Upper Gastrointestinal Bleeding in a Young Patient with Budd Chiari Syndrome due to a Mutation of Factor V Leiden: A Case Report

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INTRODUCTION

Budd Chiari syndrome encompasses a group of disorders characterised by the obstruction of the hepatic venous outflow tract represented by the main hepatic veins and the inferior vena cava [1]. The venous obstruction can be partial or complete and it is caused by thrombogenic conditions or non thrombotic factors. The most common presentation of Budd Chiari syndrome is linked to a hypercoagulable state secondary to variate factors, both hereditary and acquired, a condition encountered frequently in hematological diseases [2]. Among the acquired hematological abnormalities, myeloproliferative disorders are the most frequent etiology, particularly polycythemia vera that accounts for 10-40% of cases of the syndrome; less prevalent causes are antiphospholipid syndrome, and paroxysmal nocturnal hemoglobinuria [3].

Hereditary conditions responsible for hypercoagulability in Budd Chiari syndrome are deficiencies of protein C, protein S, antithrombin III with levels below 10-20% of normal [2] and also factor V Leiden mutation. Inherited thrombophilia that results subsequently in these abnormalities may be responsible for thrombotic events in other areas such as coronary circulation. The risk of myocardial infarction related to factor V Leiden mutation causing resistance to activated protein C is well recognized and should promptly alert genetic testing of the affected family members and initiate appropriate prophylaxis [4]. Uncommon etiologies for Budd Chiari syndrome are tumoral invasion from hepatocellular or renal cell carcinoma, the so-called secondary Budd Chiari syndrome, and at the same time inferior vena cava webs or Behcet’s disease [2]. Multiple causes of thrombophilia could be associated in the same patient [5]. The clinical presentation is usually dominated by abdominal pain, hepatomegaly and ascites [6]. Sometimes the onset of the disease is marked by the complications of portal hypertension, the most severe but fortunately less common appears to be gastrointestinal bleeding from esophageal variceal rupture [7, 8]. The diagnosis of Budd Chiari syndrome is challenging and a great deal of care should be taken to reach it. Doppler ultrasound examination establishes the diagnosis showing no blood flow or retrograde flow in one of the hepatic veins; less prevalent causes are antiphospholipid syndrome, and paroxysmal nocturnal hemoglobinuria [3].
veins, absence of visualization of a hepatic vein or demonstrates the presence of thrombotic material inside the lumen of the vein [9]. The management of Budd Chiari syndrome caused by a prothrombotic disorder is based on a “step by step” approach: first anticoagulation, then angioplasty, followed by TIPS in cases that do not respond to previous measures, and eventually liver transplantation [8].

CASE REPORT

A 32-year old man was admitted to our hospital as an emergency for upper gastrointestinal bleeding expressed through massive hematemesis. No liver disease, ulcer or other digestive condition was known until that moment. He stated that he was a former cigarette smoker but no alcohol abuse was noted.

His past medical history was relevant for heart disease. The patient suffered an anteroseptal acute myocardial infarction at the age of 20, thrombolyzed with streptokinase, followed by a favourable outcome. His family history was unremarkable for coronary artery disease and the hematological investigations performed for inherited thrombophilia were negative for protein C, S and antithrombin III deficiency and also for anti-cardiolipin antibodies. No risk factors for acute coronary syndrome were present, except for cigarette smoking. One year after the first episode of heart attack, the patient presented with unstable angina, with diffuse ischemic changes on the ECG and without serum enzyme kinetics typical for myocardial injury. The coronarography identified permeable coronary arteries and an apical left ventricular aneurysm was considered as an infarction sequela. At that time he was free of cardiac symptoms, with no exertional dyspnea or coronary pain.

At the moment of presentation to our clinic, the physical examination revealed a hemodynamically unstable patient, with tachycardia, mild pallor and cold sweat. He had neither fever nor jaundice. The abdominal examination revealed a nontender, nondistended abdomen, with no pain and normal bowel sounds. Hepatomegaly and splenomegaly were detected, but no abdominal palpable masses. Laboratory data showed mild normochromic normocytic anemia (Hb 10 g/dl) and mild thrombopenia (PLT 121,000/mm³); viral markers for hepatitis B and C were negative. Upper digestive endoscopy was performed as an emergency and identified the source of bleeding. Grade III esophageal varices with stigmata of recent bleeding, cherry-red spots were detected and esophageal band ligation was performed in order to obtain an effective hemostasis. No other episodes of bleeding were noted following the procedure.

Further investigations were required for clarifying the etiology of the gastrointestinal bleeding. Abdominal ultrasound showed hepatomegaly with hypertrophy of the caudate lobe (anteroposterior diameter 57 mm) with inhomogeneous hepatic echostructure, splenomegaly and abnormal visualization of the suprahepatic vein system, with no evidence of blood flow in the right suprahepatic vein and stenosis of the left suprahepatic vein at Doppler examination (Figs. 1-3). These changes were suggestive for Budd-Chiari syndrome. Additional imaging procedures were done. The abdominal CT scan confirmed the ultrasound findings. Based on paraclinical data, correlated with the clinical signs of portal hypertension expressed through upper gastrointestinal bleeding, Budd Chiari syndrome was diagnosed. Taking into account the patient’s medical history of myocardial infarction with onset at a young age associated with the newly diagnosed Budd Chiari syndrome, an inherited
trombophilia was suspected and specific hematological tests were ordered. Molecular genetic analysis was performed and the heterozygosity for mutation of factor V G1691A (Leiden) was detected, indicating a high risk for trombophilia. This abnormality of blood coagulation was thought to be the etiological factor of the thrombotic disease, first leading to myocardial infarction, and then to the present hepatic outflow obstruction, probably due to a clot in the hepatic vein. The patient started anticoagulation therapy with dicoumarin formulations and was then referred to the hematological department for follow-up.

**DISCUSSION**

Budd Chiari syndrome represents a complex disorder characterised by hepatic outflow obstruction localized at any level from the hepatic veins to the right atrium [10]. Several factors are incriminated in the etiology of this rare condition, but acquired and inherited thrombophilias are considered the most frequent causes [9]. A background of hypercoagulability is found in the majority of patients. Hematological diseases represent the main causative factor, especially myeloproliferative conditions that affect 50% of patients with Budd Chiari syndrome [10, 11]. An association of potential causal factors can be identified in 25% of cases [3, 9]. When an inherited prothrombotic disorder is taken into account, deficiencies of protein C, protein S, antithrombin III or factor V Leiden mutation should be suspected [2].

As we noticed in the presentation, our patient exhibited heterozygosity for factor V Leiden mutation, that explained the underlying prothrombotic state which was responsible for the thrombotic events, both the myocardial infarction and Budd-Chiari syndrome.

When the suspicion of Budd-Chiari syndrome is raised, secondary causes such as tumoral invasion, extrinsic compression of the hepatic outflow tract, inferior vena cava webs should also be ruled out [2, 8]. These possibilities were excluded from the differential diagnosis based on the imaging studies, abdominal ultrasonography and CT scan. So, further investigations were focused on identifying a prothrombotic disease by performing the genetic analysis that showed the coagulation defect already mentioned in this issue. The onset of Budd-Chiari syndrome with upper digestive bleeding is less commonly encountered in clinical practice and a high index of suspicion was needed to establish the diagnosis in our case. The typical presentation of Budd-Chiari syndrome includes ascites, abdominal pain, leg edema, symptoms that were absent in our patient. Upper digestive hemorrhage is commonly a manifestation of chronic liver disease, which was excluded from the differential diagnosis based on patient's history, clinical examination associated with laboratory assessment, namely the absence of viral markers, and the ultrasonographic findings. The diagnosis of Budd-Chiari syndrome is confirmed through imaging studies, that reveal hepatic vein obstruction at Doppler examination. Specific features are considered a turbulent or reversed flow in the hepatic vein, visualization of hepatic collaterals or flat hepatic vein wave form [8]. The absence of visualization of hepatic veins and the caudate lobe hypertrophy as an indirect sign are commonly observed in Budd-Chiari syndrome, but are not specific for this condition, because they can be noticed also in other chronic liver disease [8]. These latter elements, correlated with the underlying trombophilia, helped to establish the diagnosis in our patient.

**CONCLUSION**

Indefinite anticoagulant therapy represents the mainstay of treatment in patients with primary Budd-Chiari, including the case presented. In cases that do not respond to medical therapy, TIPS has been attempted, with favourable outcome, and liver transplantation performed as a salvage therapy.

**Conflicts of interest:** No conflict to declare.

**REFERENCES**


