

Living-donor Liver Transplant in 3 Patients With Budd-Chiari Syndrome: Case Report

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Abstract

Budd-Chiari syndrome is a rare but life-threatening disorder characterized by obstruction of the hepatic venous outflow. Treatment depends on the underlying cause, the location, and extent of the obstruction, and the functional capacity of the liver. A stepwise therapeutic approach is commonly accepted. When all other therapy options are unsuccessful, or in case of end-stage liver disease, transplant should be considered. We present case reports of 3 patients with Budd-Chiari syndrome who underwent living-donor liver transplant. Characteristic features of Budd-Chiari syndrome, diagnostic and therapeutic interventions, complications, and overall outcomes are discussed. We believe that when a deceased donor graft is unavailable, a living-donor liver transplant can be a safe option for patients with end-stage liver disease associated with Budd-Chiari syndrome.

Key words: *Budd-Chiari syndrome, End-stage liver disease, Liver transplant, Living donors*

Introduction

Budd-Chiari syndrome (BCS) is characterized by obstruction of the hepatic venous outflow. The venous obstruction can be located anywhere from the intrahepatic venules up to the junction of the inferior vena cava with the right atrium. It is rare,

but life-threatening, if left untreated. The clinical symptoms were first described by Budd in 1845; Chiari reported on the histopathology of the syndrome approximately 50 years later.^{1, 2} Treatment for BCS should be in a stepwise manner. Medical supportive treatment with anticoagulants is applied as an initial therapy. When this approach fails, more-invasive therapeutic options should be considered.³ Percutaneous transluminal angioplasty and insertion of a transjugular, intrahepatic, portosystemic shunt may be effective, depending on the extent of the obstruction. Surgical portocaval shunts also can be used. For patients with end-stage liver disease, liver transplant must be considered. Living-donor liver transplant might be a safe option, especially in countries where deceased donor grafts are of limited availability. Here, 3 cases of living-donor liver transplant for treatment of end-stage liver disease associated with BCS are presented.

Case 1

A 34-year-old man who received a diagnosis of BCS 3 months earlier was referred to our hospital for treatment of hepatic encephalopathy. Despite medical and supportive treatment, his clinical situation deteriorated progressively. After admission to our clinic, physical examination and laboratory studies revealed end-stage liver disease with high Child-Pugh and Model for End-Stage Liver Disease (MELD) scores (13 and 23). Doppler ultrasound revealed that the right and middle hepatic veins were completely obstructed (Figure 1). Hepatofugal flow was observed in the portal vein, which had a diameter of 11 mm. Computed tomography showed right lobe atrophy and left lobe hypertrophy with degenerative nodularity in the liver parenchyma, consistent with cirrhosis (Figure 2).

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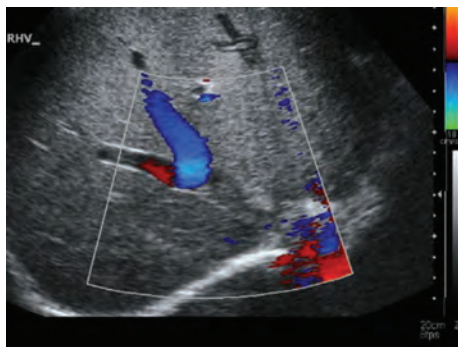


Figure 1. Patient 1. Doppler ultrasound results showing complete obstruction of the right and middle hepatic veins.

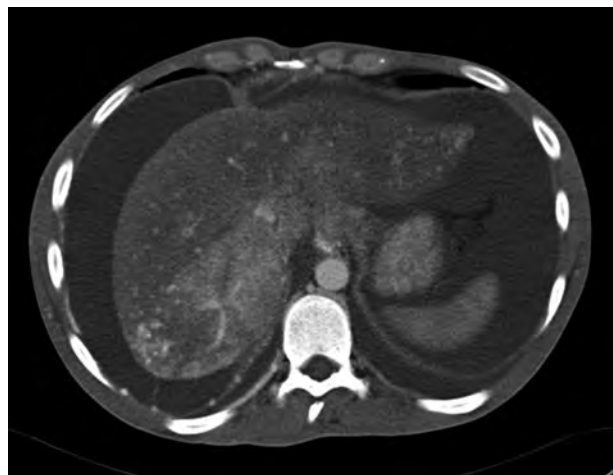


Figure 2. Patient 1. Computed tomography results showing right lobe atrophy and left lobe hypertrophy with degenerative nodularity in the parenchyma of the liver.

Case 2

A 27-year-old woman was admitted to our clinic with acute onset of jaundice, abdominal pain, and ascites. Her total bilirubin level was 59.8 mmol/L (3.5 mg/dL), the international normalized ratio (INR) was 1.63, the albumin level was 32 g/L (3.2 g/dL), and alanine transaminase (ALT) and aspartate aminotransferase (AST) levels were 85 U/L and 95 U/L. The Child-Pugh score was 8, and the MELD score was 14. Ultrasound screening showed hepatofugal flow in the portal vein, which had a diameter of 9 mm. Computed tomography revealed complete obstruction of the right and middle hepatic veins and hepatic enlargement with a heterogeneous parenchyma in the absence of nodularity.

Case 3

A 25-year-old woman, who received a diagnosis of BCS 1 month earlier, was admitted to our clinic with severe

ascites. Physical examination, laboratory studies, and ultrasound resulted in a diagnosis of BCS, with a Child-Pugh score of 7, and a MELD score of 6. Her total bilirubin level was 59.8 mmol/L (3.5 mg/dL), the INR was 1.1, the albumin level was 42 g/L (4.2 g/dL), and ALT and AST levels were 29 U/L and 34 U/L. Computed tomography showed complete thrombosis in the middle and right hepatic veins with right posterior and left lateral lobular atrophy.

To determine the cause of these cases, protein C and S activities were assessed, and mutational gene analysis was performed (Table 1). Bone marrow biopsies revealed myeloproliferative disorders (MPD) in all patients. Relatives of the patients volunteered for right lobe liver donation. After work-up of the donors, the recipients underwent surgery for living-donor liver transplant (LDLT). Standard surgical procedures were performed. The postoperative period was uneventful for the first and the third recipients, who were discharged from the hospital on postoperative days 14 and 13. These patients were prescribed tacrolimus and prednisolone for immunosuppression and acetylsalicylic acid for anticoagulation. The second patient experienced a bile leakage from the anastomosis of bile ducts (duct-to-duct type) and underwent a Roux-en-Y hepaticojejunostomy 16 days after transplant. She was discharged from the hospital 12 days after the second operation and was prescribed the same drug regimen. Histopathologic examination of the diseased livers revealed excessive parenchymal congestion, sinusoidal degeneration, and widespread fresh thromboses (Figure 3). In addition, nodular fibrosis, a marker of cirrhosis, was found in the first patient. All donors were discharged uneventfully.

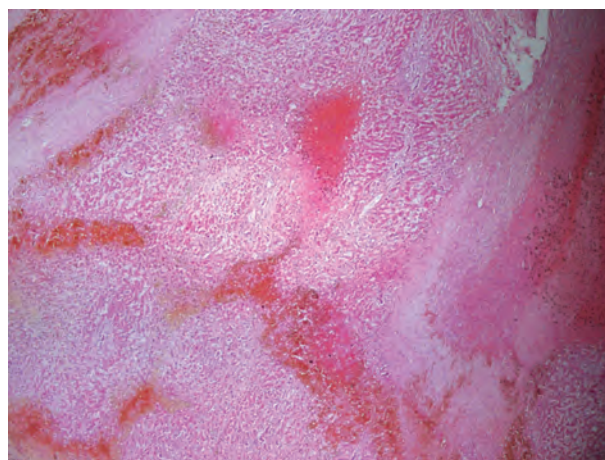


Figure 3. Patients 1 to 3. Obliteration of hepatic veins in the wall by fibrous tissue and thrombus in the lumen, with atrophy of zone 2 and 3 hepatocytes (hematoxylin and eosin stain, $\times 40$).

Table 1. Recipient and donor characteristics.

	Case 1	Case 2	Case 3
Recipient			
Age/sex	34/Male	27/Female	25/Female
Height/weight/BMI	176 cm/73 kg/23.6	159 cm/57 kg/22.5	163 cm/52 kg/19.6
Blood type	B Rh+	A Rh+	A Rh+
Child-Pugh score/MELD score	13/23	8/14	7/6
HBsAg/anti-HBs/anti-HCV	-/-/-	-/-/-	-/+/-
JAK2 gene (v617f) mutation	+	-	-
Prothrombin (G20210A) mutation	+	-	-
Factor V Leiden mutation	-	-	-
BCR-ABL gene mutation	-	-	-
Protein C activity	23%	40%	38%
Protein S activity	78%	82%	80%
Bone marrow biopsy	MPD	MPD	MPD
Weight of recovered liver	1087 g	1322 g	1124 g
Donor			
Relation	Father	Father	Cousin
Age	53 years	50 years	30 years
Height/weight/BMI	169 cm/74 kg/26.4	179 cm/92 kg/28.8	188 cm/92 kg/26
Blood type	B Rh+	A Rh+	A Rh+
Weight of graft (right lobe)	1047 g	964 g	982 g

Abbreviations: Anti-HBs, antibody to hepatitis B surface antigen; anti-HCV, antibody to hepatitis C virus; BCR-ABL, breakpoint cluster region-V-abl Abelson murine leukemia viral oncogene homolog 1; BMI, body mass index; HBsAg, surface antigen of the hepatitis B virus; JAK2, Janus kinase 2; MELD, Model for End-Stage Liver Disease; MPD, myeloproliferative disorders

Currently, after follow-up for 30, 18, and 6 months, the 3 patients are doing well and show normal results of their liver function tests.

Discussion

Budd-Chiari syndrome can be classified as primary if an endoluminal venous lesion, such as thrombosis or web, is present and secondary if the venous obstruction is caused by an extraluminal pathology, such as external invasion or compression by a nearby tumor.⁴ Thrombosis is the most frequent cause of venous obstruction, and this is mainly caused by MPD; dysfunction of the coagulation cascade, such as factor V Leiden or prothrombin (factor II) mutation; protein C or S deficiency; or other hypercoagulable conditions as malignancy or that induced by oral contraceptive use.⁵⁻⁷ The typical presentation is generally a triad of abdominal pain, ascites, and hepatomegaly, and it may vary significantly, from the absence of symptoms to severe liver failure.

During progression of the disease, portal hypertension frequently develops, such that most of the patients develop splenomegaly and gastroesophageal varices. The severity of the disease depends on the extent of thrombosis.⁸ Intrahepatic venous congestion may result in chronic ischemia, necrosis, fibrosis, and finally cirrhosis.⁹ Budd-Chiari syndrome should be suspected in patients with painful hepatomegaly, ascites, and relatively normal

liver function tests. Physical examination and laboratory studies are not specific for the disease. Noninvasive radiology imaging techniques have high diagnostic value. Doppler ultrasonography must be the initial choice because of its high sensitivity and specificity for determining the obstruction site and venous flow pattern in hepatic veins or the inferior vena cava. Computed tomography and magnetic resonance imaging are also frequently used to support diagnosis. These also provide better visualization of the liver parenchyma as well as any other possible causes of the disease.¹⁰ Hepatic venography is a reference procedure, but recently this invasive technique has been used to measure venous pressure.¹¹ Liver biopsy for histopathologic diagnosis of BCS is rarely used, but it may be performed if there is a suspicion of any other hepatic lesion. Identification of the underlying pathologies for BCS, such as MPD and coagulation cascade dysfunctions, is also important.

Diagnosis of MPD in patients with BCS can be challenging because classic changes in peripheral blood, such as a high level of hemoglobin or platelets, may not be found.¹² An acquired gain-of-function mutation in Janus kinase 2 (JAK2) tyrosine kinase can be demonstrated in the majority of patients with MPD. However, bone marrow biopsy is often required because not all cases of MPD are JAK2 mutation-positive.¹³ It is notable that 2 patients with MPD did not have JAK2 mutation.

Management of patients with BCS remains challenging. For end-stage liver disease, transplant must be considered. Ulrich and associates reported excellent long-term outcomes for 39 patients who underwent orthotopic liver transplant (3 were LDLT) owing to BCS; 5- and 10-year survival rates were 90% and 84%.¹⁴ Many recent reports have been published indicating that LDLT can be performed safely in patients with BCS.¹⁵ We conclude that LDLT can be a safe option for patients with end-stage liver disease associated with BCS, especially in countries in which deceased donor grafts are of limited availability.

References

1. Budd G. *On Diseases of the Liver*. Philadelphia, PA: Lea and Blanchard; 1846.
2. Chiari H. Ueber die selbständige phlebitis obliterans der hauptstämme der venae hepaticae als todesursache. *Beitr Pathol Anat Allg Pathol*. 1899;26:1-18.
3. Plessier A, Sibert A, Consigny Y, et al. Aiming at minimal invasiveness as a therapeutic strategy for Budd-Chiari syndrome. *Hepatology*. 2006;44(5):1308-1316.
4. Janssen HL, Garcia-Pagan JC, Elias E, et al. Budd-Chiari syndrome: a review by an expert panel. *J Hepatol*. 2003;38(3):364-371.
5. Valla D, Casadevall N, Lacombe C, et al. Primary myeloproliferative disorder and hepatic vein thrombosis. A prospective study of erythroid colony formation in vitro in 20 patients with Budd-Chiari syndrome. *Ann Intern Med*. 1985;103(3):329-334.
6. Murad SD, Plessier A, Hernandez-Guerra M, et al. Prospective follow-up study on 163 patients with Budd-Chiari syndrome: Results from the European network for vascular disorders of the liver (EN-VIE). *J Hepatol*. 2007;46:S4.
7. Janssen HL, Meinardi JR, Vleggaar FP, et al. Factor V Leiden mutation, prothrombin gene mutation, and deficiencies in coagulation inhibitors associated with Budd-Chiari syndrome and portal vein thrombosis: results of a case-control study. *Blood*. 2000;96(7):2364-2368.
8. Valla DC. Hepatic vein thrombosis (Budd-Chiari syndrome). *Semin Liver Dis*. 2002;22(1):5-14.
9. Cazals-Hatem D, Vilgrain V, Genin P, et al. Arterial and portal circulation and parenchymal changes in Budd-Chiari syndrome: a study in 17 explanted livers. *Hepatology*. 2003;37(3):510-519.
10. Brancatelli G, Vilgrain V, Federle MP, et al. Budd-Chiari syndrome: spectrum of imaging findings. *AJR Am J Roentgenol*. 2007;188(2):W168-W176.
11. Hoekstra J, Janssen HL. Vascular liver disorders (I): diagnosis, treatment and prognosis of Budd-Chiari syndrome. *Neth J Med*. 2008;66(8):334-339.
12. McNamara C, Juneja S, Wolf M, Grigg A. Portal or hepatic vein thrombosis as the first presentation of a myeloproliferative disorder in patients with normal peripheral blood counts. *Clin Lab Haematol*. 2002;24(4):239-242.
13. Kiladjian JJ, Cervantes F, Leebeek FWG, et al. Role of JAK 2 mutation detection in Budd-Chiari syndrome (BCS) and portal vein thrombosis (PVT) associated to MPD. *Blood*. 2006;16;108:116a-a.
14. Ulrich F, Pratschke J, Neumann U, et al. Eighteen years of liver transplantation experience in patients with advanced Budd-Chiari syndrome. *Liver Transpl*. 2008;14(2):144-150.
15. Choi GS, Park JB, Jung GO, et al. Living donor liver transplantation in Budd-Chiari syndrome: a single-center experience. *Transplant Proc*. 2010;42(3):839-842.