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Original Research Article **Gastroenterology**

Etiological, Therapeutic and Evolutionary Profile of Budd Chiari Syndrome (BCS): A Moroccan Experience Center

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Abstract

Background and objectives: Budd–Chiari syndrome is a vascular disorder of the liver which can cause fulminant liver injury and lethal portal hypertension-related complications. It is a rare disease and can be primary or secondary. The objective of our work is to detail the etiologies, treatment and evolution of SBC according to the experience of a Moroccan center. ***Patients and methods:*** This is a retrospective and descriptive study in the university hepato-gastroenterology department including all patients with BCS with portal hypertension (PH) over a period of 29 years. All our patients benefited from an etiological work-up and morphological explorations. ***Results:*** Out of a total of 364 cases of vascular liver disease, 29 patients had BCS, with a prevalence of 8%. Clinically, the signs of decompensated PH were predominant. Imaging confirmed BCS. The etiological work-up showed Behçet's disease in 17%. In one case each, BCS was secondary in 6.8% of cases (n=2), one of whom had HCC and the second had an association of sarcoidosis and amyloidosis. Our patients had received treatment for the causative disease and treatment of thrombosis associated with the treatment of PH complications. The evolution was marked by the death of 5 patients (17%). ***Conclusion:*** Budd-Chiari syndrome (BCS) is a rare condition. Behcet ' s disease and thrombophilia are the most frequent etiologies in our series. The prognosis is poor, mainly due to the causative disease and complications of PH, which requires a very early management.

Keywords: Budd Chiari syndrome, prothrombotics factors, treatment-evolution.

INTRODUCTION

Budd-Chiari syndrome (BCS) is a vascular disease of the liver, characterized by partial or total obstruction of hepatic venous flow in the vascular space between the hepatic veins and the junction between the inferior vena cava and the right atrium. It can be primary or secondary. The objective of our work is to detail the etiological, therapeutic and evolutionary profile in patients with BCS

MATERIALS AND METHODS

This is a retrospective and descriptive study in the university hepato-gastroenterology department including all patients with BCS with portal hypertension (PH) over a period of 29 years from 1991 to 2023.

All our patients benefited from a biological work-up including a blood count, a complete liver work-up including transaminases, alkaline phosphatases, gamma glutamyl transferase, bilirubin, prothrombin level (TP), international normalized ratio (INR), albumin, etc.

Morphologically, all our patients benefited from abdomino-pelvic ultrasound coupled with Doppler, abdominal angioscanner and hepatic MRI angiography, depending on the context.

From an etiological point of view, our patients benefited from an etiological work-up in search of prothrombotic factors according to the following classification in the table below:

Table 1

high-risk factors	low-risk factors
-Personal or family history (first degree) of spontaneous deep vein thrombosis -Myeloproliferative syndrome -Active cancer -Antiphospholipid antibody syndrome -familial antithrombin deficiency -familial protein S and C deficiency -Paroxysmal nocturnal hemoglobinuria -Behcet's disease	-Antithrombin deficiency -Protein S deficiency -Protein C deficiency -No Personal or family history (first degree) of spontaneous deep vein thrombosis -Hyperhomocysteinemia -Biermer's disease -Celiac disease -Inflammatory bowel disease -Deep abscesses

RESULTS

Out of a total of 364 cases of vascular liver disease, 29 patients had BCS, with a prevalence of 8%.

The mean age of our patients was 27 years±12.71 years with a sex ratio (M/F) of 0.4.

The table below shows the prevalence of BCS in vascular liver disease:

Table 2: Prevalence of BCS UN Vascular Liver Disease

	Portal vein thrombosis	Porto-Sinusoidal Vascular Disorders (PSVD)	BCS
Prevalence	57.69%(n=210)	35.44%(n=129)	8%(n=29)

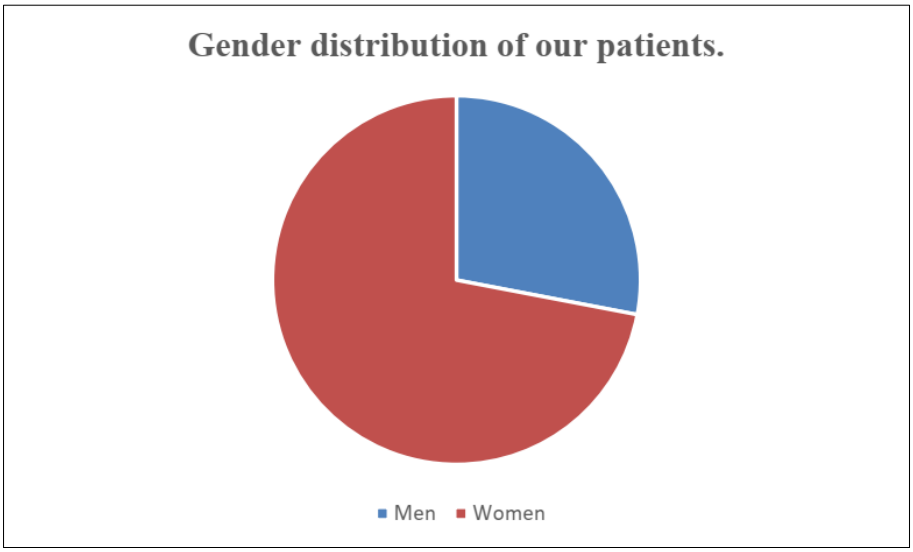

Figure 1: Gender Distribution of our Patients

Clinically, the signs of decompensated PH were predominant with ascites in 58% of cases (n=17), upper gastrointestinal bleeding in 31% of cases (n=9), jaundice in 13% of cases (n=4) and hepatocellular insufficiency in one case. Hepatic colic in 31% of cases (n=8).

The table below summarizes all the functional signs seen in our patients:

Table 3: Functional Signs in our Patients

	Number of patients	Percentage in %
Increased abdominal volume	13	52%
Hematemesis	6	24%
Melena	2	8%
Melena and hematemesis	1	4%
Hepatic colic	8	32%
Atypical abdominal pain	6	24%
Profound asthenia	5	20%
Clinical anemia syndrome	5	20%
Jaundice	4	16%

	Number of patients	Percentage in %
Pruritus	3	12%
Anorexia	3	12%
Oral aphthosis	2	8%
Bipolar aphthosis	1	4%
Genital aphthosis	1	4%

Imaging confirmed BCS with thrombosis of the inferior vena cava alone in 41% of cases (n=12), thrombosis of the two hepatic veins alone in 55% of cases (n=16), and thrombosis of the hepatic veins (HV) and the inferior vena cava (IVC) at the same time in 3% of cases (n=1). Chronic portal thrombosis was associated with 04 patients.

The table below show the results the different levels of thrombosis on Doppler ultrasound in our series:

Table 4: Showing the Different Levels of Thrombosis on Doppler Ultrasound in our Series

	IVC	2 HV	3 HV	2 HV et IVC	Associated portal thrombosis
Number of patients	10	10	4	1	4
percentage in %	40%	40%	16%	4.%	16%

The table below shows the results of Doppler ultrasound and angioscanner (CT) in our patient:

Table 5: Doppler Ultrasound and Angio CT Findings in our Patients

	Thrombosis of HV alone	Thrombosis of IVC alone	Thrombosis of HV and IVC	Associated portal vein thrombosis
Abdominal ultrasound with Doppler	56 % (n=14)	40% (n=10)	4% (n=1)	16% (n=4)
Abdominal angioscan	56% (n=14)	44% (n=11)	4% (n=1)	16% (n=4)

A liver biopsy was performed in 42% of cases (n=12) and showed cirrhosis in 13.8% of cases (n=4), an association of BCS with porto-sinusoidal vascular disease in 02 patients and an association of BCS with hepatocellular carcinoma (HCC) in one case (secondary SBC)

The table below shows the results of liver biopsy in our patients:

Table 6: The Results of Liver Biopsy in Our Patients

	Number of patients	Percentage in %
Number of patients Percentage in	2	8%
Minimal fibrosis : F1	1	4%
Moderate fibrosis : F2	1	4%
Severe fibrosis : F3	4	16%
Cirrhosis	2	8%
Associated MVPS	1	4%
HCC	1	4%
Normal	3	12%

The etiological work-up showed Behçet's disease in 17% of cases (n=5), protein S deficiency in 17% of cases (n=5), protein C deficiency in 13.8% of cases (n=4), essential thrombocythemia in 6.8% of cases (n=2), antithrombin deficiency in 6. 8% of the cases (n=2), oral contraceptive use at the time of thrombosis in 6.8% of the cases (n=2) and *paroxysmal nocturnal* hemoglobinuria (PNH) clone, Biermer's disease, celiac disease, Kahler's disease were responsible for BCS in one case each. BCS was secondary in 6.8% of cases (n=2), one of whom had HCC and the second had an association of sarcoidosis and amyloidosis

The table below shows the different prothrombotics factors in our patients:

Table 7: Etiologies of BCS in Our Patients

Etiology	Number of patients	Purcentage in %
Behçet's disease	5	20%
Protein S deficiency	4	16%
Protein C deficiency	4	16 %

Antithrombin III deficiency	1	4%
Essential thrombocythemia	2	8%
PNH clone	1	4%
Hyperhomocysteinemia with Biermer disease	1	4%
Hyperhomocysteinemia in celiac disease	1	4%
Hepatic sarcoidosis	1	4%
Hormonal cause (contraception for 13 years)	1	4%
Kahler's disease	1	4%
Hepatocellular carcinoma	1	4%
Undetermined cause	6	24%

The table below shows the associations of prothrombotic factors in our patients:

Table 8: Showing the Associations of Prothrombotic Factors in Our Series

	Number of patients	Purcentage
Protein C+protein S deficiency	2	8%
Biermer disease +Protein S and C deficiency	1	4 %
HPN clone + prolonged use of oral contraceptives	1	4%
Antithrombin III+protein C deficiency	1	4 %

The table below shows the prevalence of prothrombotic factors:

Table 9: Prevalence of Prothrombotic Factors

	At least one factor	Several factors	Loco-regional factor (BCS II)
Prevalence	76% (n=19)	20% (n=5)	4% (n=1)

Our patients had received treatment for the causative disease and treatment of thrombosis associated with the treatment of PH complications. The evolution was marked by the death of 5 patients (17%), a repermeabilization of the IVC by placement of a stent in only one patient and the persistence of thrombosis in the others

DISCUSSION

I. INTRODUCTION [1]

Budd-Chiari syndrome (BCS) is a vascular disease of the liver, characterized by partial or total obstruction of hepatic venous flow in the vascular space between the hepatic veins (minimum two veins), and the junction between the inferior vena cava and the right atrium. BCS can lead to acute liver failure, portal hypertension, liver cirrhosis and even hepatocellular carcinoma. It's classified as primary and secondary

II. Epidemiology [2, 3]

It's a rare but not exceptional disease, with an estimated prevalence of 1/1000000 worldwide. In France, the incidence of BCS is estimated at 0.68 per million per year, and in Algeria at 0.2 per million per year. BCS has a low prevalence in the general population. The gender distribution of BCS patients shows some differences between Asians and European countries.

III. Etiology: Prothrombotic Factors [4, 5]

A-Primitif BCS is the most frequent case, and is secondary to thrombosis, revealing an underlying pro-thrombotic state, and its fibrous sequel.

B-Secondary BCS

It involves local factors that are rarely identified in hepatic vein thrombosis hepatic veins, either through compression by an expansive lesion or endoluminal invasion by a tumor.

Nawel and al. in a a prospective Algerian study that included consecutive patients, over the age of 16 years with BCS, who were hospitalised in our unit from January 2004 until June 2010.The prothromobotic factors are in the table below

Table 10: Budd-Chiari syndrome aetiologies in Algeria

Aetiologies	Tested patients	*n*	% (*n*/tested *n*)
MPD	104	36	34.6
Patent		19	
Latent		17	
APL syndrome	92	20	21.7
Protein C deficiency	67	13	19.4
Protein S deficiency	59	5	8.5
Antithrombin deficiency	68	0	0
APCR	68	7	10.3
Celiac disease	88	10	11.4
Hyperhomocysteinaemia	42	5	11.9
PNH	11	4	
Systemic disease[1]	106	6	5.6
Inflammatory bowel disease[2]	60	5	8.3
Gene II mutation	21	1	4.7
Liver hydatic cyst	115	5	4.3
Hepatocellular carcinoma	115	1	0.8
Hormonal factors	70	25	35.7
Oral contraception	70	24	34.3
Pregnancy	70	3	4.3
Hormonal treatment	70	1	1.4
Unknown aetiology		24	20.9

Wen and al. in this retrospective Chinese study included 35 consecutive young Chinese patients (B25 years of age) with primary BCS between March 2011 and December 2014.

Table 11: Budd-Chiari Syndrome Aetiologies in China

Thrombophilia	
Myeloproliferative disorder	1
Polycythemia vera rubra	0
Essential thrombocythemia	1
JAK2 V617F mutation	1
Factor V Leiden mutation	0
Prothrombin G20210A mutation	0
Paroxysmal nocturnal hemoglobinuria	0
Protein C deficiency	0
Protein S deficiency	0
Antithrombin deficiency	0
Antiphospholipid antibodies	5
Hyperhomocysteinemia	14
Systemic	
Connective tissue disease	0
Behcet's disease	1
Inflammatory bowel disease	1
Vasculitis	0
Liver abscess	1
Hormonal factors	
Oral contraceptive use	2
Pregnancy within 3 months before diagnosis	2

III. Diagnostic [6- 8]

1. Clinical

The diagnosis of SBC should be suspected in the following circumstances:

Ascites, hepatomegaly and abdominal pain of the hepatic colic or atypical type,in patients with thrombogenic disorders who have developed acute liver disease, in hepatic failure accompanied by hepatomegaly

or ascites or in the case of unexplained chronic hepatopathy after classical causes have been ruled out.

2. Imaging

All imaging techniques can be used, including ultrasound coupled with Doppler, angio-MRI and MRI. Thanks to the development of imaging, arteriography, an invasive examination, is no longer of diagnostic interest.

3. Histology

Liver biopsy is rarely necessary to establish a diagnosis of BCS as imaging techniques are widely available. However, a biopsy may be recommended when neoplasia is suspected.

4. Endoscopy

Upper endoscopy is of no importance in the diagnosis of BCS, but it's the cornerstone in the search for signs of portal hypertension.

V-Management of BCS [10, 11]

The management of Budd-Chiari syndrome with portal hypertension is complex, and will involve:

- Management of PH and its complications.
- Management of BCS.
- Management of etiologies.

The Management of BCS is based on:

1. Anticoagulation

There are no randomized or retrospective studies analyzing the benefit of anticoagulation on survival or in comparison with other treatments.

In the absence of contraindications, curative anticoagulation with low-molecular-weight anticoagulation should be started as soon as possible before any decongestion procedure, and even before the even before a prothrombotic disorder is identified.

Direct oral anticoagulants (DOACs) are direct-acting oral anticoagulants that target factor IIa (e.g. dabigatran) or factor Xa (e.g. rivaroxaban, apixaban and edoxaban). They offer several potential advantages over other drugs.

Long-term anticoagulant therapy is generally recommended for patients suffering from BCS.

2. Plate-Aggregating Agents: They have a limited role in the treatment of SBC, particularly aspirin.

3. Thrombolysis

Thrombolysis or fibrinolysis is a therapeutic method involving the administration of a substance that degrades fibrin via activation of circulating or fibrin-bound plasminogen. The result is degradation of the newly-formed clot and inhibition of its extension.

4. Transluminal Angioplasty with or Without Prosthesis: This is an interventional radiology technique used in reference centers for Budd Chiari syndrome, with clearly demonstrated efficacy.

5. Transjugular Intrahepatic Portosystemic Bypass: TIPS

TIPS involves the catheterization of a transhepatic communication between a hepatic vein and a branch of the portal vein.

TIPS is always superior to medical treatment, which consists of anticoagulation and treatment of the underlying prothrombotic factors.

VI. Evolution and Prognosis [12, 13]

A good evolution is seen in asymptomatic forms, whereas in symptomatic,the mortality rate is 90% in 3 to 4 years.

BCS may progress to cirrhosis, recurrent ascites or even refractory ascites,but the main complication that may arise over the course of the is hepatocellular carcinoma (HCC).

Several prognostic models and indices have been developed by different validated in patients with BCS. Prognostic factors for SBC depend on the Child-Pugh score and the MELD score.

CONCLUSION

Budd-Chiari syndrome (BCS) is a rare condition.Behcet's disease and thrombophilia are the most frequent etiologies in our series. The prognosis is poor, mainly due to the causative disease and complications of PH, which requires a very early management

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