N. E. Daryani MD[1],
R. Fatemi MD[2],
H. Ghanaati MD[3],
A. Alipoor MD[1],
R. Taslimi MD,
J. Hamrang MD,
A. A. Hashtroudi MD[1].

Combination of Thrombolytic Therapy and Angioplastic Stent Insertion in a Patient with Budd-Chiari Syndrome

Report of a Case

Abstract: A 31-year-old female with well-established polycythemia vera since one year before, presented with the sudden onset of tense ascites and hepatic encephalopathy since 12 days prior to admission. Real-time ultrasonography revealed a suprahepatic thrombosis extending toward the inferior vena cava (IVC). Thrombolytic therapy with systemic streptokinase (250,000 IU loading + 100,000 IU/hr infusion) was started. At the end of 72 hours' infusion, the patient's general condition improved. A color Doppler ultrasonography, then showed complete and partial resolution of the thrombosis in the suprahepatic vein and IVC, respectively. Despite this good response, 12 days later, the symptoms recurred. Venography detected complete obstruction of the IVC. Percutanous balloon angioplasty with stent insertion was performed successfully and the patient was discharged without any evidence of liver disease. A combination of systemic streptokinase and radiological intervention was effective in our patient.

Keywords: Hepatic Vein Thrombosis, Anticoagulants, Thrombolytic Therapy, Stents

Introduction

Budd-Chiari syndrome (BCS) is a rare entity caused by the obstruction, usually thrombotic in origin, of the hepatic venous outflow.[1] It may be a result of various etiologies including myeloproliferative disorders (polycythemia rubra vera, chronic myelogenous leukemia, essential thrombocythemia, agnogenic myeloid metaplasia), malignancies, infections and benign hepatic lesions, oral contraceptives, pregnancy and other hypercoagulability states. It usually involves one, two or all the three major hepatic veins with or without extension of the thrombus into the inferior vena cava (IVC). The syndrome may presents with acute (sometimes fulminant), subacute or chronic signs and symptoms of abdominal pain, hepatomegaly, ascites, the lower extremities edema, and venous collateral formation. Without treatment, patients often die; primarily due to progressive liver failure resulted from chronic hepatic congestion.[2]

So far, different therapeutic modalities have been suggested. These include medical treatments (supportive measures, anticoagulants, and thrombolytics), radiological procedures (*e.g.*, angioplasty, trans-jugular intrahepatic portacaval shunt [TIPS], and stenting) and surgical interventions (shunting procedures and liver transplantation). There are only few reports of success following conventional treatments such as anticoagulants and diuretics. Radiological procedures and surgical interventions are the most effective treatments recommended for BCS. These include angioplasty, stenting, open endvenectomy,[3] shunt and TIPS operations, and more recently, liver transplantation[2].

From
1. Department of Gastroentrology, Imam Hospital,Tehran University of Medical Sciences,Tehran, IRAN.
2. Department of Gastroentrology Shahid Beheshti University of Medical Sciences, Tehran, IRAN.
3. Medical Imaging Center, Imam Hospital, Tehran University of Medical Sciences , Tehran IRAN.
Corresponding Author:
Dr N. E. Daryani,
Tel: +9821 8799446
Fax: +9821 8799840
Email: nebrahim@sina.tums.ac.ir

Fibrinolytic therapy should be restricted to acute or subacute conditions when the formed thrombus is young enough to be resolved by thrombolytic therapy.[1]

In this essay, we present a case of BCS who was treated successfully with a combination of thrombolytic therapy and angioplasty with stent insertion.

Case Presentation

A 31-year-old woman, with one-year history of polycythemia vera was admitted to our center for a progressive abdominal distension, right upper quadrant abdominal pain, nausea and vomiting for 12-15 days duration. On physical examination, a massive ascites, pitting edema of the lower extremities and hepatosplenomegaly were evident. Considering the laboratory findings (Table 1), the patient was diagnosed to be at the second stage of hepatic encephalopathy. Real-time ultrasonography ,color Doppler and Venography of abdominal veins showed a thrombosis in the hepatic vein and IVC, 5 cm proximal to the hepatic vein junction, deteriorating the blood flow of the portal vein and IVC (Figures 1 and 2). The renal vein was normal. The hepatic and splenic longitudinal diameters were measured to be 20 and 16 cm, respectively. The urinary output was slightly <400 ml/24 hrs. All these findings were clearly in favor of an acute BCS.

The initial treatment was systemic streptokinase; a loading dose of 250,000 IU run over 30 min. followed by a maintenance dose of 100,000 IU/hr for 72 hrs. She also received the standard treatment for encephalopathy. Streptokinase therapy increased the urinary flow to 35 ml/hr and reduced both the ascites and the liver size. After four days, the hepatic encephalopathy subsided completely.

Table 1: The changes in the laboratory findings, days 1-10

	Day of Submission			
	1st	2nd	4th	10th
WBC (/mm³)	18,000	16,500	14,300	8,000
Hb (g/dl)	19	16	12	11.5
Plt (/mm³)	421,000	410,000	380,000	275,000
Cr (mg/dl)	2	1.8	1.8	1.3
BUN (mg/dl)	29	25	27	18
ALT (U/L)	101	84	61	22
AST (U/L)	165	127	87	39
ALP (U/L)	315	229	218	-
BIL (T) (mg/dl)	3.7	-	-	1.8
BIL (D) (mg/dl)	1.9	-	-	0.45
PT* (sec)	20	19	15	22**
PTT (sec)	55	50	49	45

*Mean normal PT was 13"

**Patient received warfarin

During the thrombolytic therapy, the serum fibrinogen level was measured every 12 hrs, which ranged between 160 and 200 mg/dl. After completion of thrombolytic therapy (on the third day), Doppler ultrasonography showed an acceptable patency of both IVC and hepatic vein due to complete resolution of the thrombi (Figure 3). Thereafter, the standard anticoagulant therapy was started; the patient was heparinized first. It was followed by administration of warfarin for attaining a target international normalization ratio (INR) of 2 to 3. To maintain a hemoglobin level <12 gm/d1, 1,000 mg/d hydroxyurea along with repeated aggressive phlebotomy was begun since the first day on. The patient's weight and abdominal distension gradually reduced until the 15th day of admission.

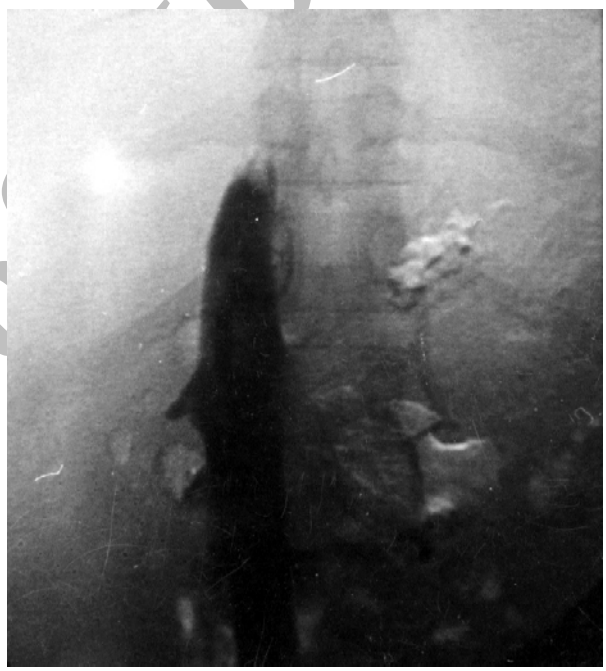

Figure 1: The venographic picture of complete obstruction of the IVC.

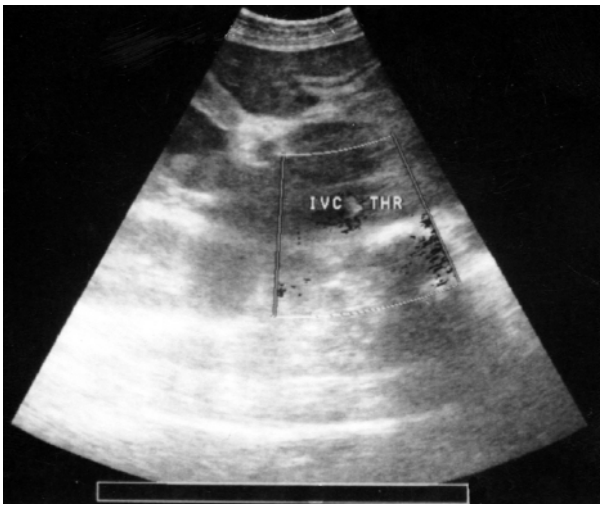

Figure 2: The location of venous thrombosis in the IVC as appears on the ultrasound.

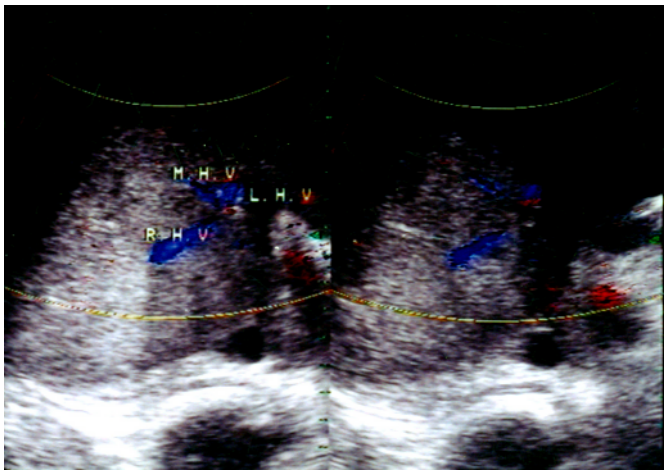

Figure 3: Post-stenting sonography, showing the right, left and middle hepatic veins.

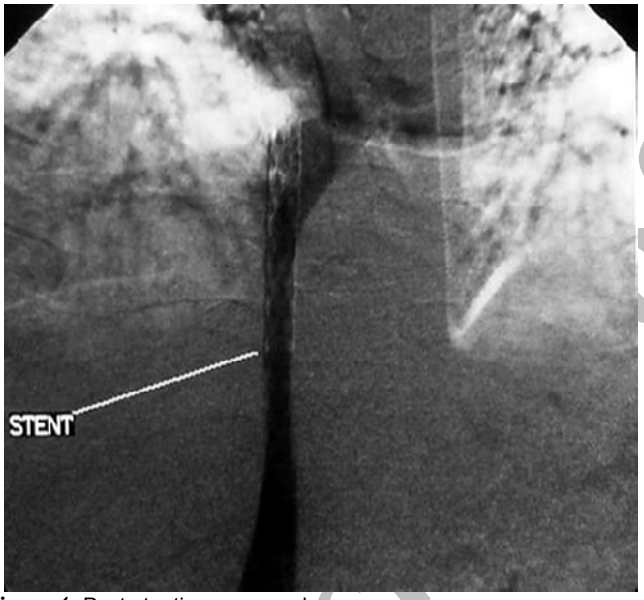

Figure 4: Post-stenting venography

After two weeks, the abdominal pain and a progressive ascites recurred, unexpectedly. Venography showed a 5-cm thrombus located in the IVC, proximal to the hepatic vein. The hepatic venous flow was minimal, yet no thrombosis was observed. Percutanous transluminal balloon angioplasty (PTA) was performed after which the blood flow of the IVC was restored. However, over the next 48 hrs, the flow decreased and recurrent stenosis made it necessary to repeat PTA with insertion of a wall stent in the IVC (Figure 4). Two wall stents were placed in the IVC. Color Doppler ultrasonography after stenting showed a complete flow with good patency of both the hepatic vein and IVC. The patient was kept under close observation during the early post-intervention period. Over the next 48 hours, the patient's symptoms subsided, the urinary output increased, and the abdominal girth returned to normal. The anticoagulant therapy was instituted. ASA 325 mg/d was added after the stent insertion. Five days post-intervention, the laboratory tests revealed a WBC of 11,000/mm^3, a Hb of 12.5 g/dl, a serum creatinine level of 1.2 mg/dl, a BUN of 23 mg/dl, ALT of 19 IU/L, AST of 25 IU/L, a total serum billirubin level of 0.6 (direct=0.2) mg/dl, PTT of 40 sec, and an INR of 2 (PT = 20 sec).

After one year of follow-up, the patient's status was satisfactory and the hepatic vein and IVC blood flow was complete as assessed by color Doppler ultrasonography at each visit.

Discussion

Budd-Chiari syndrome can be defined as any pathophysiologic process resulting in interruption or diminution of the normal blood flow out of the liver. If left untreated, it is almost always lethal owing to progressive liver failure due to chronic hepatic congestion. Medical treatment with diuretics controls the ascites. However, it just provides symptomatic relief. Radiological interventions and surgical approaches to address the underlying etiology are the best treatment to restore the hepatic venous flow.[2] A variety of non-medical approaches have been proposed. Currently, invasive methods like meso-caval or meso-arterial shunting, angioplasty, either alone or in combination with stenting and TIPS, are accepted as standard treatments of BCS. They, however, cannot be employed under certain circumstances, like severe hepatocellular damage, seriously ill patients or those with extensive thrombosis.

Angioplasty with or without stent insertion is the treatment of choice for many acute cases of BCS involving the IVC. Nontheless, in this technique, the length of thrombosis is an important limiting factor.[4] Due to recurrent stenosis following percutaneous balloon angioplasty, it is necessary to utilize wall stents in many cases. However, further evaluations are required to watch for the intimal fibrosis and subsequent obliteration of the wall stent.

While the conventional anti-coagulation therapy has been poorly effective with the 5-year venous patency of only 10%, the thrombolytic therapy with rTPA, urokinase, or streptokinase is recently reported to be hopeful.[5-7] Sholar *et al*, reported two cases of BCS due to paroxysmal nocturnal hemoglobinuria who were successfully treated with streptokinase.[8] In another report, seven patients with hepatic vein and vena caval thrombosis plus disturbed hepatic function were treated with streptokinase. The treatment was successful in four patients with no recurrence.[9] The successful treatment of two children with BCS by this method has also been reported.[10] Although, thrombolytic therapy is used mainly in acute phase of the disease, it may be used either as a temporary

treatment to improve the condition of seriously ill patients awaiting surgery, or to reduce the length of the thrombus while preparing the patient for angioplasty and stent insertion.

In conclusion, a combination of thrombolytic therapy and angioplasty with wall stent insertion might be beneficial to the patients in the acute phase of BCS. Nevertheless, more investigations are required to evaluate its definite effectiveness and safety.

References

1. Hemming AW, Langer B, Greig P, et al. Treatment of Budd-Chiari syndrome with portosystemic shunt or liver transplantation. Am J Surg. 1996 Jan;171(1):176-181.
2. Emre A, Kalayci G, Ozden I, et al. Mesoatrial shunt in Budd-Chiari syndrome. Am 1 Surg. 2000 Apr;179(4):304-8.
3. Koja K, Kusaba A, Kuniyoshi Y, et al. Radical open endvenectomy with autologous pericardial patch graft for correction of Budd-Chiari syndrome. Cardiovasc Surg. 1996 Aug;4(4):500-4.
4. Ishiguchi T, Fukatsu H, Itoh S, et al. Budd-Chiari syndrome with long segmental inferior vena cava obstruction: treatment with thrombolysis, angioplasty and intra vascular stent. J Vasc Inter Radiol. 1992; 3(2): 421-5.
5. Bell WR, Meek AG. Guidelines for the use of thrombolytic agents. N Engl J Med. 1979; 301: 1266-70.
6. Greenwood LH, yrizarry JM, Mallet GW et al. Urokinase treatment of Budd-Chiari syndrome. Am J Radiol. 1983;141: 1057-9
7. Warren RL, Schelant RC, Wenger NK et al. Treatment of Budd-Chiari syndrome with streptokinase. Gastroenterology 1972;62:200.
8. Sholar PW, Bell WR. Thrombolytic therapy for inferior vena cava thrombosis in paroxysmal nocturnal hemoglobinuria. Ann Internal Med. 1985;103;539-41
9. Pawlak J, Palester-Chlebowczky M, Michlowic ZB et al. Thrombolytic therapy of Budd-Chiari syndrome with portal vein thromb osis; Pol Arch Med Wewn 1993 Feb;89(2):171-7. Polish.
10. Sawamura R, Femandez MI, Galvaco LC, Goldani HA. Two children with Budd-Chiari syndrome were successfully submitted thrombolytic therapy. Arg Gastroenterology 1996;33(3):170-81