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ORIGINAL ARTICLE

Liver transplantation in patients with Budd-Chiari syndrome

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Abstract Patients with Budd-Chiari syndrome (obstruction of the hepatic veins) and associated hepatic insufficiency may be candidates for orthotopic liver transplantation (OLT). In our series of 405 OLT patients, 3 were transplanted due to Budd-Chiari syndrome (0.7 %). The indication for liver transplantation in these patients was severe hepatic insufficiency (chronic in two and acute in the third one). Morphologic study of the obstructions revealed apparently different causes, including thrombi, membranous webs in hepatic veins, and hydatid cyst compression. The surgical technique employed in these transplantations was similar to that for other etiologies. Due to its implications for the future course of OLT, it is important to determine the exact etiology of Budd-Chiari syndrome in the pretransplant period and to treat the patients with early and long-term anticoagulant therapy to avoid syndrome recurrence.

Key words Budd-Chiari syndrome, liver transplantation · Liver transplantation, Budd-Chiari syndrome

Introduction

Budd-Chiari syndrome (hepatic disorder caused by the obstruction of hepatic veins) is a rare indication for orthotopic liver transplantation (OLT) in most reported series [1, 2, 6]. Whereas OLT is indicated when extensive obstrucion of the hepatic veins causes severe hepatocellular dysfunction in acute or chronic form [1, 6, 8, 9], portosystemic shunting continues to be a valid therapeutic option for patients with ascites and good hepatocellular function [8, 15, 23]. Management of Budd-Chiari syndrome patients presents certain peculiarities with respect to liver transplantation. First, a determination should be made as to which patients are still in condition to be shunted and which should undergo OLT [14, 20, 23]. Second, the need for permanent anticoagulation to avoid recurrence should be determined [6, 11, 21, 23]. Third, the syndrome's underlying etiology (lymphoproliferative processes, paroxymal noctural hemoglobinuria, antithrombin III deficiency, essential thrombocytosis, extrinsic compression, etc.) should be established or it should be classified as idiopathic [9, 11, 15, 16, 20, 22, 24]. This study analyzes our experience in OLT treatment of Budd-Chiari syndrome patients in a series of 405 OLT.

Table 1 Pre-OLT characteristics of the patients [*P/OLT #* patient number/OLT number, *DUR* duration (months) from diagnosis to OLT, *CLIN PRES* clinical presentation, *PT* prothrombin activity (%), *ASC* ascites, *ENC* encephalopathy, *BIL* bilirubin (mg/ml)]

P/OLT #	AGE	SEX	ETIOLOGY	DUR	CLIN PRES	ASC	ENC	BIL	GOT/GPT (IU/l)	PT
1/39	38	Male	– Hydatidosis – Postsurgical	27	Chronic	Yes	No	3.3	240/221	35
2/192	24	Male	Idiopathic membranes?	8	Chronic	No	No	3.2	521/340	46
3/306	14	Male	Idiopathic membranes?	4	Acute	Yes	Yes	7.7	1530/1225	20

Table 2 Technical aspects of OLT and patient and graft evolution (*H-C* Hartmann-Collins preservation solution, *UW* University of Wisconsin preservation solution, *V-V* Bypass veno-venous bypass using extracorporeal bio-pump, *Consumption (u)* hemoderivatives unit consumption, *CAH* chronic active hepatitis caused by C virus)

Case no.	Preservation solution	V-V Bypass	Ischemia time (min) Cold	Warm	Consumption (u) Blood-Plasma-Platelet	Evolution		Follow-up (months)
						Patient	Graft	
1	H-C	Yes	368	52	15 – 26 – 6	Good	Normal	65
2	UW	No	200	50	40 – 20 – 10	Good	CAH	28
3	UW	No	180	58	10 – 22 – 5	Good	Normal	4

Table 3 Histopathologic findings in the hepatectomy specimens (*C-LOB* centrilubular veins, *M. Webs* membranous webs)

#	Parenchymatous lesions			Hepatic veins			
	Necrosis Hemorrhage	Nodular hyperplasia	Fibrosis	Trunk	Proximal	Mid	C-LOB
1	Mild	Diffuse	Yes	M. Webs	M. Webs	Fibrosis	Congestion
2	Moderate	Diffuse	No	M. Webs Thrombus	Normal	Normal	Congestion
3	Severe	No	No	M. Webs Thrombus	Thrombus	Thrombus	Congestion

Patients and methods

Patients

A group of 338 patients underwent a total of 405 liver transplantations between April 1986 and December 1994. Budd-Chiari syndrome was the OLT indication in only 3 of these patients (0.7 %). The pretransplant characteristics of the three patients are given in Table 1. None of them underwent prior portosystemic shunting, and the indication for OLT was established in the presence of severe hepatocellular dysfunction (Table 1). The first case (OLT no. 39) stemmed from a surgical complication after the right hepatic vein had to be ligated in a patient with hepatic hydatidosis in segments VII and VIII. In the second case (OLT no. 192), also chronic, it was not possible to determine the etiology prior to examination of the hepatectomy specimen. In the third patient (OLT no. 306), the syndrome presented in acute form, with a clinical and analytical course resembling a fulminant hepatopathy pattern: upon admission to our hospital, there was 20 % prothrombin activity and factor V less than 20 % with administration of plasma; raised transaminase levels, GOT 9850 IU/l, GPT 3720 IU/l; acute encephalopathy III/IV; ascities and the need for orotracheal intubation.

The diagnosis of the obstruction of hepatic venous return was made using cavography, venography of the efferent hepatic veins, ultrasonography, and liver biopsy (in the second case only). The syndrome's etiology could not be established preoperatively in the last two cases (OLT nos. 192 and 306), and a bone marrow biopsy was performed in both to rule out hematologic disorders as precipitating factors for the syndrome. The three patients tested seronegative for HIV and HBV markers, and only the second patient was positive for anti-HCV antibodies.

Surgical transplant technique and immunosuppression

The surgical technique employed was similar to that described for other transplanted patients [18]. Table 2 shows the ischemia times, preservation solutions, and consumption of hemoderivatives. Immunosuppression consisted of cyclosporin, prednisone, and azathioprine, as reported earlier [17].

The first patient had a clear postsurgery etiology; the other two were anticoagulated starting at 24 h post-transplant with intravenous heparin and later with dicoumarin to keep prothrombin activity at less than 50 %. Outpatient follow-up for these patients, in addition to weekly anticoagulation controls, included ultrasonography of hepatic veins every 3–4 months for the first 2 years or whenever hepatocellular dysfunction was detected.

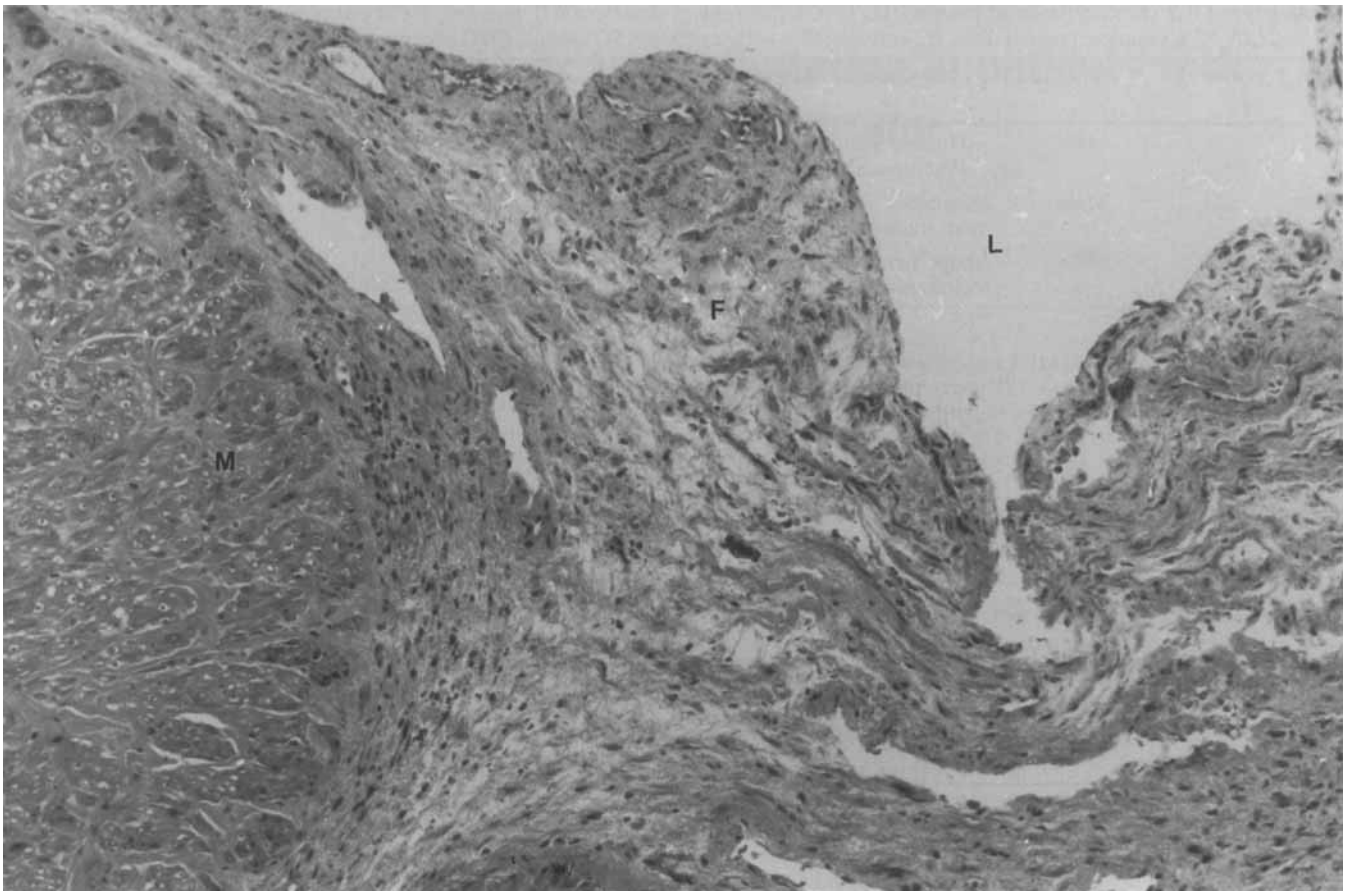

Fig. 1 (Case no. 3) Section of hepatic vein at junction with vena cava. Note intense subendothelial fibrosis *(F)* stenosing the lumen *(L)*. The recent thrombus that completely occluded the lumen was detached and is not seen. Mid-muscle layer *(M)* H & E, × 100

Results

Histopathologic analysis of hepatectomy specimens

The three grafts presented a congested aspect and enlarged size, weighing 1.95, 1.80, and 2.30 kg, respectively. In the first case, the complete hepatectomy specimen displayed a residual hydatic cyst lesion in the right liver lobe measuring 14 cm in diameter near the junction of the hepatic veins with the inferior vena cava. The lumina of the three hepatic veins were filled with fibroconnective tissue as a result of the ligation of the right hepatic vein and the compression of the left hepatic vein. The remaining macroscopin and microscopin characteristics of the grafts are shown in Table 3. Diffuse nodular regenerative hyperplasia was found in two of the patients, and in all three cases thrombi in the hepatic vein trunk were associated with organized fibrous membranes (Fig. 1, 2).

Evolution of the patients, grafts, and use of prophylactic anticoagulation

The three patients are well after follow-ups of 65, 28, and 4 months, respectively. The third patient required surgical intervention 48 h post-transplant due to intra-abdominal bleeding that was resolved with electrocoagulation of some bleeders in the retroperitoneum. Early anticoagulant therapy and thrombocytopenia (< 30,000 platelets per mm^3) were no doubt responsible for this course, as well as for a mild epistaxis on postoperative day 4. None of the patients has suffered recurrence of Budd-Chiari syndrome, and anticoagulation has not triggered any long-term complications. The second patient was a carrier of anti-HCV antibodies and his graft developed chronic active hepatitis displaying low levels of clinical and biochemical expression.

Discussion

Budd-Chiari syndrome is a rare disorder. Prior to the advent of OLT, its surgical treatment consisted of portosystemic shunting by means of portacaval, mesocaval, or mesoatrial shunts [1, 6, 13, 19, 24]. In patients maintain-

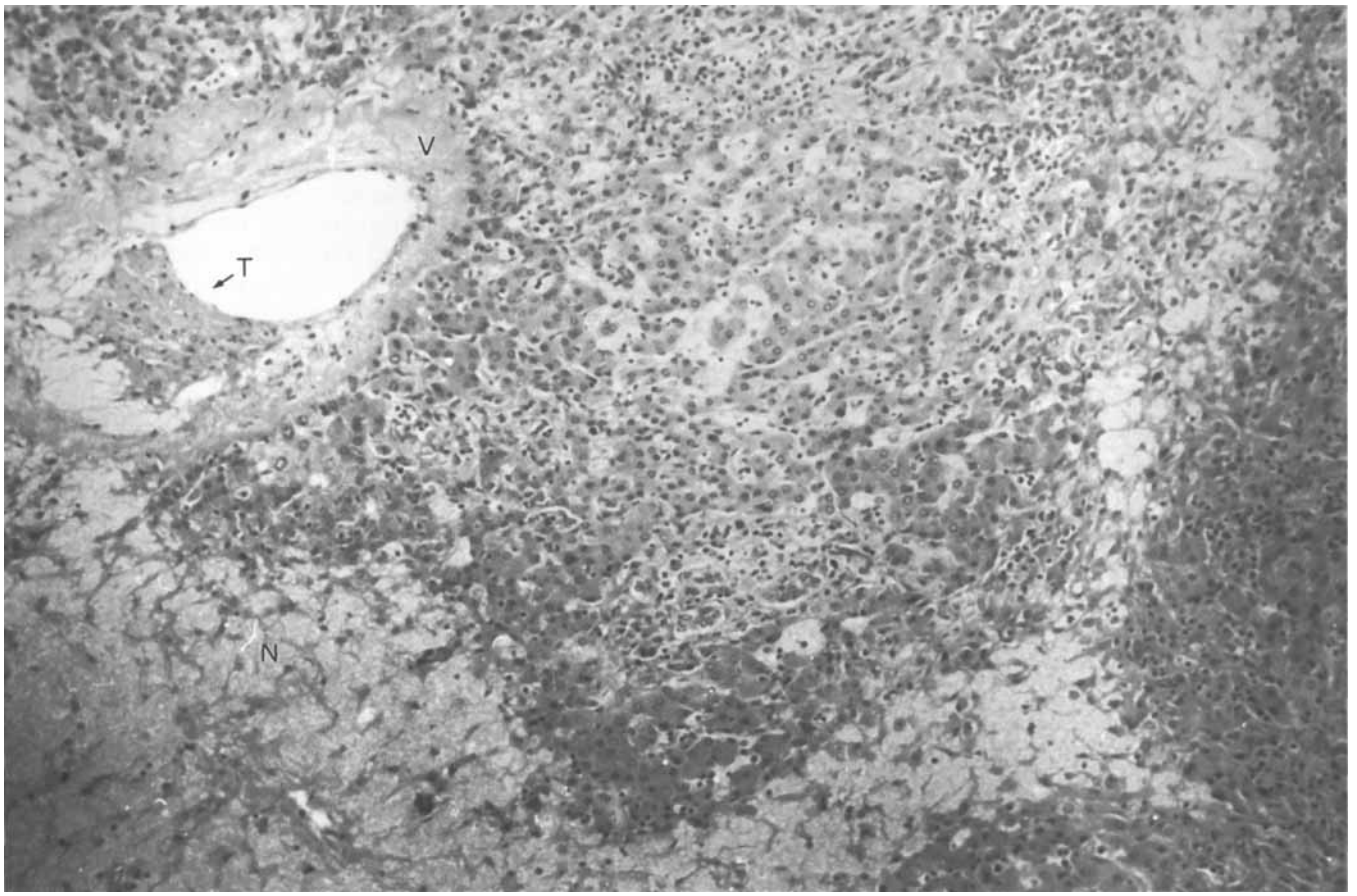

Fig. 2 (Case no. 3) Liver parenchyma with extensive confluent necrosis areas *(N)*. Medium-sized hepatic vein *(V)* with thrombus *(T)* H & E, × 100

ing hepatocellular function, portal blood shunt surgery can lead to survival rates comparable to those seen in transplanted patients [9] and can even prevent progression to cirrhosis in chronic forms of the syndrome [3, 20, 23]. Thus, it can still be used for those patients [1, 16, 23]. OLT has become the therapeutic indication for Budd-Chiari syndrome presenting with chronic liver insufficiency or acute liver insufficiency with severe encephalopathy [1, 6, 13, 23, 24]. The fact that the portacaval shunt can make a subsequent transplant technically difficult [1, 14] may make mesocaval shunting with a jugular venous graft or synthetic prosthesis the more advisable derivation procedure [8, 9, 13, 14]. Recently, it has become possible to perform a transjugular intrahepatic portocaval shunt (TIPS) in selected cases [24].

The first OLT for Budd-Chiari syndrome was performed in 1974 and the patient was still alive 16 years later [6]. Since then, a little more than 100 transplants for this syndrome have been recorded in the literature [2, 6, 23], and 158 patients were listed in the European Liver Transplant Registry in 1992 [5]. Management of patients transplanted for Budd-Chiari syndrome presents certain peculiarities as compared to the management of patients with other OLT indications. For example, the syndrome's etiology complicates diagnosis and follow-up, as it often involves hematologic factors (lymphoma, polycythemia vera) or hypercoagulative problems (paroxysmal noctural hemoglobinuria) [1, 13, 15, 22, 23] that can influence the transplanted patient's postoperative course [6, 14, 22]. In up to 30 %–40 % of the cases it is not possible to discover the etiology [6, 14, 22], or the precipitating condition is the extrinsic compression of hepatic veins (e. g., hydatid cysts). In cases where "intravascular membranous webs" are found, it is not uncommon to also find abundant thrombotic material in venous lumina [7, 8, 13, 15, 18], as occurred in the three cases reported here. The most logical explanation for the membranous webs found in Budd-Chiari syndrome cases associated with hematologic diseases appears to be intravascular thrombosis subsequently organized by granulation tissue. This theory is supported by the fact that our case of Budd-Chiari syndrome associated with hydatid cyst compression also presented membranous webs organized next to recent thrombus. This same mechanism could also explain the membranous webs

considered congenital in cases of idiopathic Budd-Chiari syndrome with membranous webs [7, 12, 20]. The onset of nodular regenerative hyperplasia in two of our cases is a rarity that has been reported previously [3]. It has been related to the need for increased liver function capacity in response to centrilobular hepatocytic necrosis caused by obstruction of venous outflow [4].

Given that the syndrome could be precipitated by hypercoagulability, long-term anticoagulant therapy with dicoumarin [2, 22, 23] or hydroxyurea (in cases of essential thrombocytosis) has been proposed to avoid syndrome recurrence [2, 6, 10, 11, 20, 21]. This was not necessary in case number one reported herein, where the underlying etiology was postsurgical and due to mechanical compression by a hydatid cyst. The other two patients, however, have remained on an anticoagulant regimen beginning immediately in the post-transplant period. These two patients have not suffered any further complication other than bleeding on the 3rd day post-transplant in patients number 3. Hemorrhagic complications have been reported by other authors in up to 44 % of such patients [2]; therefore, a closely monitored anticoagulation is necessary in the follow-up.

In the patients transplanted for Budd-Chiari syndrome, control of the etiology and the long-term anticoagulant therapy provide an acceptable survival rate [2]. At present, the actuarial survival rate at 1 and 5 years in patients transplanted for Budd-Chiari syndrome is 68.8 % and 44.7 %, respectively, in the patient group reported by Halff et al. [6], and 88 % at 3 years in Campbell's group [2].

Preoperative diagnosis of the syndrome, its etiology, and the degree of hepatocellular function together determine the most suitable therapeutic option for these patients [8, 16]. For Budd-Chiari syndrome cases presenting severe acute or advanced chronic liver insufficiency, liver transplantation is the only therapy offering acceptable long-term survival rates [8].

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