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CASE REPORT | LIVER

# Small Intrahepatic Vein Budd-Chiari Syndrome Complicated by *Fusobacterium nucleatum* Peritonitis

Ayman Bannaga, MRCP[1], Matthew J. Armstrong, MRCP, PhD[1], Homoyon Mehrzad, MRCS, FRCR[1], Rachel M. Brown, FRCPath[1], and Dhiraj Tripathi, MD, FRCP[1]

[1]*Queen Elizabeth Hospital Birmingham, Birmingham, United Kingdom*

## ABSTRACT

Budd-Chiari syndrome is a rare disorder with significant liver-related complications. We present a 28-year-old woman with a 1-month history of weight loss and ascites. Hepatic venogram showed patent hepatic veins and inferior vena cava; however, there was an increased hepatic venous pressure gradient, which is clinically significant for portal hypertension. Hereditary and acquired thrombophilia workup was unrevealing. During admission, she developed peritonitis with *Fusobacterium nucleatum* and was treated with piperacillin-tazobactam. Liver biopsy showed vascular changes with features of venous outflow obstruction, and she was diagnosed with "small hepatic vein" Budd-Chiari syndrome. She was treated with transjugular intrahepatic portosystemic stent-shunt and tinzaparin, with significant clinical improvement.

## INTRODUCTION

Budd-Chiari syndrome (BCS) is extremely rare. It is estimated at 1 per million population per year.[1] BCS is defined as the obstruction of hepatic venous outflow anywhere between the small hepatic venules up to the confluence of the inferior vena cava with the right atrium. Risk factors for BCS include hypercoagulable states, namely acquired or inherited thrombophilia, myeloproliferative disease, pregnancy, and oral contraceptives.[2] Small vein BCS remains a diagnostic challenge, and there is a paucity of cases in the literature.[3] In cases of unexplained subacute onset ascites and hepatomegaly, a liver biopsy remains the gold standard method to demonstrate evidence of outflow obstruction when large veins are patent.

## CASE REPORT

A 28-year-old Pakistani woman presented with a 1-month history of lethargy, weight loss of 3 kg, and generalized abdominal swelling. She had no significant medical history. There was a family history of deep venous thrombosis of unprovoked etiology. She had no contact with patients diagnosed with tuberculosis (TB); however, she had come in contact with visitors from her home country. She was not on any regular medications or oral contraception pills. She was a nonsmoker and never consumed alcohol. Examination revealed tender ascites without stigmata of liver disease or signs of heart failure.

Her full blood count, liver function tests, and international normalized ratio were normal. Her immunoglobulins count was normal. Her autoimmune profile was negative for antinuclear antibody, antinuclear cytoplasmic antibody, antimitochondrial antibody, anti-liver and kidney microsome antibody, and anti-smooth muscle antibody. She was also screened for viral hepatitis, with negative serology for hepatitis B and C viruses. Her HIV serology was negative.

Given the acute presentation of her ascites, the differential diagnoses were between spontaneous bacterial peritonitis (including TB), portal vein thrombosis, and BCS. Other common causes of ascites including heart failure, malignant infiltrative disease, and nephrotic syndrome were excluded after normal echocardiogram, cross-sectional imaging, and urinalysis.

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**Correspondence:** Ayman Bannaga, MRCP, Queen Elizabeth Hospital Birmingham, Mindelsohn Way, Birmingham B15 2TH, United Kingdom (Aymanbannaga@yahoo.com).

Initial ascitic fluid sampling was an exudate with protein of around 38 g/L and polymorphonuclear leucocyte count of 22 cells/mm$^3$. Microscopic assessment of the ascitic fluid was negative for malignant cells. Gram and Ziehl-Neelsen stains were also unrevealing for common bacteria. Polymerase chain reaction (PCR) assessment of the ascitic fluid was negative for TB.

Abdominal and pelvic computed tomography scan confirmed normal liver texture, large ascites, and patent portal and hepatic veins. She was further investigated with hepatic venogram to measure the portal pressure (Figure 1). It showed patent hepatic veins and inferior vena cava. However, there was an increased hepatic venous pressure gradient (HVPG) of 13 mm Hg, which is clinically significant for significant portal hypertension. She was also screened for gastroesophageal varices with normal upper gastrointestinal endoscopy. Initial transjugular liver biopsy showed vascular changes, implicating abnormal venous flow in the liver without localizing features (Figure 2).

Because she came in contact with visitors from an endemic area and in addition to results of an exudative ascites, TB was still high on the list of differential diagnoses. She underwent laparoscopic peritoneal biopsy which was normal including negative analysis for TB DNA polymerase chain reaction. She was also extensively investigated for prothrombotic causes with negative results (Table 1).

She developed spontaneous bacterial peritonitis after 4 weeks of the initial ascitic sampling, as identified by an ascitic

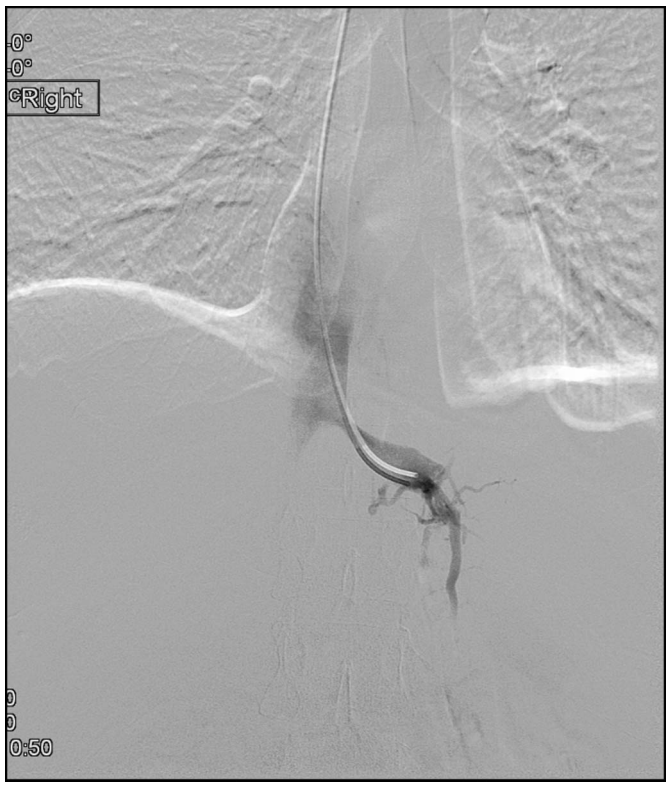


**Figure 1.** Hepatic venogram showing patent hepatic veins.

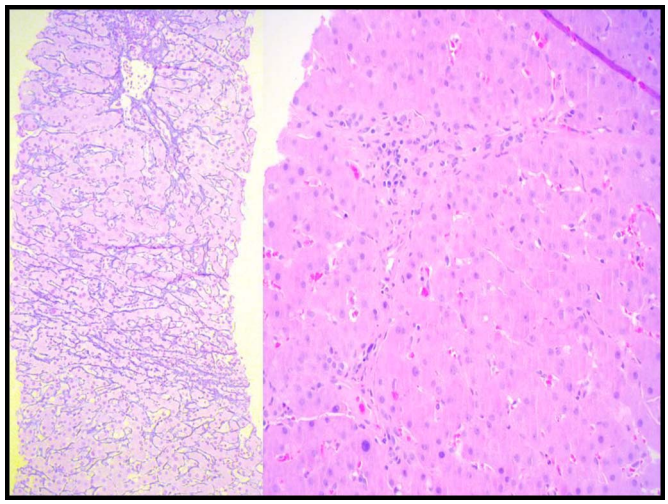

**Figure 2.** First liver biopsy showing vascular changes, implicating abnormal venous flow in the liver without localizing features. (A) Hematoxylin and eosin stain (40×) showing hepatocyte plate atrophy. (B) Hematoxylin and eosin stain (200×) showing small portal tracts lacking portal vein branches.

polymorphonuclear leucocyte count of >10,000/mm$^3$ and a positive culture with *Fusobacterium nucleatum*. She was treated with a 7-day course of piperacillin-tazobactam in addition to replacement with albumin.

No diagnosis was made, and despite diuretics, there was a progression of ascites, therefore a follow-up liver biopsy was performed. It showed progressive vascular and fibrotic changes, now with features of venous outflow obstruction (Figure 3). With the findings of the liver biopsy and unremarkable large vasculature on imaging, her clinical presentation was thought consistent with a diagnosis of "small hepatic vein" BCS.

**Table 1. Laboratory tests done for prothrombotic causes**

| Disorder | Results |
|---|---|
| Thrombophilia | Normal antithrombin, protein S, and protein C.<br>Factor V Leiden and prothrombin G20210A mutations were not detected.<br>Negative cardiolipin antibodies.<br>Negative IgG anti-beta-2-glycoprotein-1 (B2GP1). |
| Myeloproliferative neoplasms (MPNs) | Normal trephine bone marrow biopsy. Negative JAK2 mutations (no evidence of JAK2 V617F or a pathogenic variant in exon 12 of JAK2, exon 9 of CALR, and target regions of MPL and CBL). |
| Paroxysmal nocturnal hemoglobinuria (PNH) | Flow cytometric analysis of her blood showed that leukocytes have a normal expression of CD14, CD24, and fluorescently labeled aerolysin (FLAER) excluded PNH. |

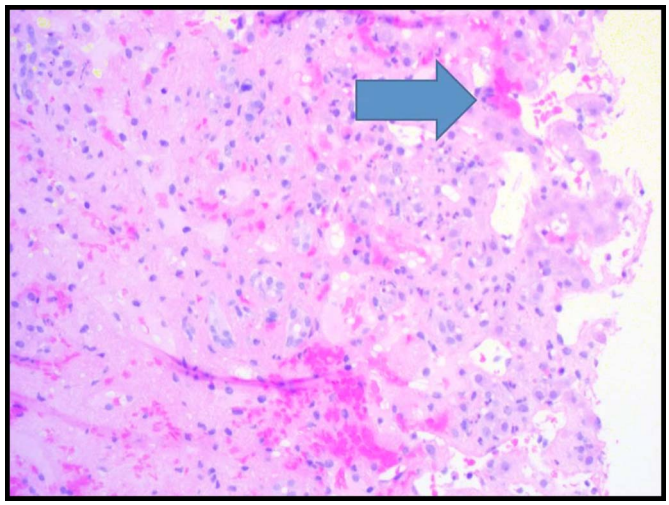

**Figure 3.** Hematoxylin and eosin stain (200×) of the second liver biopsy again showing vascular changes, now with features of venous outflow obstruction and red cells in the space of Disse (arrow).

In this case, the therapeutic goals aimed to treat portal hypertension. The patient was treated by insertion of transjugular intrahepatic portosystemic stent-shunt (TIPSS) and started on anticoagulation by tinzaparin.[4] After TIPSS, the ascites resolved completely. She was followed up with hepatic venogram to check TIPSS patency and HVPG 6 months after discharge. The HVPG was 3 mm Hg. She remains on lifelong tinzaparin, with anti-factor Xa levels being in the therapeutic range.

## DISCUSSION

BCS starts with venous outflow obstruction, which leads to portal hypertension, ascites, sinusoidal congestion, ischemia, formation of luminal and extraluminal varices, and finally hepatocellular necrosis and/or progressive liver failure.[5] Identifying BCS as the cause of the ascites was important. Treatment aimed to delay disease progression with TIPPS insertion and tinzaparin.[2] There were no identifiable etiologic factors explaining this rare idiopathic form of small intrahepatic vein BCS in this case. From the literature, there was one case described by Riggio et al.[3] They described similar presentation in a woman of the same age. The diagnosis was also made on histologic features and hepatic venogram. The biopsy also described an impaired blood outflow, and she was also successfully treated with TIPSS.[3]

Another interesting feature in this case is the infection with *F. nucleatum.* It is an anaerobic, Gram-negative bacillus. It is usually found as a commensal in the oral cavity and the rest of the gastrointestinal tract.[6] It is implicated in periodontal disease and head and neck infections. It is capable of hemagglutination, an attachment mechanism to erythrocytes which is considered a virulence trait of these bacteria.[6] It also has some thrombogenic activity and has been associated with intra-abdominal thrombosis.[7] *F. nucleatum* is described in the literature to be associated with thrombophlebitis of the portal vein (pylephlebitis in 7 case reports).[7] We conclude that liver biopsy supported by HVPG measurement are pivotal in the diagnosis of small vein BCS.

## DISCLOSURES

Author contributions: All authors contributed equally to the manuscript. MJ Armstrong is the article guarantor.

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Informed consent was obtained for this case report.

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