Liver Transplant in Budd-Chiari Syndrome: A Single-center Experience in Saudi Arabia

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Abstract

Objectives: If they do not respond to other treatments, patients with Budd-Chiari syndrome are potential candidates for a liver transplant. Timing for transplant is controversial; however, before other systems deteriorate, early intervention in relatively stable patient may improve the outcome and survival of these patients.

Materials and Methods: Six patients (2 women and 4 men) had Budd-Chiari syndrome (1.2%) among 475 patients who had undergone a liver transplant at our center between 2001 and 2012. Imaging modalities including duplex ultrasound, abdominal computed tomography angiography, and hematologic evaluation were part of our routine diagnostic work-up. Although we perform mostly living-donor liver transplants, these patients received a liver transplant from a deceased donor, because there was not enough evidence to justify a living-donor liver transplant. We thought that not replacing the caval vein might negatively influence the outcome. Postoperatively, these recipients were started on a heparin infusion and triple therapy immunosuppression; only then was warfarin introduced as long-term anticoagulant.

Results: Two patients died, 1 from uncontrollable bleeding and disseminated intravascular coagulopathy, and the other died in the intensive care unit after 5 months because of multiorgan failure and sepsis. One patient had portal vein thrombosis 9 months after the liver transplant; the other patient needed a liver retransplant after 5 years owing to liver failure, secondary to chronic rejection. Graft survival rate was 75%, and patient survival rate was 66.6%.

Conclusions: This is the first article from Saudi Arabia to describe the outcome of a liver transplant in this subgroup of patients with Budd-Chiari syndrome. Treatment of Budd-Chiari syndrome follows a therapeutic algorithm that should start with anticoagulation and may end up with liver transplant; however, it should be considered early if other treatments fail.

Key words: Budd-Chiari syndrome, Liver transplant, Saudi Arabia

Introduction

Budd-Chiari syndrome (BCS) can lead to liver cirrhosis secondary to centrilobular congestion and hepatic necrosis. Veno-occlusive disease (more accurately “hepatic sinusoidal syndrome,”) which clinically resembles BCS yet is pathologically different (in the former, the occlusion occurs at the level of hepatic sinusoids and hepatic venules, rather than the hepatic veins, as is the case in BCS). Another disorder that can present clinically as BCS is “right-side congestive heart disease,” which also leads to congestive hepatopathy. Budd-Chiari syndrome can be “primary” (if the site of obstruction is located inside the lumen of the veins), while it is considered “secondary” (if the cause of obstruction is extra luminal). The cause of BCS can be identified in 70% to 80% of cases including myeloproliferative disease in 45% to 50%, oral contraceptive use (20%), malignancy (10%), infection (10%), and hypercoagulable state (10%); in approximately 20% of cases the causes are...
idiopathic. The syndrome is rare and more common in women in their 30s and 40s. The clinical presentation of BCS includes ascites (84%), hepatomegaly (76%), and pain (61%).

Managing BCS consists of directing therapy against the underlying hematologic disorder, control of ascites, anticoagulation, and, in selected patients, relief of elevated hepatic sinusoidal pressure by creating a portosystemic shunt that can be performed either surgically or by placing a Transjugular Intrahepatic Portosystemic Shunts (TIPS). This is the first article from Saudi Arabia that describes outcomes of liver transplants in liver transplant recipients with BCS.

**Materials and Methods**

Data for 475 patients (Table 1), who underwent a liver transplant between March 2001 and October 2012, were analyzed. Six patients (1.2%) with BCS underwent a liver transplant, 2 women 4 men (mean age, 36 y). Extensive diagnostic work-up such as imaging modalities (including computed tomography angiography) and hematologic evaluation (including protein C, protein S, antithrombin 3, factor V Leiden mutation) were part of the routine work-up. The cause of BCS in our patients was myeloproliferative disease (4 patients), congenital hepatic fibrosis (1 patient), and idiopathic (1 patient); all had hepatic vein obstruction and 1 had associated portal vein and retro-hepatic inferior vena cava thrombosis.

Regarding the clinical course of the disease, it was chronic in 5 cases (which eventually developed cirrhosis) and subacute in 1 case. Mean time between the onset of the syndrome and the liver transplant was 3.14 years.

Although our center is driven mainly by living-donor liver transplants, these patients underwent a liver transplant from deceased donors because we could not find enough evidence in literature to justify using living-donor liver transplant. We thought that not replacing the caval vein might negatively affect outcomes. All patients received full liver from deceased donors, the native liver was resected with retro-hepatic inferior vena cava; vascular reconstruction was done in standard fashion and sequence, supra-hepatic inferior vena cava, infra-hepatic inferior vena cava then portal vein; after reperfusion the arterial anastomosis, we performed a duct-to-duct biliary reconstruction. Those recipients postoperatively began a therapeutic heparin infusion and triple therapy immunosuppression (tacrolimus, mycophenolate mofetil, and steroids) according to our protocol, and later on warfarin was introduced as long-term anticoagulant therapy.

**Results**

Two patients died—one from uncontrolled bleeding and disseminated intravascular coagulation, and the second from multiorgan failure and sepsis in the intensive care unit 5 months after the liver transplant. One patient had portal vein thrombosis 9 months after the liver transplant; and 1 patient required a liver retransplant 5 years after the liver transplant owing to...

<table>
<thead>
<tr>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
<th>Case 4</th>
<th>Case 5</th>
<th>Case 6</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Date of transplant</strong></td>
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<td>2008</td>
<td>2009</td>
<td>2009</td>
<td>2011</td>
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<tr>
<td><strong>Age (y)</strong></td>
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<td>35</td>
<td>40</td>
<td>27</td>
<td>49</td>
</tr>
<tr>
<td><strong>BMI</strong></td>
<td>20</td>
<td>17</td>
<td>22</td>
<td>24</td>
<td>29</td>
</tr>
<tr>
<td><strong>CPS</strong></td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td><strong>Cause</strong></td>
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<td>no</td>
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<tr>
<td><strong>Disease period (y)</strong></td>
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<td>6</td>
<td>2</td>
<td>3</td>
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<tr>
<td><strong>Portosystemic shunt</strong></td>
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<td>TIPS</td>
<td>NO</td>
<td>TIPS</td>
<td>NO</td>
</tr>
<tr>
<td><strong>Vessel Occlusion type</strong></td>
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<td>All HV</td>
<td>All HV</td>
<td>All HV</td>
<td>All HV</td>
</tr>
<tr>
<td><strong>Follow-up in Dec 2012</strong></td>
<td>Chronic rejection</td>
<td>Death 5 months after transplant by sepsis and MOF</td>
<td>Doing well</td>
<td>Doing well</td>
<td>PVT 9 months posttransplant</td>
</tr>
</tbody>
</table>

**Abbreviations:** BMI, body mass index; CHF, congenital hepatic fibrosis; CPS, Child-Pugh score; DIC, disseminated intravascular coagulopathy; Disease period, time between onset of clinical symptoms and liver transplant; ESRD, end-stage renal disease; HV, hepatic vein; IVC, inferior vena cava; JAK2, Janus kinase 2 gene; LHV, left hepatic vein; MELD, model for end-stage liver disease; MCR, multiorgan failure; MPD, myeloproliferative disorder; NO, none; PV, portal vein; PVT, portal vein thrombosis; RHV, right hepatic vein; TIPS, transjugular intrahepatic portosystemic shunt
liver failure, which was secondary to chronic rejection that resulted in graft failure. Mortality occurred in patients with renal failure, previous abdominal surgery, and low body mass index. The graft survival rate was 75%, and patient survival rate was 66.6%. The mean follow-up was 3.6 years.

Discussion

In a multicenter European study that included 248 patient with BCS who underwent a liver transplant between 1988 and 1999, overall actuarial survival was 76% at 1 year, 71% at 5 years, and 68% at 10 years. The cause of mortality was infection in 47% of cases, graft failure in 18%, the only predictor of mortality in their study was renal dysfunction. The clinical presentation and severity of signs and symptoms depend on the acuteness and rapidity of the outflow obstruction, forming formation of collateral and revascularization of thrombosed veins; however, 5% of the patients were asymptomatic. The disease can be clinically classified as follows: acute disease (severe, rapid progression of the illness, with congestion and necrosis occurring in a few days to 2 months requiring emergent surgery); subacute disease (progression from 2 to 6 months with little necrosis and an absence of cirrhosis); and chronic disease (slowly progressive disease resulting in severe fibrosis or cirrhosis). Rarely, some patients present with fulminant hepatic failure. Those patients are best served by liver transplant. Patients with acute BCS are best managed by TIPS bridging therapy to liver transplant because they are at a high risk for surgical shunts. However, portosystemic surgical shunts are given to patients with a subacute presentation with mild ascites and limited liver dysfunction, especially when the underlying hematologic disease has a good long-term prognosis. In chronic Budd-Chiari with cirrhosis, a liver transplant may be the best option. Transjugular intrahepatic portosystemic shunts have a few advantages over surgical shunts: TIPS is less invasive and has lower morbidity and mortality rates; TIPS does not complicate future liver transplant (on the other hand, surgical shunts usually must be dismantled during liver transplant to avoid an adverse effect on portal hemodynamics); TIPS allows one to bypass intrahepatic caval stenosis, compressing the inferior vena cava with an enlarged caudate lobe increases infrahepatic caval pressure, and decreases the pressure gradient between the portal vein and the infrahepatic cava to less than 10 mm Hg, ensuring that the surgical portosystemic shunt will not function; and applying TIPS may be feasible in most patients with BCS (albeit, TIPS may be technically challenging). The shunt may be constructed through the suprarehepatic inferior vena cava when no hepatic vein stump is available. In selected patients with BCS uncontrolled by medical therapy, TIPS is effective and may be associated with long-term survival. However, until more data are available, TIPS may be an option for patients with acute Budd-Chiari unresponsive to medical therapy, as a bridge to liver transplant, and in patients with subacute BCS who are not surgical candidates. Liver transplant remains the treatment of choice in patients with advanced cirrhosis and poor liver function, as well as in cases of fulminant BCS.

Generally speaking, managing BCS follows a therapeutic algorithm that should start with anticoagulation and might lead to liver transplant; this should be considered in cases of fulminant hepatic failure and failure of other treatment modalities. Also, one should consider liver transplant from a living donor in light of successful outcomes at some centers.

References