

# A rare encounter with two cases of Budd-Chiari syndrome in the Emergency Department: A case report

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**Abstract.** Budd-Chiari syndrome (BCS) is a rare disorder clinically characterized by abdominal pain, hepatomegaly and ascites. The condition is often related to thrombosis of the hepatic veins or the terminal portion of the inferior vena cava. A myeloproliferative disorder is the most identified underlying prothrombotic risk factor, although almost one-half of affected patients are now recognized as having multiple underlying prothrombotic risk factors. Doppler ultrasound may be enough to confirm the diagnosis of BCS; however, computed tomography or magnetic resonance imaging is often employed. Anticoagulant therapy is the cornerstone of BCS treatment, but most patients also need additional treatment strategies. Most patients with BCS are now treated by endovascular intervention, which has improved survival rate in those afflicted by this disease. The long-term course of the disease can be complicated by progression or recurrence of the underlying myeloproliferative disorder. The present study reports the cases of

two patients with BCS with the aim of alerting healthcare workers in Emergency Departments of this less common diagnosis in patients presenting with frequent complaints of abdominal pain.

## Introduction

Budd-Chiari syndrome (BCS) is a rare condition that is a result of thrombotic or non-thrombotic obstruction of the hepatic venous outflow, characterized by ascites, hepatomegaly and pain in the abdomen. The estimated incidence rate of BCS is 1:100,000 in the general population, with <300 cases reported by three tertiary referral centers in France, the USA and the Netherlands. Although Western countries consider BCS to be a rare disease, its presence in a population is largely affected by region; BCS is more common in Asian countries such as India, China and Nepal, with some regions of China reaching 6.8 to 12 cases per 100,000 people, while in the West, the disorder is estimated to affect one in 2.5 million individuals (1).

BCS is classified into two types: Primary BCS, when obstruction originates in the vein and thrombosis is the main cause; or secondary BCS, when there is external compression of the vein (such as from an abscess or tumor) (2). Most patients with BCS have an underlying thrombotic diathesis, for example, patients who are pregnant or those with a tumor, a chronic inflammatory disease, an infection or a myeloproliferative disorder. In >75% of patients, one hereditary or acquired hypercoagulable state can be identified, whereas more than one etiological factor is observed in the remaining 25% (3). Hepatic vein thrombosis is caused by a myeloproliferative disease, as diagnosed in 20% of cases (4); polycythemia vera accounts for 10-40% of all cases. Gene mutations in factor V Leiden and factor II have been recorded in ~25 and 5% of patients with BCS, respectively (4). Oral contraceptive use has also been identified as a risk factor for BCS (5,6).

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The presentation of BCS ranges from asymptomatic to fulminant hepatic failure, passing through the development of acute (rapid) or chronic (progressive) symptoms in a period of weeks to months prior to the diagnosis. The following circumstances are indicative of BCS: i) simultaneous presentation of ascites, hepatomegaly and upper abdominal pain; ii) massive ascites with mildly altered liver function tests; iii) sinusoidal dilation upon liver biopsy, without heart disease; iv) fulminant hepatic failure in association with hepatomegaly and ascites; and v) unexplained chronic liver disease following exclusion of diagnoses of alcoholism, autoimmunity, chronic viral hepatitis B or C, Wilson's disease, iron overload and  $\alpha$ -1 antitrypsin deficiency (6-8).

Doppler ultrasonography of the liver, with a sensitivity and specificity of  $\geq 85\%$ , is the technique of choice for detecting obliteration of hepatic veins, thrombosis or stenosis, spider web vessels, large collateral vessels or a hyper echoic cord replacing a normal vein (6,9). If the results of the ultrasonography are unclear, magnetic resonance imaging (MRI) of the blood vessels (magnetic resonance angiography) or computed tomography (CT) represent the second-line imaging investigations (10,11).

Treatment of BCS starts with anticoagulant therapy, treatment of the underlying disease and also symptomatic therapy of portal hypertension complications. In patients with short-length stenosis unresponsive to medical therapy, angioplasty/stenting is the second-line treatment, while transjugular intrahepatic portosystemic shunt represents the next step. In severe cases of BCS, liver transplantation is the last option (1,11).

The natural course of the disease is severe, with a 3-year survival rate of  $<10\%$  in patients who do not receive treatment. Following a rapid diagnosis and the early initiation of treatment, the 5-year survival rate is 76%. The long-term prognosis depends on the associated risk factors for thrombosis (11,12). Since this pathology is so rare, any encounter with a case is worth reporting in order to increase the awareness of the disorder. The present study discusses two cases of BCS in women aged 35 and 61, who presented to the Emergency Department (ED) of the Emergency Clinical Municipal Hospital (Timisoara, Romania) 1 month apart.

### Case report

*Case 1.* A 35-year-old woman presented to the ED of the Emergency Clinical Municipal Hospital in July 2020 with asthenia, a low appetite, abdominal distension and a marked decrease in weight of 13 kg in 1 month. A physical examination revealed a distended and painful abdomen, edema of the legs, palmar erythrosis and angioma stellaire on the chest. Vital parameters were recorded as follows: Blood pressure (BP), 110/70 mmHg; oxygen saturation ( $SpO_2$ ), 97%; heart rate (HR), 100 beats/min.

Abdominal ultrasound performed in the ED identified a slightly enlarged liver, with a homogenous surface and a medium amount of ascites. CT scan of the abdomen confirmed the presence of hepatomegaly and a nutmeg appearance of the liver after the administration of the contrast substance.

The pathological values of the laboratory tests performed in the ED and during hospitalization are shown in dynamic in Table I. Serial gastroscopies were performed on the 4th and 5th days after admittance, as the hemoglobin level had demonstrated a constant decrease since the admittance of the patient to the hospital. The gastroscopies revealed gastric ulcers, covered with fibrin, with no visible source of active bleeding and no esophageal or gastric varices.

Prompt intravascular volume replacement was initiated using crystalloid fluids and blood transfusions. Proton pump inhibitor (omeprazole) was administered as an intravenous bolus, followed by continuous infusion (80 mg, then 8 mg/h) for the entire hospitalization period. Despite the medication given, the patient had an episode of massive hematemesis and died 7 days from the initial presentation in the ED.

*Case 2.* A 61-year-old woman who had previously been diagnosed with breast cancer, for which mastectomy was performed 5 years before the current presentation, plus carcinomatous meningitis in the same year and bone metastases, presented to the ED of the Emergency Clinical Municipal Hospital in June 2020 with nausea and vomiting that had been persisting for 1 month, as well as abdominal pain, fatigability and edema of the legs. A physical examination revealed icteric skin, sclera and mucous membranes, diffuse abdominal pain and hepatomegaly (6 cm below the costal margin), with no pathological cardiac or respiratory findings. Vital parameters were recorded as follows: BP, 125/75 mmHg; HR, 70 beats/min;  $SpO_2$ , 96% (without supplemental oxygen).

An abdominal ultrasound exam was performed in the ED, which revealed an enlarged inhomogeneous liver, without splenomegaly, and a medium amount of ascites. Initial lab tests included a complete blood count, a comprehensive metabolic panel and a coagulation panel (Table II).

An abdominal and pelvic CT scan with contrast was also performed, which found hepatomegaly with an enlarged right hepatic lobe (20 cm), with scratchy structure, and two cysts in the 4th and 8th segments. Additional findings included the absence of visualization of the supra-hepatic veins after contrast administration, and the small caliber of the retro-hepatic segment of the inferior vena cava, suggestive of BCS. Furthermore, a medium/large amount of ascites, a normal spleen, a portal vein with a diameter of 0.8 cm (normal range, 0.7-1.5 cm), a common bile duct with a diameter of 0.7 cm (normal value, 0.4 cm), a dilated pancreatic duct of 4 mm measured at the level of pancreatic body (normal value, 2.00 mm) and normal kidneys, uterus and urinary bladder were recorded. Bilateral basal pleural effusions of  $\sim 2.2$  cm on the right side and 3.8 cm on the left side were noted, as well as thoraco-lumbar osteolytic lesions (Fig. 1A and B).

The patient was admitted to the Department of Gastroenterology. Following treatment with analgics, antispastics, oral anticoagulants and gastric protection medication, the patient's condition improved, and they were discharged from the hospital with the recommendation to continue the oral anticoagulant treatment (4 mg acenocumarol, half a tablet per day) until further follow-up at 1 month.

Table I. Case 1: Pathological values of the laboratory tests performed in the Emergency Department, at 1 and 6 days post-admittance.

Laboratory parameter	Conventional units	Value 1 (in the ED)	Value 2 (1 day post-admittance)	Value 3 (6 days post-admittance)	Reference range value
WBC	$\times 10^3/\mu\text{l}$	12.2	21.6	17.8	4-10
RBC	$\times 10^6/\mu\text{l}$	2.39	2.72	1.76	3.8-4.8
HGB	g/dl	9.2	8	5.4	12-15
HCT	%	28.3	24.4	16	36-46
PLT	$\times 10^3/\mu\text{l}$	212	112	103	150-410
AST	U/l	118	171	500	15-37
ALT	U/l	29	44	234	14-59
Blood glucose	mg/dl	77	64	107	74-106
BT	mg/dl	3.3	5.65	6.5	0.2-1
BD	mg/dl	2.81	4.83	5.01	0.0-0.2
Cholinesterase	U/l	3522	3789	4321	5320-12920
Creatinine	mg/dl	0.45	1.22	2.02	0.55-1.02
FAL	U/l	250	304	320	35-105
INR	INR	1.63	1.75	2.5	0.8-1.2
aPTT	Sec	44.9	50	52	21.6-28.7

WBC, white blood cell; RBC, red blood cell; HGB, hemoglobin; HCT, hematocrit; PLT, platelet; AST, aspartate aminotransferase; ALT, alanine aminotransferase; BT, total bilirubin; BD, direct bilirubin; FAL, alkaline phosphatase; INR, international normalized ratio; aPTT, activated partial thromboplastin time.

Table II. Case 2: Pathological values of the laboratory tests performed in the Emergency Department.

Laboratory parameter	Conventional units	Value (upon presentation in ED)	Reference range value
RBC	$\times 10^6/\mu\text{l}$	3.35	3.8-4.8
HGB	g/dl	10.8	12-15
AST	U/l	289	15-37
ALT	U/l	82	14-59
Lipase	U/l	1033	73-393
Blood glucose	mg/dl	112	74-106
BT	mg/dl	4.6	0.2-1
BD	mg/dl	3.41	0.0-0.2
Cholinesterase	U/l	3065	5320-12920
Creatinine	mg/dl	1.22	0.55-1.02
FAL	U/l	565	35-105
Ferritin	ng/ml	1417	15-150
CRP	mg/l	50.1	0.0-5.0
INR	INR	1.48	0.8-1.2
aPTT	Sec	29.1	21.6-28.7

RBC, red blood cell; HGB, hemoglobin; AST, aspartate aminotransferase; ALT, alanine aminotransferase; BT, total bilirubin; BD, direct bilirubin; FAL, alkaline phosphatase; CRP, C-reactive protein; INR, international normalized ratio; aPTT, activated partial thromboplastin time.

## Discussion

The cause of BCS remains unknown in a large number of cases. In a series of 163 cases, the etiology was reported as either unidentified or inadequately established in 70.1%, while in the rest of the patients, myeloproliferative neoplasm, celiac

disease, antiphospholipid syndrome, factor V Leiden mutation and hyperhomocysteinemia were found as causes (13). In the present study, case 1 experienced a rapid fatal evolution and extensive blood tests were not possible to identify the cause of the BCS. Since the uncontrolled bleeding led to the death of the patient, it may be hypothesized that an imbalance

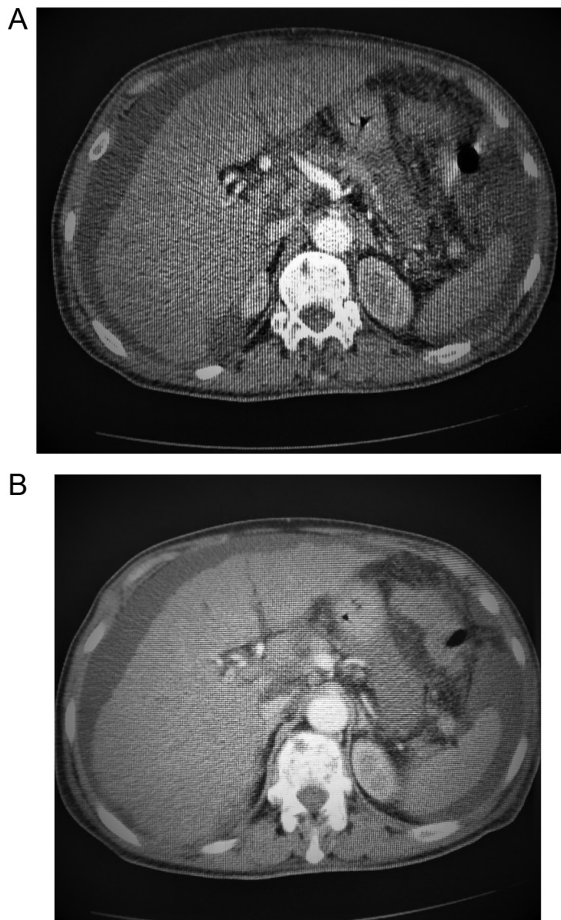


Figure 1. CT results of case 2. (A) Abdominal CT showing hepatomegaly with inhomogeneous contour, and two cysts in the 4th and 8th segments. (B) Common bile duct with a diameter of 0.7 cm and a dilated pancreatic duct. CT, computed tomography.

of pro- and anti-coagulation factors was present, which was also demonstrated to be the case in patients with BCS in a study by Chen *et al* (14). In case 2 of the present study, the most relevant etiological factor appeared to be thrombosis, probably secondary to the neoplastic disease, similar to 7 patients out of 163 from the study by Seijo *et al* (13). Patients with cancer have an altered hemostatic system, increasing the risk of both hemorrhagic and thrombotic complications, particularly venous thromboembolism. This association is well described for solid tumors (15). In both cases in the present study, the association of ascites, hepatomegaly and upper abdominal pain, presented simultaneously, was highly suggestive of BCS; however, it was the CT scan that confirmed the diagnosis.

Complications of BCS are generally related to underlying conditions and the severity of liver failure. Left untreated, BCS can lead to hepatic encephalopathy, variceal hemorrhage, hepato-renal syndrome, portal hypertension, bacterial peritonitis if ascites is present and hepatocellular carcinoma (16,17). Case 1 of the present study had a fatal outcome, although it is hard to confirm whether this was due to complications from BCS. The serial gastroscopies performed did not reveal any variceal hemorrhage as the source of the massive bleeding. The blood tests demonstrated altered liver function and mild thrombocytopenia, either in the context of liver injury

or due to the platelet consumption secondary to BCS acute thrombosis (18). Case 2 had a favorable evolution despite the patient comorbidities. The patient was discharged with anti-coagulant therapy, which represents the first-line treatment in BCS (19,20).

In conclusion, BCS is an uncommon life-threatening hepatic vascular disorder. With regard to the present cases, the following should be highlighted: i) The pro-thrombotic state associated with neoplastic disease; and ii) that emergency physicians should be aware of the association of ascites, hepatomegaly and upper abdominal pain, which are commonly encountered in the ED, and therefore perform an extensive work-up for BCS. Since the outcome is poor in numerous cases, a timely diagnostic and therapeutic approach is of vital importance.

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#### Availability of data and materials

All data generated or analyzed during this study are included in this published article.

#### Authors' contributions

AS and AP were responsible for the study concept and visualization, the original draft preparation, writing and reviewing the manuscript. SDC, MI, MVB, NB and OAM analyzed the patient data contributed to writing, reviewing and editing the manuscript. OAM and NB confirm the authenticity of all the raw data. All authors read and approved the final manuscript.

#### Ethics approval and consent to participate

Not applicable.

#### Patient consent for publication

The patients provided written informed consent for publication.

#### Competing interests

The authors declare that they have no competing interests.

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