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Budd-Chiari syndrome in a young patient with Celiac sprue: A case report

Genç bir hastada Budd-Chiari sendromu ve Çölyak spru birlikteliği: olgu sunumu

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Budd-Chiari syndrome is thrombosis of the hepatic veins, and associated conditions vary. Budd-Chiari and celiac sprue association is a rare condition. A 24-year-old woman was admitted to the clinic with complaints of weakness, distended abdomen and weight loss for four months. Results of investigation showed Budd-Chiari syndrome and malabsorption with endomysial antibodies and intestinal villous atrophy. All known etiological factors for Budd-Chiari syndrome were negative. Three months after initiation of a gluten-free diet and replacement therapy, she died from infection of ascitic fluid and renal failure following umbilical hernia rupture. Celiac sprue must be remembered especially in the event of Budd-Chiari syndrome and malabsorption.

Key words: Celiac sprue, Budd-Chiari syndrome

Budd-Chiari sendromu hepatik venlerin trombozudur ve çeşitli durumlarla birlikte olabilir. Budd-Chiari sendromu ve çölyak spru birlikteliği nadirdir. 24 Yaşında bayan hasta, kliniğimize dört aydır süregelen güçsüzlük, karın şişliği ve kiloj kaybı yakınmaları ile başvurdu. Tetkikler sonucu Budd-Chiari sendromu ve malabsorpsiyon saptandı. Endomisyal antikorlar pozitifti ve intestinal villöz atrofi mevcuttu. Budd-Chiari etiyolojisinde bilinen nedenlerin araştırılması sonuçsuz kaldı. Glutensiz diyete alınan ve replasman tedavisi başlanan hasta, üç ay sonra umbilikal herni rüptürü ve bunu takiben gelişen asit infeksiyoınu ve renal yetmezlik tablosu ile kaybedildi. Budd-Chiari ve malabsorpsiyon durumlarında çölyak spru akla getirilmelidir.

Anahtar kelimeler: Çölyak spru, Budd-Chiari sendromu

INTRODUCTION

Budd-Chiari syndrome (BCS), comprising hepatomegaly, abdominal pain and ascites, is a rare disorder caused by obstruction of hepatic venous outflow, leading to sinusoidal congestion, ischemic injury to liver cells, and portal hypertension. The main mechanism of obstruction is thrombosis of hepatic veins or of the terminal portion of the inferior vena cava. Thrombosis at these sites usually occurs in association with various prothrombotic disorders, including primary myeloproliferative disorders, antiphospholipid syndrome, paroxysmal nocturnal hemoglobinuria, inherited deficiency in natural coagulation inhibitors, and miscellaneous prothrombotic disorders (1-6). Pregnancy and oral contraceptive use are regarded as precipitating cofactors (7). However, in 10-30% of patients, a prothrombotic state cannot be identified.

Celiac sprue (CS), also known as celiac disease or gluten-sensitive enteropathy, is characterized by malabsorption resulting from inflammatory injury to the mucosa of the small intestine after the ingestion of wheat gluten or related rye and barley proteins. CS results from an inappropriate T-cell-mediated immune response against ingested gluten in genetically predisposed people (8). Classically, infants with CS present between the ages of four and 24 months with impaired growth, diarrhea, and abdominal distention (9). About 20% of cases occur in patients who are older than 60 years of age (10). Hematological and biochemical tests (deficiencies of iron, Mate, calcium, and vitamin D), the availability of highly sensitive and specific serologic markers (antiendomysial antibodies, tissue transglutaminase), tests of intestinal absorption (D-xylose-absorption test) and biopsy

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of the small intestine (striking mucosal architectural changes, with absent villi and hyperplastic crypts, and increased numbers of intraepithelial lymphocytes and of plasma cells and lymphocytes in the lamina propria) are cornerstones of the diagnosis (11, 12).

In this report, we present a case of BCS in a patient in whom CS was diagnosed. All prothrombotic disorders for BCS were investigated but none was detected except CS. This report will discuss Budd-Chiari syndrome and its relationship to celiac sprue.

CASE

A 24-year-old female presented to her internist with a four-month history of abdominal distension, adynamia and edema. Her doctor initially prescribed diuretics, and when this led to no improvement in her symptoms he performed some tests to investigate gynecological and gastrointestinal malignancies and tuberculosis. Results were inconclusive and she was referred to our clinic for further evaluation.

Her past history was significant for Cesarean section two years previously and weight loss of 25 kg in two months. Her mother was nefrectomized and had been treated for six months for tuberculosis in her childhood. She denied any current or past alcohol, tobacco and drug use, except for furosemide. Her physical examination was significant for a cachectic woman; the liver edge was nonpalpable, spleen was nonpalpable but percussable, abdomen was distended by tense ascites, and edema of both lower extremities to the knee and of abdominal collaterals were noted. Workup at the clinic included negative hepatitis A, B, and C viral serologies and negative autoimmune markers. Routine laboratory studies showed Hb and Hct 10.4g/dl and 35.5%, respectively; white blood cell 4,500/mm^3, platelet count 159,000/mm^3, MCV 74fL, erythrocyte sedimentation rate 36 mm/h, prothrombin time 24 seconds, INR 2.26, glucose 90 mg/dl, total bilirubin 3.22 mg/dl, alanine aminotransferase 149 U/L, aspartate aminotransferase 228 U/L, albumin 3 g/dl, y-g-globulin 1.3 g/dl, serum iron 22 mcg/dl, transferrin iron binding capacity 314 mcg/dl, ferritin 4.9 mcg/L, Ca 7.1 mg/dl, P 1.5 mg/dl, Na 133 IU/L, and K 3.2 IU/L. An a-fetoprotein level was 2.8 ng/ml. Analysis of ascitic fluid showed uncomplicated portal hypertensive ascites with total protein 1.6 g/dl, albumin 1 g/dl, glucose 101 mg/dl, LDH 162 U/L, cholesterol 23 mg/dl, WBC 180/mm^3, and serum-ascites albumin gradient of 2.0 g.

Imaging studies included computerized tomography (CT) and Doppler ultrasonography; hepatic venography followed. These studies showed an enlarged caudate lobe with surrounding underperfused parenchyma, absence of blood flow in hepatic veins, narrow occluded veins, and adjacent veins with tortuous lace-like spider web pattern (Figure 1). Splenomegaly was seen. Upper gastrointestinal endoscopy evidenced grade III esophageal varices and duodenal mucosal edema. Mucosal forceps biopsies showed absence of villi and hyperplastic crypts with intraepithelial lymphocytic infiltration (Figure 2). IgA antiendomysial antibodies were detected.

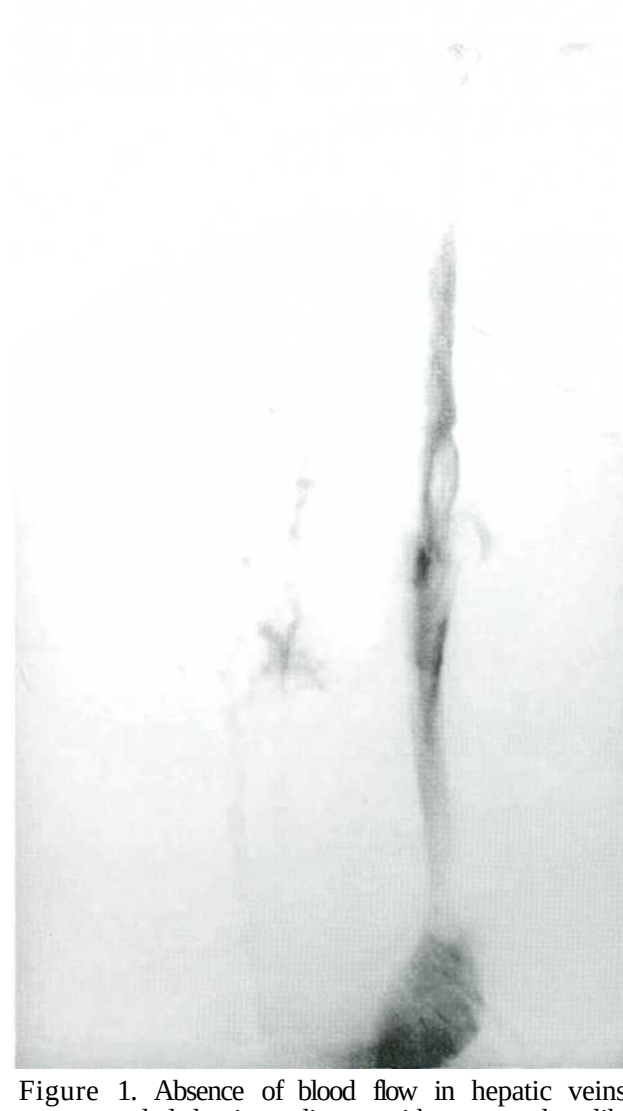

Figure 1. Absence of blood flow in hepatic veins, narrow occluded veins, adjacent with tortuous lace-like spider web pattern

On microscopical evaluation of the stool, fatty acid, starch and muscle fiber were observed. A peripheral blood smear showed no alterations in cell morphology except for iron deficiency. Laboratory analysis to detect etiology of Budd-Chiari syndrome (myeloproliferative disease; antithrombin III, protein S and C deficiency; lupus anticoagulant; anticoagulant activated protein C-factor V Leiden; Behcet's disease; hyperhomocysteinemia) was unrevealing.

Strict gluten-free diet and treatment with spironolactone and furosemide were started. Iron, minerals and vitamins were replaced. She had symptomatic improvement within two weeks after starting a gluten-free diet. Three months after discharge from hospital, she was admitted to emergency service with complaints of spontaneous rupture of umbilical hernia and abdominal pain. Ascites infection was diagnosed, and she died of septic shock and renal failure.

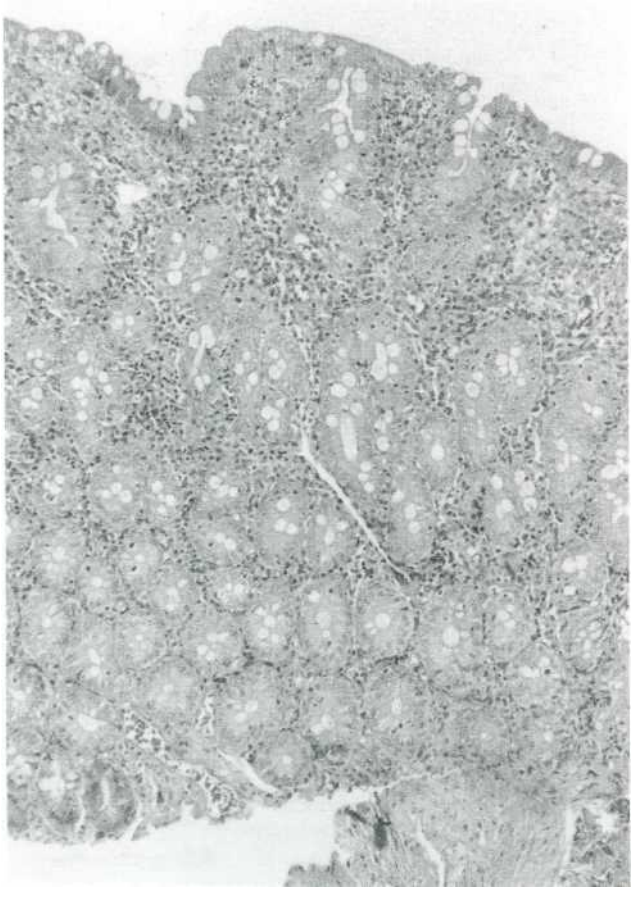

Figure 2. Absence of villi and hyperplastic crypts with intraepithelial lymhocytic infiltration of the smal intestinal mucosa (HE, 125x).

DISCUSSION

This is a case of a 24-year-old woman with BCS who presented to our hospital with abdominal distension, adynamia, loss of weight, and pretibial edema. Imaging and histopathological studies confirmed BCS and celiac disease. Celiac disease can present great clinical heterogeneity. Its association with a series of intestinal and non-intestinal diseases, whether immunologically mediated or otherwise, presents a higher than normal frequency (13). Many conditions such as dermatitis herpetiformis, autoimmune diseases, especially type 1 diabetes mellitus and autoimmune thyroiditis, occur in association with celiac sprue (14-17). BCS and celiac disease association has previously been described in isolated cases in Northern Africa (13). The appearance of this case in Turkey reveals that the coexistence of both processes in a single patient is unlikely to be due to environmental or geographical factors, in contrast with previous literature in which this was claimed (18).

The unexplained hypercoagulable state in celiac disease may affect the hepatic veins, the mesenteric veins or the splenoportal axis, causing different syndromes; it is merely the different expression of the same abnormality related to different sites. We believe that the reason for the hypercoagulable state may be hyposplenism, and celiac disease with abdominal venous thrombosis may be more frequently found if carefully searched. A peripheral blood smear in this patient showed no alterations in erythrocyte morphology typical of hyposplenism due to celiac disease. On the other hand, we could not find any other cause for the development of BCS, such as myeloproliferative disease, antithrombin III, protein S and C deficiency, lupus anticoagulant, anticoagulant activated protein C-factor V Leiden, Behcet's disease, or hyperhomocysteinemia. Mortality rates for Budd-Chiari syndrome have declined with advances in medical techniques. A recent review indicates a current 10-year survival rate of 75% for patients with Budd-Chiari syndrome (19). But our patient had celiac disease additionally and her general condition was poor due to malabsorption. She partially responded to a strict gluten-free diet but later died of a complication.

The current case report presents an unusual association of BCS and celiac disease. In conclusion, despite the fact that no definitive relationship between these diseases could be elucidated, we think this association, which was previously reported in only a couple of patients, must be remembered, especially in the setting of Budd-Chiari syndrome and malabsorption.

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