CASE REPORT

A rare association of celiac disease with gastric antral vascular ectasia and Budd-Chiari syndrome

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Abstract

We are reporting a case of 11 year girl with Budd-Chiari syndrome (BCS) & gastric antral vascular ectasia (GAVE) occurring in a patient with celiac disease, who presented with symptoms of abdominal distension, easy fatigability, pallor for one year and shortness of breath for 2 days prior to admission. Initial assessment revealed the presence of severe pallor and splenomegaly. Blood investigation showed pancytopenia and USG abdomen with doppler was suggestive of portal hypertension. On routine endoscopy, she was found to have antral nodularity, GAVE, changes of portal hypertensive gastropathy and duodenal nodularity in first and second part of duodenum. Suspecting celiac disease, she was investigated further. Her serum IgA antitissue transglutaminase antibody titers were elevated (> 100 units/mL) and duodenal biopsy was suggestive of celiac disease. She showed functional deficiency of protein C and protein S. There was narrowing of inferior vena cava as the possible cause of portal hypertension. Patient was kept on gluten free diet (GFD) and GAVE completely resolved in 6 months. Literature on BCS with celiac disease is present but associated GAVE is interestingly rare finding. We are reporting first case of GAVE with celiac disease in India.

Introduction

Celiac disease (CD) is an immune-mediated systemic disorder elicited by gluten and related prolamines in genetically susceptible individuals and characterized by the presence of a variable combination of gluten-dependent clinical manifestations, CD-specific antibodies, human leukocyte antigen (HLA) -DQ2 or -DQ8 haplotypes and enteropathy. CD-specific antibodies comprise auto antibodies against transglutaminase-2 (TG2), including endomysial antibodies (EMA), and antibodies against deamidated forms of gliadin peptides (DGP) [1]. The prevalence of CD has been estimated to approximate 0.5%-1% in different parts of the world [2]. However, the population with diabetes, autoimmune disorder or relatives of CD individuals have even higher risk for the development of CD, at least in part, because of shared human leukocyte antigen (HLA) typing. The prevalence of celiac disease in north Indian community is 1 in 96. Celiac disease is more common than is recognized in India [2]. Over the past four decades, several CD associated hepato-biliary disorders have been documented, including isolated hypertransaminasemia, autoimmune hepatitis, primary biliary cirrhosis, primary sclerosing cholangitis, and non-alcoholic fatty liver disease [3].

Gastric antral vascular ectasia is characterized by presence of dilated small blood vessels in the gastric antrum, an uncommon but important cause of gastrointestinal blood loss and iron deficiency anemia that is characterized by a distinctive endoscopic appearance consisting of parallel erythematous folds traversing the gastric antrum. Several mechanisms have been described in literature such as mechanical stress,

humoral/immunological factors and hemodynamic alterations. GAVE is associated with autoimmunity, portal hypertension, chronic kidney failure, and collagen vascular diseases (4).

Budd-Chiari syndrome comprises a heterogeneous group of disorders characterized by hepatic venous outflow obstruction, in the absence of right heart failure, constrictive pericarditis, or sinusoidal obstruction syndrome. BCS is a relatively rare condition, with an estimated prevalence at one case per 100,000 individuals [5]. Several case reports published in the past two decades suggested an association between CD and BCS [5,6].

We are reporting a rare case of GAVE with celiac disease and BCS, with response to gluten free diet (GFD).

Case

A 11-year old girl, presented with a one year history of increasing abdominal distension, easy fatigability, pallor and shortness of breath for 2 days. On examination her weight was 26 kgs (at 25th centile), height was 131cm (between 3rd and 10th centile). Patient was in moderate respiratory distress due to significant pallor. Per abdominal examination showed massive splenomegaly (8cm below left costal margin) with no free fluid. Investigations revealed hemoglobin of 3.1 gm/dL, total leukocyte count of 1510/mm^3, platelet count of 11000/mm^3, and peripheral blood film showed hypochromic microcytic red blood cells. Liver function tests revealed serum bilirubin of 1.7 mg/dL, aspartate aminotransferase of 41 IU/mL, alanine aminotransferase of 16 IU/mL, alkaline phosphatase of 273 KAU/dl (cut-off 30 KAU/dl), and serum albumin levels of 3.9 g/dL with globulins of 3 g/dL. High performance liquid chromatography (HPLC) was normal and direct Coombs test (DCT) was negative. A complete serological screen for autoimmune hepatitis produced normal results. Fasting lipid profile, kidney and thyroid function tests were within normal limits. Her hepatitis B surface antigen and anti hepatitis C virus antibodies were negative and serum ceruloplasmin level was normal (34 mg/dl); no Kayser–Fleischer ring was observed on slit lamp examination.

Investigations of a hypercoagulable state showed functional deficiency of protein C 31% (normal: 75–165); protein S free 45% (normal: 50–120), but she was negative for lupus anticoagulant and factor V Leyden mutation. Her serum folate level was 23 ng/ml (normal: 5-21 ng/mL), serum iron 24 mcg/dL (normal: 60 to 170 mcg/dL), total transferrin iron binding capacity 400 mcg/dL (normal: 240 to 450 mcg/dL), serum ferritin 3.3ng/mL (normal: 12 to 150 ng/ml) . Her plasma homocysteine level was normal (10.4 umol/L).

Abdominal ultrasound revealed hypoechoic liver with massive splenomegaly (long axis 16 cm). Doppler ultrasound of the liver showed IVC narrowing with intrahepatic collaterals (figure1 and figure2). All three hepatic veins were patent. Portal vein was dilated with prominent splenoportal axis, collaterals also noted near falciform ligament and gastro-oesophageal junction

The diagnosis of BCS was confirmed by a contrast-enhanced computed tomography (CT) of the abdomen which showed all 3 patent hepatic veins, intrahepatic collaterals, and with narrowing of the supra hepatic segment of the inferior vena cava(figure3 and figure 4). Liver biopsy was planned but could not be done because of persistent thrombocytopenia due to hypersplenism. Oesophago-gastroduodenoscopy revealed no oesophageal varices but signs of mild portal hypertensive gastropathy were present. Marked antral nodularity with gastric antral vascular ectasia was present in antrum (figure 5). The duodenal nodularity was present in first part and second part of the duodenum, but there was no scalloping while histopathological examination of biopsies taken from the bulb and the second part of the duodenum revealed an increase in intraepithelial lymphocytes with crypt hyperplasia and subtotal villous atrophy (modified Marsh type 3A). Her serum IgA antitissue transglutaminase antibody titers were elevated (> 100 units/mL cutoff 15 units/mL).

She was given blood transfusion (2 units) and started on a gluten-free diet, propranolol and

nutritional supplements (iron, multivitamin and calcium). Six months later, she has clinically improved and gained weight & height. Her hemoglobin (12 gm/dL) and total leukocyte (2400/ mm^3) and platelet counts (95000/ mm^3) have increased (Table-1). On USG abdomen, there was significant decrease in intrahepatic collaterals and improved flow through IVC. Repeat Endoscopy after 6 months of GFD showed complete disappearance of GAVE & reduction in antral nodularity (figure 6).

Discussion

The case describes the occurrence of GAVE and BCS in a female child with CD. GAVE is a distinct condition also associated with portal hypertension that can cause acute and chronic upper gastrointestinal blood loss. These conditions frequently, but not invariably, are diagnosed by upper endoscopy. Although they are fairly prevalent, only 15% to 20% of subjects experience symptomatic gastrointestinal blood loss. GAVE is often associated with systemic illnesses, such as cirrhosis of the liver, autoimmune connective tissue disorders, bone marrow transplantation and chronic renal failure. The pathophysiological changes leading to GAVE have not been fully explained and remain controversial. Patient presentation varies from chronic iron-deficiency anaemia to heavy acute gastrointestinal bleeding[7]. An understanding of the pathophysiologic changes that lead to GAVE is lacking because most theories are based on single case reports or on reports of smaller series of fewer than 15 cases.

Interestingly, in 16 out of 28 cases of CD-associated BCS, the diagnosis of CD was established upon investigating patients for symptoms of BCS in the absence of typical symptoms of CD, confirming that ′silent′ and atypical presentations of CD have become very common. On the other hand, hepatic vein thrombosis can be asymptomatic, especially in the setting of chronic occlusion with large collaterals, which explains the incidental finding of BCS in some patients known to have CD [8]. In BCS, the IVC may show localized narrowing or marked narrowing consistent with a web or a thrombus and intrahepatic collaterals are a specific diagnostic criterion for BCS. [9] Similarly in our case localized IVC narrowing with intrahepatic collaterals were present.

Other mechanisms have been suggested as explaining the pro-thrombotic potential of CD[8], including (i) malabsorption of vitamin K causing protein C, S and antithrombin III deficiency, (ii) hyperhomocysteinemia secondary to folate deficiency and/or variants in the methylenetetrahydrofolic acid reductase (MTHFR) gene (iii) an association with serum lupus anticoagulant (iv) autoimmune vasculitis (v) magnesium deficiency and (vi) myointimal proliferation leading to thrombosis.

GAVE does not respond to measures that decrease portal pressures in PHG, including transjugular intrahepatic shunt and β-blocker therapy. The primary treatment of actively bleeding GAVE as well as recurrent bleeding from GAVE is endoscopic ablation (Nd:YAG-laser or argon plasma coagulation). Surgical antrectomy should be reserved for unresponsive cases as it is associated with a high mortality [7]. Ultimately, treatment of the underlying medical co-morbidities may lead to resolution of GAVE as we found complete resolution of GAVE on repeat endoscopy after 6 months of GFD (Figure 6).

We suggest that a diagnosis of CD should be pursued in the setting of BCS and GAVE of undetermined etiology. Similarly, CD patients with unexplained manifestations of acute or chronic liver injury should be assessed for BCS. To conclude, we report a rare occurrence of GAVE and BCS in a patient with CD from India.

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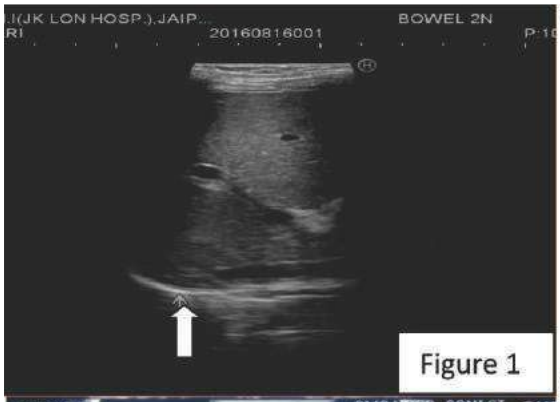
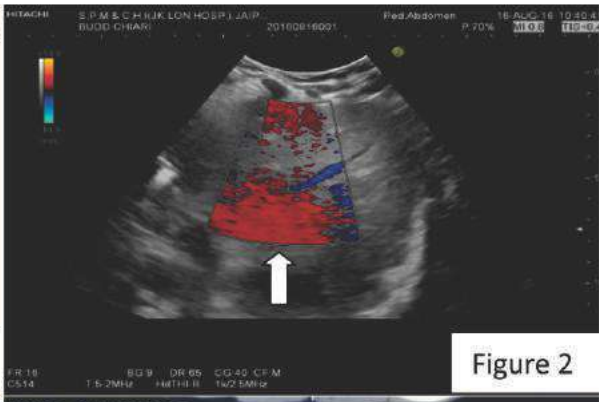
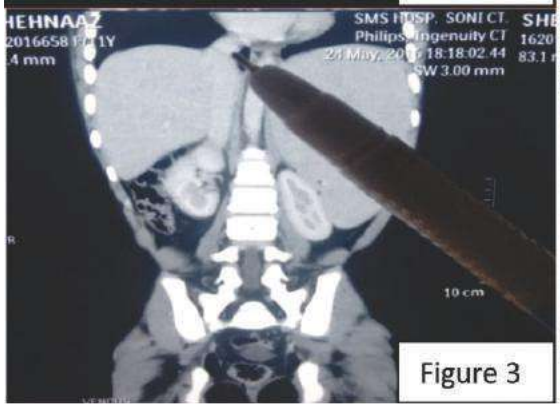
Table1. Investigations and anthropometry before and after 6months of gluten free diet(GFD)

	Before GFD (on Admission)	After 6months of GFD
Hemoglobin(>11.5g/dL)	3.1 g/dL	12g/dL
Total Leukocyte count (4000-11000/mm^3)	1510/ mm^3	2400/ mm^3
Total red blood cell count (4.2 -5.4million/mcL)	2.2million/mcL	4.85million/mcL
Mean corpuscular volume (80-96 fL/redcell)	60.9 fL/red cell	77.9 fl/red cell
Platelet count (150000-400000/ mm^3	11000 / mm^3	95000 / mm^3
Weight (kg)	26kg	30kg
Height (cm)	131 cm	133.5 cm







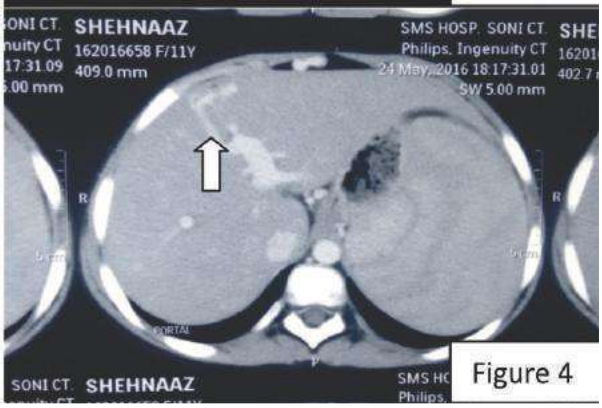
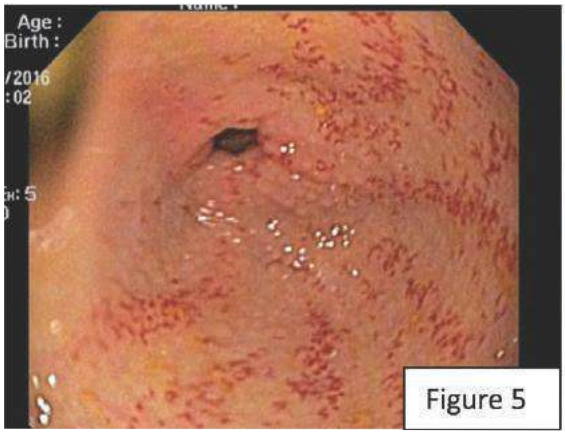


Figure 1. Ultrasound abdomen showing narrowing of IVC.
Figure 2. Ultrasound Doppler showing intrahepatic collaterals,
Figure 3. CT triphaisc angio abdomen showing IVC narrowing,
Figure 4. CT triphaisc angio abdomen showing intrahepatic collaterals



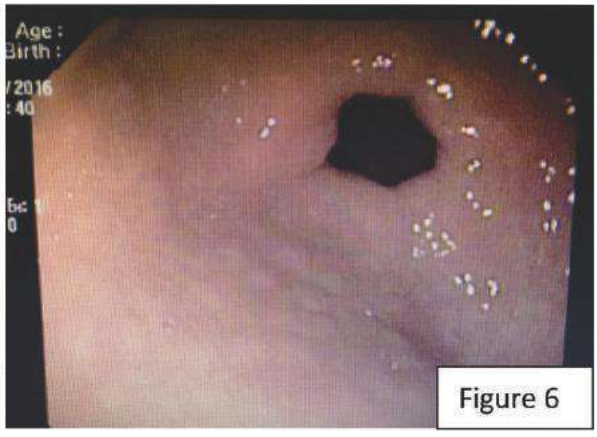


Figure 5. Gastroscopy showing GAVE with Antral nodularity,
Figure 6. Gastroscopy showing mild antral nodularity with disappearance of GAVE (after 6months of gluten free diet)