

# Budd-Chiari Syndrome Secondary to Polycythemia Vera. A Case Report

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## Abstract

Budd-Chiari syndrome still represents a challenge for the hepatologist with regard to its causes and its most effective therapy. Polycythemia vera is considered to be the most frequent condition causing the Budd-Chiari syndrome (10-40% of cases). We present a 34-year-old patient in post-partum who was admitted for right upper abdominal quadrant pain and asthenia. Laboratory data, abdominal echography and angioMRI all raised the suspicion of BCS, but it was in the haematological department that polycythemia vera was diagnosed as the cause of the hepatic condition.

## Key words

Budd-Chiari syndrome – polycythemia vera.

## Introduction

Budd-Chiari syndrome (BCS) represents a rare hepatic condition characterized by vascular obstruction of the efferent hepatic flow at a site that may vary from the small hepatic veins up to the place where the inferior vena cava enters the right atrium [1].

## Case presentation

A 34 year old patient was admitted to the 3rd Medical Clinic, Cluj-Napoca, in January 2008 for right upper abdominal quadrant pain and asthenia. She had no relevant personal history, and no smoking or alcohol abuse in her past. Her family history revealed a mother with liver cirrhosis and ischemic heart disease. The patient had given birth three months before and was still breastfeeding her child. She recalled having had similar symptoms before her pregnancy,

but they had worsened during pregnancy. A more complex evaluation in a specialized center after child delivery was then recommended.

She was in the third month post-partum when she was admitted to our clinic. The physical examination showed palmar and facial erythema, important and firm hepatomegaly, and splenomegaly.

Laboratory data indicated polyglobulia (Hb= 17.1g/dL, Ht= 51.5%), thrombocytosis (PLT= 517,000/mm<sup>3</sup>), coagulation abnormalities (Quick Time= 24sec, prothrombin index= 46.3%, INR=1.58, APTT= 43.7sec), hepatocytolysis (AST= 49IU/l, ALT= 49IU/l) and cholestasis (FA= 491 IU/l, GGT= 150 IU/l), normal ceruloplasminemia and normal renal function tests. Viral markers and immunological tests (autoantibodies) were negative.

Abdominal ultrasonography showed marked hypertrophy of the caudate hepatic lobe and a very inhomogeneous structure of the left hepatic lobe, which had an irregular capsular line (Fig. 1). The suprahepatic vein presented a stenosis (Fig. 2). The right hepatic lobe could not be visualized (possible atrophy?), the right portal vein was also not visible, the portal vein axis was dilated; only the median suprahepatic vein could be seen with monophasic flow at the power angio examination (Fig. 3). Other findings were: collateral vessels between the tributary territory to the hepatic vein and those tributary to the left and right lobes, multiple vascular tracks in the caudate lobe which led to the inferior vena cava, congestive splenomegaly with important collateral circulation at the hilum, and a small quantity of ascites in the pelvis.

The upper digestive endoscopy indicated the presence of 1st degree esophageal varices and no signs of portal hypertensive gastropathy. Budd-Chiari Syndrome was suspected.

The angioMRI performed at the Clinical Institute Fundeni, Bucharest described: pseudotumoral hypertrophy of the caudate lobe, the segments II, III and IV, pronounced hypotrophy of the right lobe (Figs. 4, 5), inhomogeneous hepatic structure. The 3D postcontrast examination revealed a heterogeneous stained image of “confluating snowballs” and only the median hepatic vein and the precaval segment

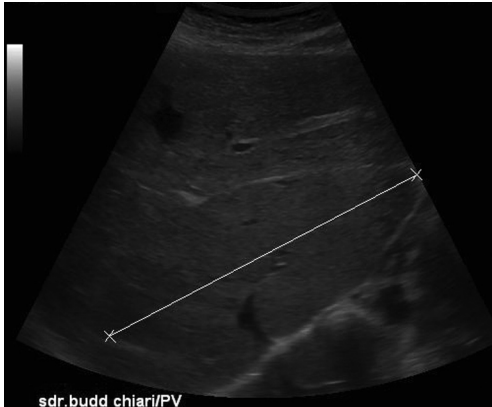
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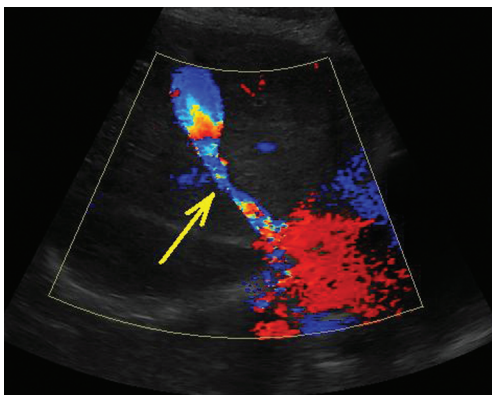
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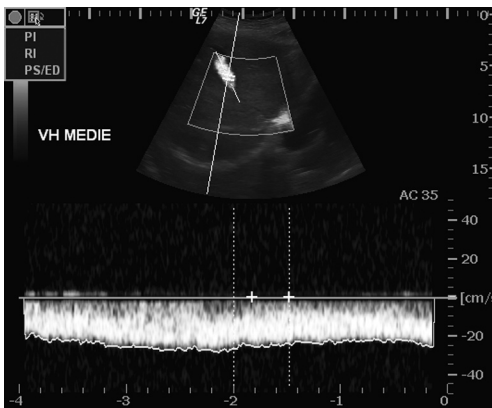
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**Fig 1.** Ultrasound examination of the liver in sagittal section: important hypertrophy of the caudate lobe and of the left hepatic lobe.



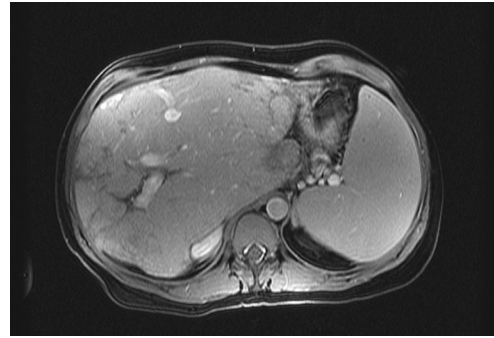
**Fig 2.** Colour Doppler US examination: only the median suprahepatic vein is visible with a stenosis (arrow).



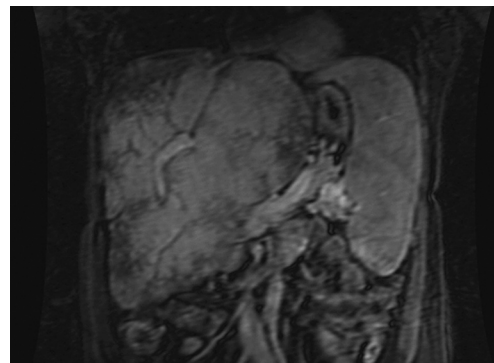
**Fig 3.** Pulsatile Doppler examination: monophasic flow in the median suprahepatic vein.

of the right superior hepatic vein were visible. There was an important collateral circulation which replaced the one in the caudate lobe, with direct flow into the inferior vena cava and the dilatation of porto-spleno-mezenteric axis and important splenomegaly.

Abdominal CT scan with contrast confirmed asymmetrical hepatomegaly, with the hypertrophy of the left and caudate lobe and hypotrophy of the right hepatic lobe, inhomogeneous structure with multiple nodular structures. Venous ultrasound in real time in axial section did not



**Fig 4.** Axial T1-weighted MRI section with contrast: global hepatomegaly with important hypertrophy of segments I, II and III. Marked hypotrophy of the right hepatic lobe.



**Fig 5.** Coronal T1-weighted MRI section plus contrast plus fat saturation: alternations in hepatic perfusion, macronodular aspect. Global hepatomegaly, splenomegaly, collateral circulation.

visualize the hepatic veins. On reconstituted coronal and sagittal images, short paths of the juxtacaval hepatic veins were visible (Figs. 6, 7).

The haematological investigation revealed the bone marrow (osteomedullary biopsy) with predominantly erythroid and megakaryocytic precursors, indicating a chronic myeloproliferative syndrome, namely polycythemia vera (Fig. 8). The recommended therapy was periodical phlebotomy (until the hematocrit reached normal level), myelosuppressive therapy (Hydroxyurea), low doses of acetyl-salicylic acid and hepatoprotective drugs. Ablactation was also recommended.

The patient was reevaluated one month after starting therapy. She still complained of right upper abdominal quadrant discomfort. Clinical examination showed the liver and spleen significantly reduced as compared to the previous examination. Laboratory data revealed a normal hemoleucogram, normal values of serum transaminases, mild cholestasis (FA= 347IU/l, GGT= 114IU/l) and coagulation abnormalities (TQ= 22.1sec, IP= 57.2%, APTT= 34.9sec.). Abdominal ultrasound revealed a decreased volume of the caudate lobe and of the spleen, with the maintenance of the other abnormalities previously described.

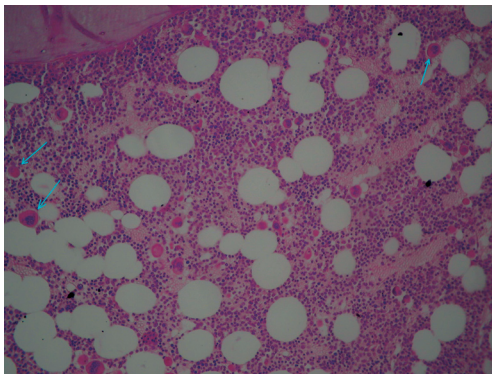
The clinical and biological reevaluation of the patient after 18 months (June 2009) showed normal values of transaminases and cholestasis enzymes, normal coagulation



**Fig 6.** CT section with contrast, sagittal multi planar reconstruction: only a suprahepatic vein that drains the IInd and IIIrd hepatic segments is visualized.



**Fig 7.** Multiplanar reconstruction: frontal section plus venous phase plus contrast: the permeable portal vein and inferior vena cava are revealed.



**Fig 8.** Pathological examination of the osteo-medullary biopsy: presence of erythroid and megakaryocytic precursors, several megakaryocytes with dysplastic nucleus.

parameters (TQ= 18.7sec, INR= 1.3, APTT= 29.3sec.) and hemoleucogram.

Abdominal ultrasound described a decreased size of the caudate lobe (95 mm) and of the spleen (165 mm).

The patient is presently under haematological therapy.

## Discussion

Budd-Chiari Syndrome can be primary, when obstruction of the hepatic flow is determined by an endoluminal lesion (thrombosis, membranes) or secondary, when the cause

of vascular obstruction is an extrinsic compression or nearby invasion [1]. The main conditions which cause BCS are: conditions accompanied by hypercoagulable states (myeloproliferative disorders – especially polycythemia vera, antiphospholipid syndrome, antithrombin III, protein C and S deficiency, factor V Leiden mutations), neoplasias (hepatocellular carcinoma, kidney cancer/Wilms tumor, suprarenalian cancer, bronchopulmonary carcinoma, leukaemia), oral contraceptives, pregnancy, inflammatory bowel disease, celiac disease and trauma [2-4].

Clinical manifestations depend on the extension and rapidity of venous occlusion as well as on the development of collateral circulation that decompresses the hepatic sinusoides. Different clinical forms of BCS are described: the fulminate form, in the presence of hepatic encephalopathy, the acute, subacute and chronic forms, the latter being the most frequent, with clinical manifestations and complications similar to liver cirrhosis. Abdominal pain, hepatomegaly, ascites are present in almost all BCS patients. Nausea, vomiting and jaundice are more common in the fulminate and acute forms, while splenomegaly and esophageal varices appear in the chronic forms [2, 5].

In establishing the diagnosis in our patient, we excluded other causes of liver cirrhosis (viral hepatitis B and C infections, alcohol abuse, autoimmune liver disease, Wilson disease, hemochromatosis,  $\alpha 1$  antithrypsin deficiency). The patient did not use oral contraceptives. In her case, the clinical onset of the disease occurred during pregnancy and worsened in post-partum.

Abdominal gray scale and Doppler ultrasonography were the first investigations performed in this patient. The method has a sensitivity and a specificity over 80% in BCS. The defining features of BCS are: the nodular aspect of the liver, compensatory hypertrophy of the caudate lobe (vascularized by vessels that directly open into the inferior vena cava), the absence of the vascular signal in the suprahepatic veins, intraluminal echogenic fill at this level, and the development of collateral circulation [1, 6, 7]. The necrotic areas of the liver are better visualized by abdominal CT scan with contrast, which is recommended for description of the venous anatomy and hepatic configuration when a transjugular intrahepatic portosystemic shunt is taken into consideration. The angioMRI shows a deep inhomogeneous hepatic parenchyma image of “confluent snowballs”, hepatic vein thrombosis and is more efficient in visualizing the whole length of the inferior caval vein [8, 9]. The BCS diagnosis is confirmed by the “spider web” aspect of hepatic vascularization, showed by hepatic venography and transjugular hepatic biopsy (vascular dilation, hemorrhage and centrolobular necrosis, followed in time by centrolobular fibrosis and eventually leading to cirrhosis) [7].

The treatment of BCS starts with treatment of the cause. Antiplatelet treatment necessary for preventing the extension of venous thrombosis is associated with specific therapy for liver cirrhosis. When the medical treatment is no longer efficient, percutaneous transluminal angioplasty and stent placing are taken into consideration for short stenoses.

Surgical porto-systemic shunt or TIPS are recommended for therapy of the acute forms of BCS [2, 3]. Hepatic transplantation is reserved for the fulminate forms or after failure of other treatments [10].

The main complications of BCS are those of liver cirrhosis: hepatic insufficiency, encephalopathy, portal hypertension, esophageal varices with hemorrhage, hepatorenal syndrome.

Our patient had some factors predictive for a good prognosis: the young age, the absence of ascites or ascites in a small quantity, and a low level of serum creatinine.

Polycythemia vera is a clonal hematopoietic stem cell disease characterized by sustained medular and excessive erythroid proliferation, the main clinical consequence being the increased risk of thromboembolic accidents [6]. The WHO diagnosis criteria include: increase of the total erythrocyte volume ( $> 32\text{ml/kg}$  in women and  $> 36\text{ml/kg}$  in men), blood O<sub>2</sub> saturation  $> 92\%$ , splenomegaly accompanied by thrombocytosis  $> 400,000/\mu\text{l}$ , leukocytosis  $> 12,000/\mu\text{l}$ , low serum erythropoietin levels, elevated serum alkaline phosphatase, the myelogramme showing predominantly erythroid and megakaryocytic precursors [6, 11]. Most patients develop thromboembolic complications (BCS, deep venous thrombosis, myocardial infarction, mesenteric ischemia), bleeding (epistaxis, gastrointestinal bleeding), or acute leukemia on myeloid metaplasia with myelofibrosis.

Recently, a specific mutation V617F in the JAK2 tyrosine kinase gene on the 9th chromosome was described in patients with polycythemia vera [12, 13].

The first line treatment for polycythemia vera is phlebotomy: 300-500 ml blood should be removed every other day until the hematocrit is decreased to 45% for men and 42% for women [6, 14]. The association of small doses of acetylsalicylic acid (75-100mg) decreases the risk of thrombosis. Myelosuppressive therapy may be indicated for patients with a high requirement of blood emissions, important splenomegaly, persistent leukocytosis and thrombosis. Patients are given Hydroxyurea 1-1.5g/day after a normal value of the hematocrit has been reached. IFN- $\alpha$  reduces stem cell proliferation and lowers the risk of thromboembolic complications. Anagralide is recommended to patients with persistent thrombosis after standard treatment. Administration of radioactive phosphorus (<sup>32</sup>P) might be an alternative for patients over 70, its mutagenous effects being well known. Recently, bone marrow treatment has been taken into account for young patients with rapid progression towards leukaemia or myelofibrosis [11, 14]. Several studies do currently question the efficiency of tyrosine kinase inhibitors in polycythemia vera, therapeutically proven for other chronic myeloproliferative conditions (chronic myeloid leukaemia) [15-17].

## Conclusion

The Budd-Chiari Syndrome is a rare disorder, and

polycythemia vera is one of its major causes. The characteristics of the presented patient were: the young age, the pregnancy/post-partum state at the clinical onset of the Budd-Chiari Syndrome, and the fact that the underlying disease, polycythemia vera, was diagnosed after its complication.

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