thrombocytosis</td>
<td>Cavogram</td>
<td>Yes</td>
<td>Liver transplantation, death</td>
</tr>
<tr>
<td>Ambrosi et al., 1992 (20)</td>
<td>53/F</td>
<td>Yes 1.7°</td>
<td>Operative interruption of 2 hepatic veins</td>
<td>Autopsy</td>
<td>Yes</td>
<td>Death</td>
</tr>
<tr>
<td>Clive et al., 1993 (21)</td>
<td>39/F</td>
<td>Yes Hemodialysis</td>
<td>Bilateral nephrectomy</td>
<td>CT, cavogram</td>
<td>Yes</td>
<td>Death</td>
</tr>
<tr>
<td></td>
<td>50/F</td>
<td>Yes Hemodialysis</td>
<td>Bilateral nephrectomy</td>
<td>Cavogram</td>
<td>No</td>
<td>Death</td>
</tr>
<tr>
<td>Johnstone et al., 1993 (22)</td>
<td>63/F</td>
<td>No Normal</td>
<td>Choangitis</td>
<td>CT, Doppler ultrasound</td>
<td>No</td>
<td>Recurrence after fenestration, recovery after resection/fenestration</td>
</tr>
<tr>
<td>This Series</td>
<td>53/F</td>
<td>Yes 4.5°</td>
<td>None</td>
<td>CT, MR</td>
<td>No</td>
<td>Recovery after resection fenestration</td>
</tr>
<tr>
<td></td>
<td>61/M</td>
<td>Yes Hemodialysis</td>
<td>Bilateral nephrectomy</td>
<td>CT, MR</td>
<td>No</td>
<td>Recovery after resection fenestration</td>
</tr>
<tr>
<td></td>
<td>58/F</td>
<td>Yes Hemodialysis</td>
<td>None</td>
<td>CT, MR</td>
<td>No</td>
<td>Recovery after resection fenestration</td>
</tr>
<tr>
<td></td>
<td>74/F</td>
<td>Yes 1.1°</td>
<td>Renal transplantation, cyclosporine</td>
<td>CT, cavogram</td>
<td>Yes</td>
<td>Recovery after portocaval shunt</td>
</tr>
</tbody>
</table>

a Serum creatinine in milligrams per deciliter.

relieving the obstruction of the intrahepatic IVC and hepatic veins. If the obstruction is caused by a large dominant cyst, this may be accomplished by alcohol sclerosis (33–37) or laparoscopic fenestration (38–40). If the obstruction is caused by an enlarged cystic liver without dominant cysts, then combined hepatic resection and cyst fenestration is the only practical alternative. In the presence of hepatic vein thrombosis where reestablishing hepatic venous flow is precluded, a nonselective portosystemic shunt with or without decompression of the IVC should be performed (28) or liver transplantation should be considered (41).

REFERENCES


