Budd-Chiari Syndrome: Rare Cause, But Important of Portal Hypertension

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Budd-Chiari syndrome (BCS) (artery-occlusive hepatic disease) is a rare disease characterized by the obstruction of the blood flow at the level of the suprahepatic veins till their flow in the inferior vena cava (IVC) or at the level of IVC on the segment between the suprahepatic veins and the right atrium. The most frequent symptoms are abdominal pains, hepatomegaly and ascites. The imagistic investigations have an essential role in the early establishment of the diagnostic, evaluating the extension of disease and the management of BCS. Treatment depends on the presence or absence of symptoms and how acute the disease is.We present the case of a 43-years old woman, who had had for two month dyspeptic symptoms, increase of volume of the abdomen and oedema in the lower limbs. The biological investigations indicated hepatic dysfunction and thrombocytosis. The abdominal ultrasound showed modifications of chronic hepatopathy with signs of portal hypertension. The abdominal computer-tomography emphasized hepatomegaly with multiple nodules of regeneration, signs of portal hypertension (splenomegaly, moderate ascites), caudate lobe hypertrophy and thrombosis IVC. The patient was diagnosed with BCS and essential thrombocythemia. She started the medical treatment and was listed for liver transplantation. Budd-Chiari syndrome has to be taken into account every time we investigate the etiology of an acute or chronic hepatopathies, because the early diagnose can improve the patient's prognostic.

*Keywords: Budd-Chiari syndrome, ascites, portal hypertension, hepatic vascular diseses, essential thrombocythem*ia

Budd-Chiari syndrome (BCS) is a rare form of vascular hepatic illness. It was reported for the first time in 1845 by George Budd, when he described the classical symptom triad consisting in abdominal pains, hepatomegaly and ascites, and in 1899, Hans Chiari presented the histopathological characteristics of the syndrome [1, 2]; it is also called hepatic vein-occlusive disease or the Rokitansky syndrome.

BCS is defined as hepatic vascular obstruction at any level of the suprahepatic veins until their junction with IVC and at the level of IVC until the right atrium, regardless of the aetiology of the obstruction. BCS is considered to be primary when the vein blocking is intrinsic and secondary in case the obstruction or compression of the vein is produced from its exterior. This complex disease presents a wide range of aetiologies and clinical manifestations [3]. BCS can manifest as an acute or chronic hepatic disease, asymptomatic or severe. The myeloproliferative syndrome is met in 50% of the cases, being sometimes associated with other conditions, such as infections and neoplasias. The most frequent symptoms are abdominal pains, hepatomegaly and ascites. Nonetheless, up to 20% of the cases are asymptomatic, which suggests an insidious debut of the hepatic vein obstruction and the formation of hepatic vein collateral circulation [4]. Regardless of the cause of the hepatic vein blood flow obstruction, it is produced the rapid increase of hepatic sinusoidal pressure and portal hypertension, determining vein congestion and ischemic injury of the adjacent sinusoidal hepatocytes. If pressure in the hepatic sinusoids does not decrease, by therapeutic interferences or by developing a collateral vein circulation, then the following appear: nodular regeneration, fibrosis and finally cirrhosis [5]. Imagistic investigations such as hepatic Doppler ultrasound and abdominal computer-tomography (CT) decide the diagnostic in most cases [6]. Management of BCS consists in a gradual strategy.

Treatment comprises anticoagulation on long term associated with measures that try to remake the blood flow in the thrombosed vein (thrombolysis or angioplasty) or with procedures of interventional radiology (they are porto-systemic trans-jugular intra-hepatic) or surgical (by-pass surgical). Surgical treatment has limited indications, but important, especially in the cases with obstruction at the level of IVC, which do not apply for endovascular treatment; nonetheless, the prognostic is often sombre. Orthotopic hepatic transplant represents the ideal therapy [7, 8].

Experimental part

Material and methods

Case presentation

We present the case of a patient aged 43, who was hospitalised for pains in the right hypochondrium, nausea, loss of appetite, abdominal distension and oedema in the inferior limbs appeared a couple of months ago. The patient denied having smoked, the consumption of alcohol, medicine, contraceptive, antecedent in blood transfusion, personal pathologic antecedents or family history in digestive diseases or thrombosis.

Results and discussions

Portal hypertension by post-sinusoidal extra-hepatic block is the consequence of a chest vein stasis and can be

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found, apart from Budd-Chiari syndrome, in *concretio pericardii* and in right heart failure.

Intra-hepatic cirrhotic structural alterations and portal hypertension that results can cause hemodynamic modifications, both in hepatic circulation and in the systemic one.

The physical examination showed malnutrition, oedema in the lower limbs, increase in abdomen volume with dullness slapper on sides and parietal vein collateral circulation, painful hepatomegaly at 3 cm under the right costal splenomegaly degree I.

Investigations in the laboratory underlined non-specific inflammatory syndrome (increase ESR 70 mm/L h), normal values of haemoglobin (12.5 g/dL, normal values 12-14 g/dL) and leucocytes (9.600/mm^3, normal values 4000-10000/mm^3), thrombocytosis (558000/mm^3, normal values 150000-400000/mm^3), slight increase of transaminases (AST 53 UI/L, ALT 48 UI/L, normal values 0-40 UI/L), gammaglutamyl-transferase (GGT 103 UI/L, normal values 11-40 UI/L), alkaline phosphatase (FA 395 UI/L, normal values 98-280 UI/L), blood urea (54 mg/dL, normal values 15-44 mg/dL) and normal serum albumin (3.92 g/dL, normal values 3-5 g/dL). Electrophoresis of serum proteins detected a polyclonal hypergammaglobulinemia. Antigen HBs, antibodies antiVHC, antinuclear antibodies (ANA), hepatic anti-cytosol (anti-LC), anti smooth muscles (ASMA), antimitochondrial (AMA) and hepatic and kidney anti-microsomes (LKM-1) were negative. Tests for the assessment of the iron profile and the ceruloplasmin were normal. Carcinoembrionar antigen (CEA), alpha-fetoprotein (AFP), CA19-9 and CA125 had normal values. Rheumatoid factor, reaction latex Waaler-Rose, antibodies anti-ADN- double stranded, anti-phospholipid antibodies were negative. The research of a possible state of hypercoagulable nature associated infirmed the mutation of the factor V Leiden, and the levels of protein C and S were normal. The exploratory paracentesis underlined a liquid of ascites serocitrin, with total protein 3.6 g/dL, albumin 2.14 g/dL, gradient of albumin serum-ascites (SAAG) 1.78 g/dL, adenosine deaminase of 17.1 UI/L (normal values 10-33 UI/L), glucose 109 mg/dL, 5 cells/mm^3, absence of Koch bacillus and malign cells, negative culture.

Abdominal ultrasound showed moderate ascites, hepatomegaly with heterogeneous eco-structure and hypertrophy of the caudate lobe (fig. 1).

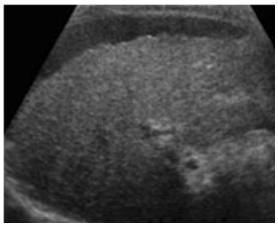

Fig. 1. Abdominal ultrasound showed hepatomegaly with non-homogeneous eco-structure and ascites

Computer-tomography of the abdomen showed hepatomegaly with multiple nodules of regeneration, signs of portal hypertension (splenomegaly, moderate ascites), hypertrophy of the caudate lobe and thrombosis IVC (fig. 2).

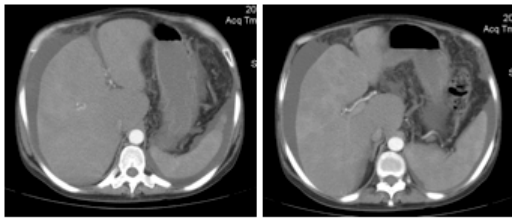

Fig. 2. Computer-tomography of the abdomen showed hepatomegaly with multiple nodules of regeneration, signs of portal hypertension (splenomegaly, moderate ascites), hypertrophy of the caudate lobe and thrombosis IVC

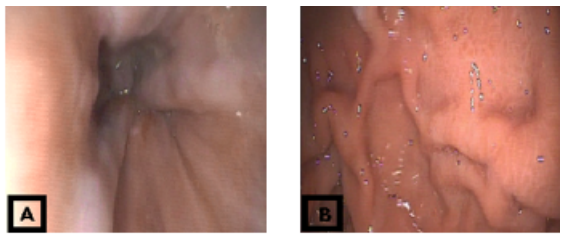

Fig. 3. Upper digestive endoscopy showed: A) esophageal varices degree II; B) portal-hypertension gastropathy

Upper digestive endoscopy showed esophageal varices degree II and portal-hypertension gastropathy (fig. 3).

Patient was diagnosed with BCS, and the hematologic evaluation resulted in the diagnostic of essential thrombocythemia (ET), based on bone marrow biopsy and the results of the molecular tests.

It was initiated the anticoagulant treatment associated with diuretics and beta-blocking. The patient received at the beginning heparin with low molecular weight, then the antagonists of vitamin K (Acenocumarol), in order to obtain and maintain the INR between 2 and 3. In a short while, the patient developed refractory ascites, complicated with an episode of spontaneous bacterial peritonitis with Staphylococcus aureus Methicillin-sensitive (SAMS) treated efficiently with azithromycin. At the moment, the patient is under anticoagulant treatment, being monitored gastroenterologic and hematologic. Also, the patient was assessed and inscribed on the waiting list for hepatic transplant.

BCS is a hepatopathy characterized by hepatic vein obstruction, which in most cases is due to the suprahepatic vein thromboses or inferior vena cava. It causes hepatic congestion, ascites, portal hypertension and collateral circulation developed between the occluded segment and the adjacent vein territories [9].

BCS is a rare disease, but with severe prognostic. Prevalence of BCS varies from one geographical area to the other. Thus, if BCS is more frequent in certain Asian countries, the disease is rare in the western countries, where the annual incidence is about 1/2.5 million inhabitants [10, 11].

Pathogenesis of BCS is incompletely clarified, but it seems to be a multi-factorial disease. The factors that cause BCS include chronic myeloproliferative syndromes (MPS), such as polycythemia vera, ET, paroxysmal nocturnal hemoglobinuria, hematologic and liver metabolic abnormalities, such as deficit of antithrombin, protein C and protein S, resistance to protein C activated, mutation of factor V Leiden, mutation G20210A of the gene that codifies the factor II, neoplasias, administration of oral contraceptive, pregnancy and the period of postpartum. The most frequent factor of risk prothrombotic is MPS, even if it was proved that almost half of the patients have multiple factors of risk prothrombotic [12-14]. Among the factors that cause it mentioned above, ET is associated with high risk of deep vein thrombosis. At the same time, ET is one of the most frequent MPS that determine BCS, and in some cases it can be the initial manifestation of this syndrome [9, 15-17]. In the case presented, the patient presented as risk factor for BCS a myeloproliferative

disorder (essential thrombocythemia), without having antecedent of deep vein thrombosis.

Ascites, hepatomegaly and abdominal pains form the classical triad of BCS produced by suprahepatic vein thrombosis or IVC. The clinical manifestations less frequent include the digestive haemorrhage by intrusion of esophageal varices (5%) and hepatic encephalopathy (9%) [11]. Nonetheless, it is surprising the fact that about 20% of the patients are asymptomatic [18]. The clinical manifestation of BCS can be acute or chronic: a) the acute form is produced by acute thrombosis of the hepatic veins or IVC, when the debut is sudden, by the appearance of ascites; b) the chronic form is determined by the fibrosis of the intra-hepatic veins, probably by inflammatory mechanism. Our patient presented a chronic form of disease manifested clinically by the triad: abdominal discomfort, hepatomegaly and ascites. A particularity of the case was the complicated evolution with an episode of spontaneous bacterial peritonitis produced by Staphylococcus aureus Methicillin-sensitive (SAMS) treated efficiently with azithromycin.

Usually, in BCS the modifications of the biochemical tests are non-specific, and in 25-50% of the cases there is slight increase of transaminase and alkaline phosphatase. Ascites liquid has a gradient of albumin serum-ascites increased (SAAG> 1.1 g/dL) and high content in proteins (> 2.5 g/dL), similar to ascites in heart diseases [1].

The imagistic features characteristic to BCS, detected by CT, imagistic by magnetic resonance (IRM), ultrasound and angiography, are the occlusion of the hepatic veins, IVC, or both (18-53% of the cases), the hypertrophy of the caudate lobe, non-homogenous aspect of the liver, the presence of the intra-hepatic collateral circulation and the nodules of regeneration, hyper-vascularized [19, 20]. The identification of these aspects is essential to decide the early diagnostic and initiate proper treatment. In the case presented, the abdominal ultrasound presented modifications of chronic hepatopathy with signs of portal hypertension, and the abdominal CT showed hepatomegaly with multiple nodule of regeneration, signs of portal hypertension, hypertrophy of the caudate lobe and thrombosis IVC, giving the diagnostic BCS.

The main objectives of the treatment are to improve the hepatic congestion and prevent the subsequent thrombosis. Management of BCS, from medical treatment to hepatic transplant, is done according to the clinical form of the disease (acute or chronic) and the degree of hepatic insufficiency. The therapeutic measures can be divided into three major categories: medical, surgical and endovascular [21]. The initial therapeutic strategy includes anti-coagulation, correcting the risk factors, diuretics and prophylaxis of portal hypertension; then it follows the angioplasty for the short vein obstructions, then the transjugular intrahepatic portosystemic shunt and at the end the hepatic transplant indicated in the patients presenting the worsening of the clinical evolution, to those reticent to the medical treatment and/or the interventional radiologic treatment [22, 23]. In clinical practice, overcoming the therapeutic resources is guided by the response to the previous treatment. The progress recorded during the last three decades in the management of BCS has improved significantly these patients' survival, reaching a quota of survival for five years of 80-90%. The prognostic on medium term depends on how severe the hepatic disease is [11, 24-26]. In some cases, on long term, the evolution of BCS can be complicated by the recurrence or progression of MPS associated, or the development of the post-transplant lymphoma in patients with transplant who require immune-suppressor treatment [7, 12]. The anticoagulant therapy with oral antagonists of vitamin K, as well as acenocoumarol or warfarin, represent the first line of treatment in BCS secondary to the obstruction IVC and ET [27]. It seems that there is no difference in respect of the efficiency of glycosaminoglycans (unfractionated heparin or heparin with small molecular weight (LMWH), comparing with the antagonists of vitamin K [28]. Zaman and collab. reported a worrying percentage of thrombocytopenia induced by heparin in BCS treated with unfractionated heparin comparing with other therapeutic indications (28.1%, versus 0.2-5.%) [29]. The advantages of the new oral anticoagulants (that inhibit selectively either thrombin (dabigatran etexilate) or factor Xa (rivaroxaban, apixaban), related to rapid action, the predictable pharmacokinetic and pharmacodynamic properties, lack of food or medicine interactions and relatively high therapeutic diversity, the fact that it does not require monitoring the coagulation, makes them preferred in the detriment of oral antagonists of vitamin K. In the case presented, the anticoagulant treatment was initiated with HGMM, followed by acenocoumarol, which the patient continued to take after leaving the hospital. The patient is currently following anticoagulant treatment and was inscribed on the waiting list for hepatic transplant.

After the diagnostic BCS, we must assess the prognostic factors before deciding on the therapeutic strategies. Thus, the following prognostic factors have been identified: rapidity of installation and degree of extension of the occlusion at the level of the hepatic veins, how severe the subjacent hepatic disease is, and the presence of hepatic decompensation [5]. The additional prognostic factors include age, the score Child-Pugh, the score MELD, presence of ascites, serum creatinine, as well as the presence of modifications that indicate acute injuries overlapped on the chronic injuries at the moment of diagnostic [30].

Conclusions

Budd-Chiari syndrome is a less frequent disease, where the strategy of the diagnostic and the success of the therapy are essential for the patient's survival. It is important to take into account this diagnostic in patients who present signs or symptoms of obstruction hepatic vein flow, such as painful hepatomegaly, ascites suddenly installed or refractory. The complete screening of the states of thrombophilia must be carried out at all the patients with diagnostic BCS. Also, we must carry out in-depth investigation to identify the cause of the hepatic vein flow obstruction. Hepatic ultrasound Doppler and CT abdominal allow to decide the diagnostic in most cases. Knowing the clinical manifestations and the imagistic characteristics contribute to deciding the correct diagnostic, on taking into account the fact that the early diagnostic of the disease has a major impact on the patient's management. The treatment of this disease requires a multi-disciplinary approach.

APPROVAL: To publish this case presentation and the images associated, we obtained the patient's written informed approval.

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Manuscript received: 21.11.2016