Presentation of Hospital Outcomes and Different Treatment Methods of Patients with Budd-Chiari Syndrome: A Report from Two Tertiary Hospitals in Iran

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Key Words

Budd-Chiari syndrome • Etiology • Treatment methods

Abstract

Objective: The aim of this study was to report common presentations of Budd-Chiari syndrome (BCS) and the early outcome of different treatment methods in two tertiary hospitals in Iran. **Subjects and Methods:** This case series study was performed on 21 patients (mean age: 42 ± 13.09 years; 11 male, 52.4%, and 10 female, 47.6%) admitted for treatment of BCS in two tertiary referral centers in Mashhad, Iran, between 2002 and 2008. All required data of signs, underlying etiology, treatment methods and in-hospital mortality were gathered from patients' medical records. **Results:** Angiographic and sonographic findings showed that the most frequent isolated location of obstruction was the inferior vena cava ($n = 12$, 57.1%). No distinct underlying disease was found in 6 (28.6%) patients. Eleven (52.4%) patients had web obstruction and 4 patients had other related underlying diseases. Treatment modalities consisted of medical follow-up in 12 (57.1%), angioplasty in 6 (28.6%), and surgery in 3 (14.3%) patients. Medical follow-up of 3 patients, 1 with angioplasty and 2 who had undergone surgery, disclosed that they had died before discharge from hospital. **Conclusion:** Higher age at diagnosis may reflect late diagnosis at an advanced stage

of disease. We suggest that the early symptoms of this disease should be taken into account more seriously in differential diagnosis. Balloon angioplasty seems to be a more efficient method for treatment of BCS.

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Introduction

Budd-Chiari syndrome (BCS) is characterized by a group of uncommon varied disorders defined by hepatic venous outflow obstruction at the level of the hepatic venules, large hepatic veins, inferior vena cava, or right atrium [1]. This syndrome occurs in 1/100,000 of the general population [2]. There is some evidence that BCS is a result of acquired predisposing factor(s) affecting a susceptible individual with one or more underlying thrombophilic conditions [3]. The presentations of BCS are as follows: hematological disorders, inherited thrombotic diathesis, pregnancy and postpartum, web obstruction (as a presentation), use of oral contraceptives, chronic infections, chronic inflammatory diseases (as in Behçet's disease), tumors and miscellaneous (trauma) and idiopathic (or unidentified) disorders [2, 4, 5]. An underlying disorder can be identified in over 80% of patients with BCS [6, 7].

Myeloproliferative disorders are the leading cause of BCS in Western countries, occurring in 20–53% of BCS patients [2, 8]. Various types of medical therapy, such as transcatheter interventions, different kinds of open surgery, and liver transplantation are considered for patients with BCS [5, 9]. Based on our current experience, BCS will be one of the important health problems in Iran. Due to lack of sufficient data regarding a general overview of presentations of BCS, different treatment methods and in-hospital outcomes for patients with BCS in Iran, a retrospective analysis of this syndrome was conducted for two tertiary hospitals in Iran.

Subjects and Methods

This study was carried out on all patients admitted for treatment of BCS in two tertiary referral centers, Imam Reza and Ghaem Hospitals, in Mashhad, Iran, between 2002 and 2008. The following data were obtained from the patients' medical records: signs (ascites, esophageal varices, hepatomegaly, edema, icterus, abdominal pain, splenomegaly and encephalopathy); underlying etiology and presentations (hematological disorders, inherited thrombotic diathesis, pregnancy and postpartum, membranous webs, use of oral contraceptives, chronic infections, chronic inflammatory diseases, tumors) and idiopathic.

All the patients' records showed a documented diagnosis of BCS based on clinical features, biochemical tests, sonography and angiography.

Treatment methods included medical therapy (efforts to control the further development of ascites, the use of anticoagulation therapy to prevent further extension of the venous thrombosis, and treatment of detectable underlying causes), intravascular interventions and different kinds of open surgery that were gathered from the medical records of all patients. The data were analyzed using Mini-Tab (release 13, Minitab Inc., 2000, USA), with descriptive statistics (mean and standard deviation) being determined for all variables.

Results

A total of 21 patients, 11 (52.4%) males and 10 (47.6%) females, were studied; mean age was 42 ± 13.09 years (range: 28–69) (table 1). The age distribution was <30 years: n = 4; 30–40 years: n = 6; 40–50 years: n = 9, and >50 years: n = 2.

Nineteen (90.5%) patients presented with ascites, varicose vein: n = 6 (28.6%), hepatomegaly: n = 8 (38.1%), edema: n = 14 (66.6%), abdominal pain: n = 5 (28.85%) and encephalopathy: n = 12 (57.1%). Obviously, some patients had more than one presenting symptom. Imaging (angiography and sonography) findings showed that the

Table 1. Age and gender characteristics of the sample population, site of obstruction and causes of BCS

Age, years	42 ± 13.09
Gender	
Male	11 (52.4%)
Female	10 (47.6%)
Site of obstruction	
Isolated IVC	12 (57.1%)
Hepatic vein	6 (28.6%)
IVC and hepatic	3 (14.3%)
Presentation/underlying disease of BCS	
Web	11 (52.4%)
Unidentified underlying disease	6 (28.6%)
Behçet's disease	2 (9.5%)
Hepatitis C	1 (4.8%)
Leukemia	1 (4.8%)

IVC = Inferior vena cava.

most frequently identified location of obstruction was the inferior vena cava, which occurred in 12 (57.1%) patients (table 1).

Our findings showed that 11 (52.4%) of the BCS patients had web obstruction. However, 6 (28.6%) of the patients were categorized with unidentified underlying disease or idiopathy. The underlying disease of the remaining patients was as follows: Behçet's disease: n = 2 (9.5%), hepatitis C: n = 1 (4.8%), leukemia: n = 1 (4.8%) (table 1). Behçet's disease was also found in 1 patient who had a web obstruction as the major cause of BCS.

The chosen methods of treatment were medical therapy: n = 12 (57.1%), angioplasty: n = 6 (28.6%), and surgery: n = 3 (14.3%). In 9 patients with web obstruction as a cause of BCS, balloon angioplasty was successfully performed in 6 (28.6%) and 3 (14.3%); others were referred for surgery because of thickening of the web lesions.

Three patients with encephalopathy upon admission died before discharge from the hospital. One who had been admitted with acute liver failure and encephalopathy died 5 days after successful angioplasty. In the surgical group, 2 with some degree of encephalopathy and liver failure upon admission succumbed after surgery.

Discussion

In this study, the mean age of patients diagnosed with BCS was 10 years older than that reported in India and Turkey [4, 10], which might be due to different causative

factors or later diagnosis in Iran. The most frequent presenting sign for Iranian patients with BCS was ascites, consistent with an Indian report [10], indicating that BCS should be suspected in patients with abrupt onset of ascites and painful hepatomegaly and also massive ascites with liver function relatively preserved [11].

Isolated inferior vena cava obstruction was the commonest disease in our study, consistent with a previous report [4]. However, in more recent reports a combination of inferior vena cava and hepatic vein obstruction was the commonest type [3], which in our study was the second type. Longer duration of illness has been shown to be associated with inferior vena cava obstruction [3, 12] and indicates a late diagnosis of BCS in Iran.

According to our experience, web obstructions are the most common presenting sign of BCS in Iranian patients, consistent with other reports from the East [4, 13, 14], but not in the Western hemisphere, where myeloproliferative disorders are the most prevalent underlying disease in BCS patients [2, 8, 15]. It is often thought that membranous lesions are congenital in origin; however, the mechanisms that result in their formation are not clear despite numerous epidemiological studies [16]. The interesting point in this regard is that the higher number ($n = 5$) of older patients with web-based BCS is not consistent with the congenital formation of web obstructions. Until the present time, there are rare reports of BCS in children. Some investigators believe that formation of membranous occlusions can occur during adulthood [17].

About 30% of Iranian patients with BCS remained unidentified, consistent with another report from Turkey [4]. Other researchers have reported an exact diagnosis of BCS for about 80% [6, 7] of patients, which clarifies the lower rate of exact diagnosis in Iran that might be due to medical and technical problems.

Vasculitis is a major component of Behçet's disease. Hepatic vein vasculitis, which occurs in patients with Behçet's disease, may cause BCS [18], which again, is not uncommon in Behçet's disease patients [19]. In patients with Behçet's disease, BCS is often associated with inferior vena cava as well as hepatic venous thrombosis [19], exactly the finding in our study: 2 of the patients with BCS in Iran had Behçet's disease.

Comorbidity of hepatitis C and BCS was observed in 1 patient. We do not believe that hepatitis C can be a causative factor for the development of BCS, a view that may be corroborated by an investigation of the causes of BCS by Mesa [20], who also reported a co-infection of hepatitis C in a patient with BCS, but did not conclude that hepatitis C was a causative factor of BCS [21].

Interventional therapy or radical resection of web lesions is now an accepted method [6]. Percutaneous transluminal angioplasty is another safe and useful method for the management of BCS due to membranous obstruction of the hepatic portion of the inferior vena cava or the hepatic veins [22]. In our study, 6 patients with BCS caused by web obstruction were successfully treated with balloon angioplasty. Perhaps new interventional transcatheter methods that are minimally invasive will replace surgical techniques.

If BCS is not treated punctually and properly, the outcome may be fatal [23]. Seven of 21 (33%) patients died in hospital before discharge. The observed 33% death rate of our patients in the hospital before discharge is a very high rate of mortality. However, others have reported higher survival rates for BCS: 87% at 1 year and 82% at 2 years [24] and survival rates at 1, 3, and 5 years after shunting of 83, 78, and 75%, respectively [25].

Inclusive imaging evaluations, in combination with pathologic analyses and clinical testing, are necessary for determining the severity of disease, stratifying risk, selecting the suitable therapy, and impartially assessing the response [23]. Our results demonstrated that the current status of the patients with BCS in Iran is critical. Urgent systematic reactions for proper screening and precise follow-up of patients with BCS are required in Iran. It seems that special attention should be paid in this regard by physicians and medical associations.

In comparison with Western countries, Iranian patients with BCS had more web obstructions than hematologic disorders, as shown in the study by Darwish Murad et al. [24] where myeloproliferative disorder was a common cause of BCS. A probable explanation for the difference is that we did not measure JAK2 V617F mutation as an indicator of myeloproliferative disorder, as was done by Darwish Murad et al. [24].

Conclusion

Higher age at diagnosis may reflect late diagnosis in an advanced stage of disease. We suggest that the early symptoms of this disease should be taken into account more seriously in differential diagnosis. Balloon angioplasty seems to be a more efficient method for treatment of BCS.

References

- Menon KV, Shah V, Kamath PS: The Budd-Chiari syndrome. *N Engl J Med* 2004;350:578-585.
- Aydinli M, Bayraktar Y: Budd-Chiari syndrome: etiology, pathogenesis and diagnosis. *World J Gastroenterol* 2007;13:2693-2696.
- Eapen CE, Mammen T, Moses V, Shyamkumar NK: Changing profile of Budd-Chiari syndrome in India. *Indian J Gastroenterol* 2007;26:77-81.
- Uskudar O, Akdogan M, Sasmaz N, Yilmaz S, Tola M, Sahin B: Etiology and portal vein thrombosis in Budd-Chiari syndrome. *World J Gastroenterol* 2008;14:2858-2862.
- Zhang XM, Li QL: Etiology, treatment, and classification of Budd-Chiari syndrome. *Chin Med J* 2007;2:159-161.
- Dilawari JB, Bamberg P, Chawla Y, Kaur U, Bhusnurmath SR, Malhotra HS, Sood GK, Mitra SK, Khanna SK, Walia BS: Hepatic outflow obstruction (Budd-Chiari syndrome): experience with 177 patients and a review of the literature. *Medicine* 1994;73:21.
- Case records of the Massachusetts General Hospital. Weekly clinicopathological exercises. Case 51-1987. Progressive abdominal distention in a 51-year-old woman with polycythemia vera. *N Engl J Med* 1987;317:1587.
- Denninger MH, Chait Y, Casadevall N, Hillaire S, Guillin MC, Bezeaud A, Erlinger S, Briere J, Valla D: Cause of portal or hepatic venous thrombosis in adults: the role of multiple concurrent factors. *Hepatology* 2000;31:587-591.
- Klein AS: Management of Budd-Chiari syndrome. *Liver Transpl* 2006;12(11 suppl 2):S23-S28.
- De BK, De KK, Sen S, Biswas PK, Das TK, Das S, Hazra B: Etiology based prevalence of Budd-Chiari syndrome in eastern India. *J Assoc Physicians India* 2000;48:800-803.
- Ohta M, Hashizume M, Tomikawa M, Ueno K, Tanoue K, Sugimachi K: Analysis of hepatic vein waveform by Doppler ultrasonography in 100 patients with portal hypertension. *Am J Gastroenterol* 1994;89:170-175.
- Iwai M, Kitagawa Y, Nakajima T, Takeda M, Okanoue T, Nakajima T, Ogasawara T, Suyama Y, Miyoshi M, Kashima K: Clinical features, image analysis, and laparoscopic and histological liver findings in Budd-Chiari syndrome. *Hepatogastroenterology* 1998;45:2359-2368.
- Shrestha SM, Okuda K, Uchida T, Maharjan KG, Shrestha S, Joshi BL, Larsson S, Vaidya Y: Endemicity and clinical picture of liver disease due to obstruction of the hepatic portion of the inferior vena cava in Nepal. *J Gastroenterol Hepatol* 1996;11:170-179.
- Okuda H, Yamagata H, Obata H, Iwata H, Sasaki R, Imai F, Okudaira M, Ohbu M, Okuda K: Epidemiological and clinical features of Budd-Chiari syndrome in Japan. *J Hepatol* 1995;22:1-9.
- Hirshberg B, Shouval D, Fibach E, Friedman G, Ben-Yehuda D: Flow cytometric analysis of autonomous growth of erythroid precursors in liquid culture detects occult polycythemia vera in the Budd-Chiari syndrome. *J Hepatol* 2000;32:574-578.
- Wang ZG: Budd-Chiari syndrome. *Curr Probl Surg* 1996;33:83-211.
- Li XQ, Duan PF, Qian AM, Sang HF: Reoperation for postoperation recurrence in Budd-Chiari syndrome patients undergoing radical resection. *Chin J Gen Surg (Chin)* 2005;20:274-275.
- Bayraktar Y, Balkanci F, Kansu E, Dundar S, Uzunalimoglu B, Kayhan B, Telatar H, Gurakar A, Van Thiel DH: Cavernous transformation of the portal vein: a common manifestation of Behçet's disease. *Am J Gastroenterol* 1995;90:1476-1479.
- Ben Ghorbel I, Ennaifer R, Lamoum M, Khanfir M, Miled M, Houman MH: Budd-Chiari syndrome associated with Behçet's disease. *Gastroenterol Clin Biol* 2008;32:316-320.
- Mesa RA: How I treat symptomatic splenomegaly in patients with myelofibrosis. *Blood* 2009;113:5394-5400.
- Shrestha SM: Liver cirrhosis and hepatocellular carcinoma in hepatic vena cava disease, a liver disease caused by obstruction of inferior vena cava. *Hepatol Int* 2009;3:392-402.
- Sparano J, Chang J, Trasi S, Bonanno C: Treatment of the Budd-Chiari syndrome with percutaneous transluminal angioplasty: case report and review of the literature. *Am J Med* 1987;82:821-828.
- Cura M, Haskal Z, Lopera J: Diagnostic and interventional radiology for Budd-Chiari syndrome. *Radiographics* 2009;29:669-681.
- Darwish Murad S, Plessier A, Hernandez-Guerra M, Fabris F, Eapen CE, Bahr MJ, Trebicka J, Morard I, Lasser L, Heller J, Hadengue A, Langlet P, Miranda H, Primagiani M, Elias E, Leebeek FW, Rosendaal FR, Garcia-Pagan JC, Valla DC, Janssen HL; EN-Vie (European Network for Vascular Disorders of the Liver): Etiology, management, and outcome of the Budd-Chiari syndrome. *Ann Intern Med* 2009;151:167-75.
- Slakey DP, Klein AS, Venbrux AC, Cameron JL: Budd-Chiari syndrome: current management options. *Ann Surg* 2001;233:522-527.