

Late onset ulcerative colitis complicating a patient with Budd–Chiari syndrome: a case report and review of the literature

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We report a case of a 33-year-old female patient with Budd–Chiari syndrome because of polycythemia vera. A transjugular intrahepatic portal-systemic shunt was performed because of refractory ascites 7 months after diagnosis. She had a stable hepatic function receiving anticoagulants until 3 years later when she presented with bloody diarrheas, liver function deterioration with prolonged prothrombin time and hypoalbuminemia, encephalopathy, and ascites. Colonoscopy revealed ulcerative pancolitis and the patient was treated with corticosteroids and antibiotics. Hepatic function was stabilized in parallel to controlling ulcerative colitis and the patient is in good health until now receiving maintenance therapy for ulcerative colitis and anticoagulants for Budd–Chiari syndrome. *Eur J Gastroenterol Hepatol* 21:109–113 © 2009 Wolters Kluwer Health | Lippincott Williams & Wilkins.

Introduction

The Budd–Chiari syndrome (BCS) is a clinical condition caused by hepatic venous outflow obstruction and is a rare cause of portal hypertension and liver failure [1]. The BCS may present as acute, subacute or chronic liver disease and its etiology is associated with acquired and inherited hypercoagulation states and other rare causes [2].

Ulcerative colitis (UC) is associated with increased risk of thromboembolic events, both venous and arterial [3]. BCS complicating UC has been rarely reported in the literature [4–7], whereas inflammatory bowel disease complicating BCS has not been described to our knowledge.

We report a case of a 33-year-old woman with established BCS because of polycythemia vera who presented with sudden deterioration of liver function in parallel with onset of active UC. We also describe the clinical course and the improvement in both the liver disease and UC after controlling bowel inflammation and induction of UC remission.

Case report

A 33-year-old Caucasian female patient was admitted to our department in 2003 because of abdominal distention, mild right upper quadrant pain, bloating, and constipa-

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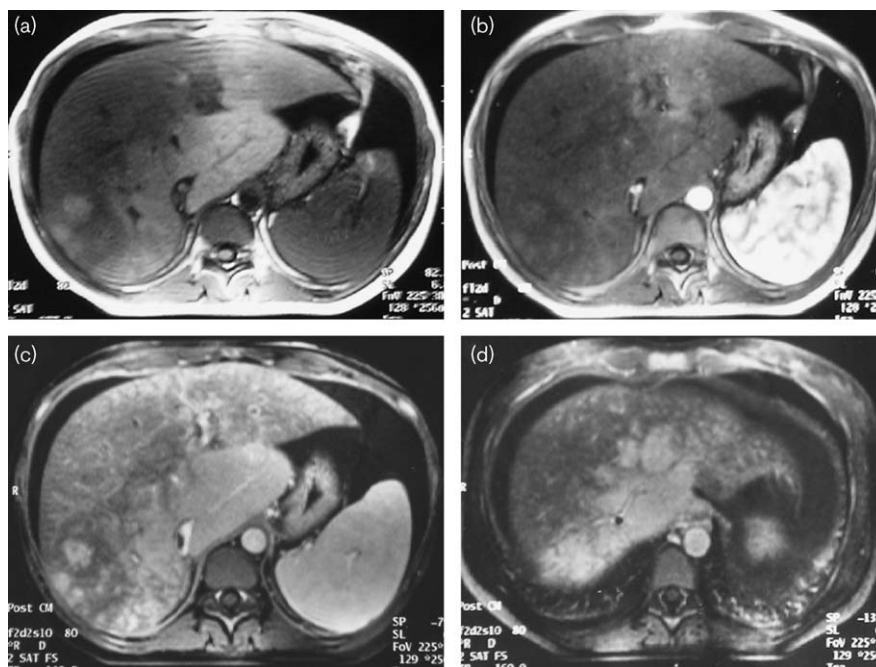
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tion. She had no past medical history and she did not abuse any alcohol or use hepatotoxic drugs. On clinical examination she had no signs of chronic liver disease, had distended but not tense abdomen with presence of fluid on percussion and the liver edge was palpable, soft and mild tender. The spleen was not palpable. She had edema of the legs and no signs of encephalopathy. On laboratory examination she had a slight elevation of prothrombin time (17.6 s, normal range: 10–14), hypoalbuminemia (2.9 g/dl, normal range: 3.4–5.0) and mild thrombocytosis (PLT: 544 000, normal range: 280 000–440 000). All other laboratory examination, including hepatic function tests, viral hepatitis markers, autoantibodies (ANA, SMA, AMA) were within normal range. A Doppler ultrasound showed enlarged and coarse liver, presence of ascitic fluid and no flow in hepatic veins, with normal flow in portal vein and inferior vena cava, which was suggestive of BCS. On paracentesis, 7 l of ascitic fluid were removed and the examination of the fluid revealed a serum-ascites albumin gradient more than 1.1 g/dl, while there was no evidence of spontaneous bacterial peritonitis. A magnetic resonance angiography (Fig. 1) had similar findings with Doppler ultrasound consistent with the diagnosis of BCS showing thrombosis of hepatic venous and normal portal vein and inferior vena cava. Upper gastrointestinal (GI)

Fig. 1



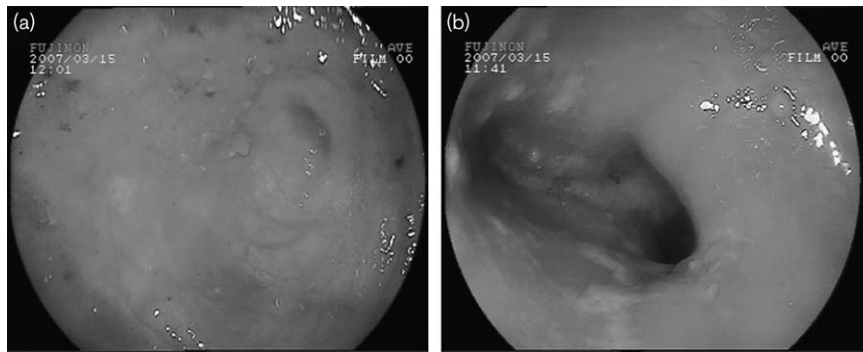
Magnetic resonance imaging of the abdomen showing presence of ascitic fluid, heterogeneity of liver parenchyma with enlargement of caudate lobe, possible presence of thrombi in inferior vena cava and a lesion in the right lobe which represents a nodule due to Budd-Chiari syndrome.

endoscopy revealed grade II esophageal varices. A thorough investigation for the cause of BCS [bone marrow biopsy for myeloproliferative diseases, laboratory investigation for paroxysmal nocturnal hemoglobinuria, antiphospholipid syndrome, deficiencies of natural anticoagulants (antithrombin III, protein C, and protein S), factor V Leiden mutation, prothrombin II mutation, hyperhomocysteinemia] revealed polycythemia vera along with low levels of antithrombin III (68.9%, normal range: 68–144%) and protein C (55%, normal range: 70–149%). The patient was treated with furosemide 40 mg/day, spironolactone 100 mg/day, and asenocumarol 3 mg/day along with sodium restriction. Despite intense diuretic therapy, ascites was poorly controlled and a transjugular intrahepatic portal-systemic shunt (TIPS) was placed 7 months later.

The ascitic fluid disappeared 1 month after TIPS placement and liver function tests returned to normal, except from a mild elevation of g-glutamyl transpeptidase (62 IU/l, range: 0–55). For 3 years the patient was in good condition with normal life and regular visits at our outpatient clinic every 3 months. On October 2006, she was admitted to our department because of bloody diarrheas. For 10 days she had more than 10 liquid bowel movements per day with blood and mucus and more than three nocturnal diarrheas, tenesmus, fever, and abdominal pain.

On admission she had elevated temperature (38.2°C), abdominal tenderness, presence of ascites, leg edema, and signs of stage I encephalopathy. On laboratory examination, she had elevated white blood cell count (13 440/mm³, normal range: 3800–10 500) with polymorphonucleosis (92%), low hemoglobin level (8.2 g/dl, normal range: 14–18), thrombocytosis (PLT: 662 000), raised erythrocyte sedimentation rate (65 mm, normal range: 0–20), C-reactive protein (82 mg/dl, normal range: 0–5) and fibrinogen (1044 mg/dl, normal range: 220–400), prolonged international normalized ratio (INR) (4.72, normal range: 0.85–1.15 under asenocumarol), hypoalbuminemia (2.3 g/dl, normal range: 3.5–5.0) and elevated g-glutamyl transpeptidase (102 U/l, normal range: 0–55), and alkaline phosphatase (153 IU/l, normal range: 30–120). Blood ammonia levels were 70 mg/dl (normal range: 0–35). To exclude a possible thrombosis of the shunt that could explain hepatic function deterioration, ascites and encephalopathy, an urgent Doppler ultrasound revealed normal flow in TIPS (Fig. 2). Sigmoidoscopy revealed edematous, friable mucosa, superficial ulcers, and spontaneous bleeding, findings suggestive of active UC. Abdominal radiograph showed no evidence of toxic megacolon or thumbprinting and computed tomography scan of the abdomen was performed to exclude possible thrombosis of mesenteric vessels in the setting of polycythemia vera and showed no evidence of ischemic colitis. Asenocumarol was discontinued and low molecular

Fig. 3

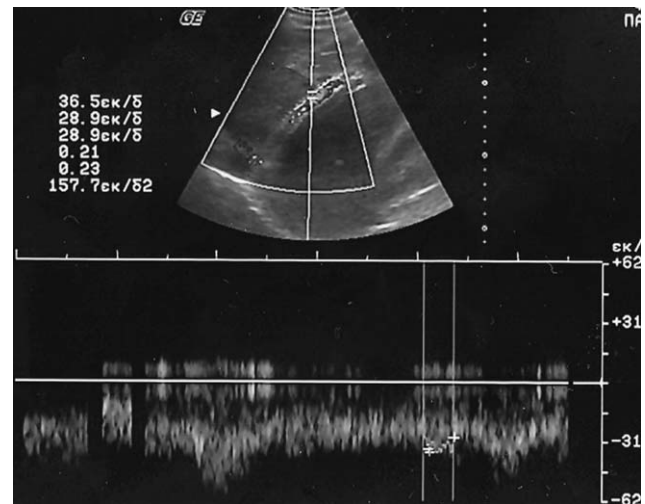


Endoscopic appearance of cecum (a) and sigmoid colon (b) with mucosal edema, friability and superficial ulcers in sigmoid colon and cecum, evident of active ulcerative colitis (pancolitis)

weight heparin was initiated because of the bleeding rate and the difficulty to control INR in therapeutic ranges. After excluding other possible causes of fever [blood, urine and stool cultures negative, normal chest and abdominal radiograph, viral agents (cytomegalovirus, Epstein–Barr virus, herpes simplex virus negative)], prednisone 75 mg intravenously (i.v.) was initiated along with i.v. albumin 40 g/day, ciprofloxacin 400 mg \times 2 i.v., lactulose enemas and bowel rest. A total colonoscopy, which was performed at day 3 to assess disease extent and severity, was suggestive for severe ulcerative pancolitis with mucosal edema and friability, multiple erosions and superficial ulcers in a continuous manner (Fig. 3). The histological examination of the multiple biopsies obtained during colonoscopy revealed neutrophilic and eosinophilic infiltration, crypt abscesses, and crypt distortion along with depletion of goblet cells suggestive of active UC. An upper GI endoscopy (to estimate portal hypertension) revealed esophageal candidiasis and grade II esophageal varices for which propranolol 100 mg/day was initiated. The disease was controlled after 5 days of treatment; mesalamine was initiated at 3.2 g/day per os along with rectal enemas whereas prednisone was tapered off over a 12-week period according to guidelines 5 mg/week up to 20 mg prednisone/day and 2.5 mg/week thereafter. Along with UC remission, synthetic liver function (INR and albumin levels) returned to near normal values and ascites was controlled with low doses of diuretics.

In the following 8 months UC is still in remission and ascites is well controlled with low doses of diuretics (furosemide 20 mg and spironolactone 50 mg per day). The patient experienced an upper GI bleeding episode from esophageal varices and we performed two sessions of banding ligation. She is in low priority transplantation (orthotopic liver transplantation) list and is a regular visitor at our outpatient clinic every month.

Fig. 2



Doppler ultrasonography showing normal flow within TIPS.

Discussion

BCS is defined as hepatic venous outflow obstruction at any level from the small hepatic veins to the junction of the inferior vena cava and the right atrium, regardless of the cause of obstruction with cardiac diseases and venoocclusive disease excluded from this definition [8]. The hepatic vein obstruction leads to hepatic congestion, portal hypertension, ascites, esophageal varices, reduction in hepatic blood flow, hepatocyte necrosis, and eventually cirrhosis and liver failure [9]. The presentation ranges from asymptomatic to fulminant disease [2,10]. The etiology of BCS is identifiable in 75% of patients [11]. Myeloproliferative disorders are the most common causes with polycythemia vera accounting for 10–40% of cases of BCS [12] and essential thrombocythemia and

myelofibrosis identified less frequent. In the remaining 25% of patients with BCS and no obvious cause identified with the regular work up, a high proportion seems to have a latent myeloproliferative disorder with a positive JAK2 tyrosine kinase mutation V617F [13].

An association between BCS and inflammatory bowel diseases is reported in the literature mainly as case reports presenting patients with established inflammatory bowel disease (IBD) complicated with BCS symptoms [4–7]. Patients with IBD are at increased risk for thromboembolic events, both venous and arterial [3]. This association is explained in part by the hypercoagulable state that correlates with disease activity and in part by the acquired or inherited thrombophilia associated with hyperhomocysteinemia, Leiden mutation in the gene-encoding factor V and antiphospholipid syndrome [14]. Miehsler *et al.* [15] reported a 3.6-fold higher risk of thromboembolism in IBD patients compared with controls with 60% of thromboembolic episodes occurring during disease activity or complications such as abscess. A possible explanation is that during the acute phase of IBD, the increased intestinal permeability and bacterial translocation results in systemic endotoxemia [16], which along with elevated levels of proinflammatory cytokines (IL-1, IL-6, and TNF- α) [17–19], activate the inflammatory and coagulation cascades in the local intestinal microenvironment and in the systemic circulation [20].

Our patient had BCS because of polycythemia vera and apart from refractory ascites that was controlled with TIPS, she had a steady liver function and was in good health for 3 years after diagnosis. The sudden onset of UC complicated her condition with hepatic deterioration, ascites, and encephalopathy. These clinical and laboratory findings (hypoalbuminaemia, prolonged INR, and elevated ammonia levels) raised the suspicion of thrombosis of TIPS or decompensation of cirrhosis that would be an indication of high priority in liver transplant list. Although Doppler ultrasound has conflicting results in detecting stent malfunction [21–25], it was performed by an experienced radiologist and showed no evidence of stent occlusion or stenosis so we proceeded with endoscopy to evaluate the etiology of bloody diarrheas. Other possible causes of colitis (ischemic and infectious) were ruled out and histological examinations showed active UC so the patient was treated for severe UC with intravenous prednisolone. Both her clinical and the laboratory findings improved rapidly along with the remission of UC with corticosteroids, which is in favor of TIPS patency. A second Doppler ultrasound was performed a few days later by a second radiologist, and it showed no evidence of stent malfunction.

The possible explanation for the hepatic deterioration/decompensation in our patient during the flare of UC is complex. Firstly, endotoxemia and bacterial translocat-

ion from the gut along with inflammatory cytokines and the defective immune status in cirrhosis can lead to liver dysfunction because of hepatic necrosis by disruption of the microcirculation and lipid peroxidation [26–28]. Secondly, the hemodynamic alterations resulting from increased synthesis of nitric oxide [29,30] and other vasoactive agents can further aggravate arterial dilatation and decompensation of cirrhosis [31], and thirdly, the activation of the coagulation and fibrinolysis cascade because of UC in the setting of a myeloproliferative disorder could have resulted in microthrombosis in liver parenchyma contributing to the liver dysfunction. Coexistence of polycythemia vera and UC have only been reported as cases in the literature [7,32]. Both these conditions, however, show common hemostatic abnormalities that can lead to thrombosis, such as thrombocytosis, activated platelets and elevated plasma homocysteine levels [33–35].

In conclusion, this is the first case report of a patient with a BCS that presented with a decompensation of the hepatic disease during a flare of severe new-onset UC.

Acknowledgement

Conflict of interest: none declared.

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