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CAUSAL LINK BETWEEN BUDD-CHIARI SYNDROME AND POLYCYTHEMIA VAQUEZ: CASE REPORT AND REVIEW OF THE LITERATURE

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ABSTRACT

The aetiologies of Budd-chiari syndrome are multiple dominated by myeloproliferative syndromes, present in 50% of carriers of primary SBC. Myeloproliferative syndromes group together several pathologies, namely polycythemia vera, essential thrombocythemia and myelofibrosis. The PV is the entity most frequently associated with a primitive SBC. The blood count abnormalities are often masked by portal hypertension in splanchnic thrombosis. The diagnosis of polycythemia vera is based on BMB and the therapeutic management must be multidisciplinary using hematology, gastroenterology and cardiology in order to manage anticoagulants on the one hand and the complications of portal hypertension on the other hand.

KEYWORDS: Budd-Chiari syndrome, myeloproliferative syndrome, polycythemia vera.

Abbreviations

SBC : Budd-chiari syndrome
PV: polycythemia vera
BMB : Bone Medullary Biopsy
PMS: myeloproliferative syndromes

INTRODUCTION

Budd Chiari syndrome results from obstruction of the hepatic venous drainage, from the hepatic venules to the terminal part of the inferior vena cava, resulting in progressive hepatic fibrosis with hepatomegaly and portal hypertension. One or more thrombogenic conditions are usually present, the most frequent of which is polycythemia vera with a prevalence of 30 to 50%.[1]

The association between Budd-Chiari syndrome and polycythemia vera was first described by Fitzgerald and al in 1956.[2] This combination poses a diagnostic problem, because the abnormalities of the blood count are masked by hypersplenism and a therapeutic problem due to the management of anticoagulants, especially in cirrhotic patients.

We will study this association through an case report and treat it in the light of data from the literature.

CASE REPORT

40-year-old patient, followed for a year for polycythemia of vaquez treated by Hydroxycarbamide Cureaml * 500mg /d, admitted to the gastroenterology department for management of abdominal distension evolving for a month in a context of apyrexia and preservation of general condition.

Clinical examination found moderate ascites with edema of the lower limbs taking the scoop, splenomegaly and conjunctival sub-jaundice without other signs of hepato-cellular insufficiency.

The results of the cytobacteriological and chemical study of ascitic fluid are shown in the following table (Table 1):

Table 1: analysis of ascites fluid.

Aspect	Trouble
Protein	23.4 g/l
White-blood cells	320/mm3
Neutrophils	192/mm3
Lymphocyts	128/mm3
Direct examination	Negative
Culture	Sterile

An abdomino-pelvic CT scan performed objectifying.

- A dysmorphic liver with crenellated contours and hypertrophy of the left liver
- Portal trunk increased in caliber measuring 15 mm
- Splenomegaly measuring 18 cm homogeneous
- Peritoneal effusion of moderate abundance

Doppler ultrasound was performed to show thrombosis of the median and right hepatic veins in favor of Budd-Chiari syndrome.

Biological analysis objectified a hemoglobin at 16.8 g / dl with a hematocrit at 55% the rest of the analysis is shown in table 2.

Table 2: results of the biological assessment.

Hemoglobin	16.8g/dl
Hematocrit	55%
Red cells	6.8 x106/mm3
White cells	12760/mm3
Neutrophils	11360/mm3
Lymphocyts	1400/mm3
Platelets	392.000
Transaminases ASAT	131 UI/l
Transaminases ALAT	97UI/l
Gamma GT	185UI/l
Alkaline phosphatase	239UI/l
Total bilirubin	44.9 UI/l
Conjugate bilirubin	34.8 UI/l
Prothrombin rate	49%
Albumine	32.8g/l
Uree	0.28
Creatinine	5.2
Soduim	132
Potassium	3.1

In the light of these results, the diagnosis of hepatic cirrhosis classified as CHILD C10, MELD 17 at the portal hypertension stage was retained, the etiology is very probably secondary to polycythemia, however an etiological assessment was requested revealed negative (serology HVB, HVC and autoimmune hepatitis).

The therapeutic goal was to manage ascites as well as to look for complications of cirrhosis.

Concerning ascites, the patient was treated by diuretics with good efficacy and tolerance, a fibroscopy had objectified VO guard I without red signs with the appearance of hypertension gastropathy.

Our patient had no HCC with AFP negative at 2 and absence of hepato-renal syndrome, hepato-pulmonary syndrome, no malnutrition or hepatic encephalopathy.

The patient is put on an anticoagulant treatment based on low molecular weight heparin backed up by anti-vitamin K.

DISCUSSION

The aetiologies of Budd-chiari syndrome are multiple dominated by myeloproliferative syndromes, present in 50% of carriers of primary SBC.[1] Therefore they must be systematically retrieved.

Myeloproliferative syndromes group together several pathologies, namely polycythemia vera, essential thrombocythemia and myelofibrosis. The PV is the entity most frequently associated with a primitive SBC.

After the myeloproliferative syndromes, other pathologies can be incriminated in the genesis of a SBC namely the syndrome of the primary anti-phospholipid antibodies, the isolated deficiency in protein C, in protein S, and in antithrombin III, or a mutation of the factor V Leiden.[3]

Other causes are more rarely incriminated: paroxysmal nocturnal hemoglobinuria, Behçet's disease, celiac disease, sarcoidosis or even hypereosinophilia syndrome. As a result, SBC is considered to be a multifactorial disease since two thrombogenic factors are found in 50% of SBC.[4]

The main short-term risk of PMS is arterial and / or venous thrombotic risk, with a reported incidence of up to 40%.[5]

The pathophysiology of thrombosis is multifactorial: platelethyperaggregability, hyperviscosity, inflammation, acquired resistance to activated protein C and increased thrombin generation, activation of endothelial cells.[6-8] At the hepatic level, endothelial cells, carriers of the JAK2 mutation have been described.[9]

Abnormalities in the blood count are often masked by portal hypertension in splanchnic thrombosis.[10] a circulating platelet count greater than 200,000 / mm3 and a splenomegaly greater than 17 cm is an argument in favor of myeloproliferative syndrome in a context of portal hypertension.

A meta-analysis published in 2012 reported a prevalence of PMS and the JAK2 V617F mutation, respectively, of 40.9% and 41.1% in patients with SBC and of 31.5% and 27.7% in patients with TVPEH.[11] In patients without CBC abnormalities suggestive of SMP, testing for the JAK2 V617F mutation identifies an underlying SMP in 17.1% of patients with SBC. It is therefore recommended to include the search for the JAK2 V617F mutation in the first-line examinations to be performed in patients with splanchnic thrombosis.[12]

Confirmation of the diagnosis of polycythemia vera is done by

- Bone medullary biopsy which will note clusters of megakaryocytes and panmyeloid hypercellularity, and which will also allow the detection of endogenous erythroid colonies with spontaneous growth, which is an important argument for the diagnosis of occult PV.
- The demonstration by allele-specific PCR of the JAK2 mutation observed in 61% to 97% of patients with polycythemia vera. This JAK2 mutation is the primary molecular event leading to the development of PV.

  The diagnosis of a myeloproliferative syndrome as the etiology of a primary SBC helps guide treatment modalities.

In the acute phase, anticoagulant treatment for splanchnic thrombosis does not differ, whether or not there is an underlying PMS. It is recommended to use low molecular weight heparins (LMWH), and not unfractionated heparins (UFH) in view of the risk of heparino-induced thrombocytopenia, especially in this category of patients.

Effective anticoagulation should be continued for the long term, or even for life.[13] Some patients with splanchnic thrombosis are candidates for liver transplantation. the presence of PMS does not affect survival after liver transplantation, but increases the risk of thrombotic and hemorrhagic complications.[13, 17]

Aspirin is usually indicated for the prevention of arterial cardiovascular risk in polycythemia vera or essential thrombocythemia.

The occurrence of thrombosis during PMS is an indication for cytoreductive therapy[18]: the combination of cytoreductive and anticoagulant therapy improves survival and decreases the risk of hepatic complications in patients with splanchnic thrombosis.[19]

The proposed cytoreductive therapy may be hydroxyurea, interferon alpha, or ruxolitinib.[18,20] Outside of a context of splanchnic thrombosis, the goal of cytoreductive therapy is hematocrit below 45% and platelets below 400,000 / mm3.[21]

During splanchnic thrombosis, blood count may be normal despite confirmed PMS. The treatment objectives are more stringent taking into account hypersplenism and hemodilution, therefore a hematocrit of less than 42% and platelets less than 250,000 / mm3.[22]

Percutaneous angioplasty techniques with or without endovascular prosthesis with or without thrombolysis at the sites of obstruction by fibrous stenosis of the hepatic veins and / or the inferior vena cava, make it possible to control the manifestations of the syndrome by Budd Chiari (digestive hemorrhage, ascites, functional renal failure). In the event of ineffectiveness of the above-mentioned means, the establishment of a portosystemic intrahepatic shunt (TIPS) should be considered.[23]

CONCLUSION

The causal link between SBC and SMP is a fairly frequent phenomenon in gastroenterology, the chief of which is polycythemia vera. The diagnosis is based on BOM and the therapeutic management must be multidisciplinary involving hematology, gastroenterology and cardiology.

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