Budd Chiari Syndrome: Three Case Reports and a Literature Review

Ana Catalina Ramírez,[1] Simón Correa Gaviria,[1] Yeinis Paola Espinoza Herrera, MD,[2] Juan Ignacio Marín, MD,[3] Octavio Muñoz, MD,[4] Oscar Santos, MD,[4] Sergio Hoyos Duque, MD,[5] Carlos Guzmán, MD,[6] Álvaro Mena, MD,[7] Juan Carlos Restrepo Gutiérrez, MD, MSc. PhD.[8]

1 Student of Medicine at the Universidad de Antioquia, member of the Gastrohepatology group at the Universidad de Antioquia in Medellin, Colombia
2 Surgeon at the Universidad de Antioquia, member of the Gastrohepatology group at the Universidad de Antioquia in Medellin, Colombia
3 General Practitioner, Specialist in Internal Medicine and Clinical Hepatology, Hepatologist in the Hepatology and Liver Transplant Group at the Hospital Pablo Tobon Uribe. Professor in the Faculty of Medicine at the Universidad Pontificia Bolivariana in Medellin, Colombia
4 General Practitioner, Specialist in Internal Medicine and Clinical Hepatology, Hepatologist in the Hepatology and Liver Transplant Group at the Hospital Pablo Tobon Uribe. Professor in the Faculty of Medicine at the Universidad de Antioquia in Medellin, Colombia
5 General Practitioner, Specialist in General Surgery and Hepatobiliary and Pancreatic Surgery, Master's Degree in Epidemiology, member of the Gastrohepatology group at the Universidad de Antioquia, Surgeon in the Hepatology and Liver Transplant Group at the Hospital Pablo Tobon Uribe, Professor in the Faculty of Medicine at the Universidad de Antioquia in Medellin, Colombia
6 General Practitioner, Specialist in General Surgery and Vascular and Intra-abdominal Organ Transplant Surgery, Surgeon in the Hepatology and Liver Transplant Group at the Hospital Pablo Tobon Uribe in Medellin, Colombia
7 General Practitioner, Specialist in General Surgery, Transplant Surgery, Intra-abdominal organs, Surgeon in the Hepatology and Liver Transplant Group at the Hospital Pablo Tobon Uribe in Medellin, Colombia
8 General Practitioner, Specialist in Internal Medicine, Clinical Hepatology and Liver Transplantation. Master's Degree in Organs and Tissues, Doctor of Medical Sciences, member of the Gastrohepatology group at the Universidad de Antioquia, Coordinator of the Hepatology and Liver Transplant Group at the Hospital Pablo Tobon Uribe, Professor in the Faculty of Medicine at the Universidad de Antioquia in Medellin, Colombia

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Abstract

This article describes the cases of three female patients who were diagnosed with Budd-Chiari syndrome. One patient was subacute and could be successfully managed by placement of a transjugular intrahepatic portosystemic stent (TIPS). Another patient who had the Factor V Leiden mutation developed associated progressive liver dysfunction and required liver transplantation. A hematologic disease was identified as the underlying disorder in two of the three cases. For one patient, the use of oral contraceptives was a risk factor. Since all three patients were undergoing anticoagulant therapy, surgical management was determined according to each patient's clinical condition. Nevertheless, the one patient who that presented acute hepatic failure did not survive.

Keywords

Budd-Chiari syndrome (BCS), myeloproliferative disorders, thrombosis, thrombophilia, TIPS, anticoagulation, angioplasty, Factor V Leiden, liver transplantation.

CASE DESCRIPTION

Case 1

The patient was a 42 year old women who was born and lives in Medellin. She has no children and is a housewife. In March 2011 she was sent to the emergency department of our institution after being tentatively diagnosed with acute BCS (Budd-Chiari Syndrome). She reported that her symptoms had begun a month earlier with gradual worsening of non-dysenteric diarrhea, edema of her legs, decreased volume of urine and increased abdominal girth associated with progressive dyspnea.

An abdominal CT scan was suggestive of thinning of the hepatic veins. A complete blood count showed thrombocytosis with a platelet count of 460,000/mm^3 (Normal range= 150,000-450,000); alanine aminotransferase (ALT) elevated to 205 IU/L (NV <29); aspartate transaminase (AST) at 86 U/L; INR 1.4 (NV = 0.0 to 1.0); electrolytes normal; albumin at 3.8 g/dL (NV = 3.8-5); total bilirubin 1 mg/dL (NV = 0.6-1.0) and GGT at 545 U / L. Doppler ultrasound of the portal system showed suprahepatic portals with flow in the middle hepatic vein but no flow in the left and right hepatic veins.

Given all of this, treatment was initiated with diuretics and anticoagulants. Later TIPS (transjugular intrahepatic

portosystemic shunts) were placed. Following treatment the patient's recovery was satisfactory as measured clinically and through laboratory tests. While hospitalized, a blood test showed that the patient had, "chronic myeloproliferative neoplasm due to essential thrombocythemia with heterozygous positive JAK." The patient is currently receiving oral anticoagulation with warfarin and is being followed up as an outpatient.

Case 2

The patient was a 20 year old women who was born and lived in Medellin. She had one daughter and was a housewife. She had no relevant medical history, except for the use of combined oral contraceptives.

The patient was admitted to the emergency department of our institution after being referred with a diagnosis of acute liver failure. Her test results showed her CRP level elevated to 15 mg/dL (Normal range: = 0.0 – 1.0); PT of 20 seconds; an INR of 1.9; a platelet count of 80,000/mm3, a white blood cell count of 24,5007mm3 (Normal range: 4,000 to 12,000); AST at 7,432 IU/L; ALT at 2,300 IU/L; serum creatinine at 2.5 mg/dL (Normal range: 0.5 to 1.2) and blood urea nitrogen at 43 mg/dl (Normal range: 7 to 20). Her virological study was normal, but imaging showed a prominent hepatic caudate lobe, hypertrophy of the left liver lobe and multiple confluent solid images.

She reported her symptoms had begun with cramping abdominal pain located in the right upper quadrant, nausea, vomiting, jaundice and progressively increasing abdominal girth. An exploratory laparotomy found ascites (2,500 ml of clear fluid), collateral circulation and a nodular liver.

The patient was admitted to the Intensive Care Unit of our institution and Doppler ultrasound showed thrombosis of the hepatic veins. Anticoagulants were administered and the patient became stable but with declining transaminases and INR for the first two days of hospitalization. However, her clinical condition progressively worsened, and she suffered multiple organ failure including compromised cardiovascular, renal, hematologic, and central nervous systems which subsequently led to her death.

Case 3

The patient was a 40 year old women who was born and lives in La Estrella, Antioquia. She is a single mother of two children with a history of hypertension, and cirrhosis of the liver. She had been diagnosed with Budd-Chiari syndrome by pathology which showed grade I-II/IV macrovacuolar steatosis and fibrosis but no etiology had been established. When she came to the outpatient clinic of the Department of Hepatology, she was hospitalized for testing for any bleeding disorders in order to assess the possibility of placing a portosystemic shunt depending on the etiology of the disease. By the time she was admitted she had already been referred to the ER various times for complications secondary to advanced cirrhosis.

The results of laboratory tests done on admission were creatinine of 1.1 mg/dL; a platelet count of 419,000/mm3; PT of 17.3 seconds; PTT of 146 seconds (Normal range: 25 to 35); AST at 127 IU/L, ALT at 99 IU/L; total bilirubin at 1.6 mg/dL; direct bilirubin at 1.2 mg / dL (Normal range: 0.0 to 0.3); albumin of 3.4 mg/dL; alkaline phosphatase at 282 IU/L (Normal range: 44 to 147) and GGT at 321 U/L. Budd-Chiari syndrome was secondary to mutation of the V Leiden factor which is why it was decided to perform a mesocaval bypass. The patient's postoperative clinical course was satisfactory.

Following the bypass, the patient presented bleeding in her abdominal cavity with obstructed drainage, but her subsequent development was successful with anticoagulation as the goal of examinations. An upper endoscopy showed esophageal varices surrounding the entire esophageal passageway. The patient underwent orthotropic liver transplantation after being diagnosed with advanced cirrhosis of the liver with a vascular etiology which is secondary to Budd-Chiari syndrome in patients with V Leiden factor. Currently the patient being followed up as an outpatient in our Department of Hepatology (1-4).

LITERATURE REVIEW

Budd-Chiari Syndrome (BCS) is a rare condition which was first described in 1845 by Budd and later in 1899 by Chiari. They described clinical manifestations secondary to partial or complete obstruction of the venous outflow from the small hepatic veins to the hepatic portion of the inferior vena cava (1-4). Later, in 2003, the result of a consensus on the subject was published by a panel of experts who excluded from this definition obstructions caused by heart disease or tumor processes and sinusoidal obstruction syndrome. The new definition of the disease limits it to the result of obstruction of hepatic venous flow which can be located from the hepatic venules anywhere in the journey that the inferior vena cava makes until it arrives at the right atrium (5).

Budd-Chiari syndrome is classified as primary or secondary depending on the cause of the obstructive lesion. It is considered primary if the blockage is the result of an endoluminal venous injury, i.e. thrombosis, and secondary when the obstruction is due to extrinsic compression of the venous system or by invasion of a tumor (6, 7).

Similar to reports in articles such as that by Murad et al., the first case reported here had a myeloproliferative disease

which predisposed her to BCS (17-20). In the results of a study published in 2009, Murad et al. described the natural history of 163 patients diagnosed with BCS over a seventeen-month period during which they found that 84% of patients with BCS had at least one type of thrombophilia and that 49% of the patients had myeloproliferative disease (20). As in Case 1 reported above, of the Of the total study population of Murad et al., 56% were treated with TIPS, as was the first patient reported above. The one year survival rate was 87% and the two year rate 82% (20).

In 1989 Richter et al. first described the use of TIPS. Their patient was 49 year olds and had severe portal hypertension due to Child C cirrhosis. The procedure succeeded in reducing portal pressure from 38 mmHg to 18 mmHg. Since then, this technique has become an important treatment for portal hypertension complications and for BCS (21, 22). Many other studies describe positive results with the use of TIPS to treat BCS. One example is a study of twenty-one BSC patients by Perello et al. with a four year follow-up period. Nevertheless, another study of 237 patients with BCS by Murad et al. which was published in 2004 had more nuanced findings. The patients were classified into three groups: class I, class II and class III according to prognoses determined by evaluation of the presence or absence of encephalopathy, PT and bilirubin values. The study found that this invasive procedure was only successful for intermediate-risk patients (23-25).

Case 2 in this article is that of a patient whose only relevant personal medical history was the use of oral contraceptives, but she developed an acute case of BCS which led to severe clinical deterioration and death. The relationship between the BCS and the use of oral contraceptives has been studied since the 1980s. A case-control study published in 1986 by Valla et al. showed that patients who had recently taken oral contraceptives had a 2.37 times higher risk of developing thrombosis of the hepatic veins than did those who had not taken these medicines (26). It has been suggested that many patients who develop BCS after use of contraceptive or during pregnancy may have some form of subjacent thrombophilia (27, 28).

The cause of BCS in the patient in case 3 was a Factor V Leiden mutation. Some authors like Deltenre et al. state that it is unlikely that such mutations can produce isolated thrombosis in the absence of other congenital or acquired prothrombotic factors (29). Deltenre et al. make this argument on the basis of their finding that 20 (31%) of their 63 patients with CBS had factor V Leiden mutation, but 70% of those with Factor V Leiden mutations also presented one or more other risk factors associated with thrombosis (29). In case 3, the patient required liver transplantation, as in the cases reported by Avenhaus et al. (1999) and Tan et al. (2000) in which positive results were obtained with this technique. In the cases described by Avenhaus et al. and Tan et al., transplantation corrected thrombophilia since Factor V is primarily synthesized in the liver (30, 31). Similarly, a study that included 248 BCS patients from 51 European centers who underwent liver transplantation showed a one year survival rate of 76%, a five year survival rate of 71%, and a ten year survival rate of 68% (32). In this study 77% of the deaths occurred in the first three months, 47% as a result of infections and multiorgan failure and 18% as the result of graft failures or thrombosis in the hepatic artery. The main predictor of mortality was renal dysfunction (32).

Taking all of the above into account, our conclusion is that each particular case diagnosed with BCS requires individualized treatment related to the clinical stage of the disease. Anticoagulation is indicated in all cases, but other therapeutic options such as percutaneous placement of shunts and TIPS depend on the progression of the disease. Liver transplantation is the first therapeutic option when there is an underlying hematological factor, associated structural liver damage, or when the BCS develops suddenly. Proper post-transplant monitoring of these patients is also critical because of the necessity of maintaining INR in therapeutic ranges in order to prevent bleeding.

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