INTRODUCTION

Celiac Disease (CD), also known as non-Tropical sprue, and Celiac sprue is an immune-mediated disorder, triggered by gluten containing grains in genetically susceptible people. The disease may be diagnosed at any age and can affect many organ systems. Its diagnosis and management can often be challenging. A high index of suspicion is required to diagnose this disease at an early stage in patients presenting with atypical symptomatology and delayed onset. Although serological tests are widely used, duodenal biopsy remains the gold standard for diagnosis of CD. Even though CD affects various body systems, Microscopic Colitis (MC) and refractory sprue are among the main gastrointestinal complications of CD, which are resistant to Gluten-Free Diet (GFD). A thorough and appropriate evaluation is mandatory for an early and accurate diagnosis of these complications. Herein, we report a case of a young female with CD in early phase in concordance with MC and splenomegaly.

CASE REPORT

An 18-year female presented to the Outpatient Department (OPD) with symptoms of small bowel diarrhea for the past one year associated with easy fatigability, generalized weakness and undocumented weight loss. She also complained of non-itching rashes over her legs for one month. She denied any history of abdominal pain, fever, nausea or vomiting, passage of worms in stools, joint pain or swelling, photosensitivity or blood loss. She also denied use of medications or drug abuse.

The mother was a known case of refractory CD associated with MC. The physical examination revealed a young girl weighing 30 kg and 5 feet tall with pallor, peripheral pitting edema and non-blanching purpuras on legs bilaterally. Tip of spleen was palpable on abdominal examination with no hepatomegaly or other stigmata of chronic liver disease.

Ultrasound abdomen revealed 14 cm spleen with no splenic varices, normal size liver and portal vein of 1.1 cm and no ascites. Complete blood picture revealed microcytic hypochromic picture with hemoglobin (Hb): 5.1 g/dl (normal: 11.5-15.5 g/dl in females), Mean Corpuscular Volume (MCV): 64.6 fl (78 - 95 fl), total leukocyte count: 4.1 x 10^9/L (normal: 4 - 11 x 10^9/L), platelets: 82 x 10^9/L (normal: 150 - 400 x 10^9/L). Iron profile consistent with iron deficiency anemia with serum iron: 08 ug/dl (normal: 40 - 170 ug/dl in females), total iron binding capacity: 507 ug/dl (normal: 250 - 450 ug/dl), transferrin saturation: 1.57%, ferritin: 5.3 ng/ml (normal: 6.9 - 282 ng/ml), serum folate: 1.1 ng/ml (normal: 5.9 - > 24/8 ng/ml) and normal vitamin B12: 324 pg/ml (normal: 180 - 914 pg/ml). Coagulation profile and Hb electrophoresis was normal while Erythrocyte Sedimentation Rate (ESR): 45 mm after 1st hour (normal: 0 - 9 mm after 1st hour). Liver function tests showed hepatocellular injury with total bilirubin: 0.45 mg/dl (normal: 0.2 - 1.0 mg/dl), direct bilirubin: 0.07 mg/dl (normal: 0 - 0.25 mg/dl), alkaline phosphatase: 242 U/L (normal: 50 - 136 U/L), aspartate transaminase: 50 U/L (normal: 10 - 42 U/L), alanine transaminase: 59 U/L (normal: 10 - 40 U/L), gamma glutamyl transferase: 50 U/L (normal: 7 - 64 U/L). Viral serology for hepatitis B and C was negative. Autoimmune profile including Anti-Nuclear Antibodies (ANA), Anti-Smooth Muscle
Antibodies (ASMA), Liver Kidney Microsomal antibody (LKM), anti-mitochondrial antibodies was negative. Serum IgM level was normal. Serum cryoglobulins were checked for suspicion of vasculitis, which came to be positive.

Esophagoduodenoscopy demonstrated no varices and normal stomach. A duodenal biopsy was obtained which was consistent with sprue fulfilling criteria for Marsh type 3 (Figure 1A). Serological tests for CD were positive with high titters (tissue transglutaminase antibodies (anti-tTG) IgA: > 100 Units (positive: > 10 Units), Anti Gliadin Antibodies (AGA) IgA: 203 Units, AGA IgG: 186 Units). Human leukocyte antigen typing revealed DQ2 positivity. Patient was commenced on oral iron supplement and GFD. A flexible sigmoidoscopy was performed to rule out MC in view of positive family history. Biopsy was consistent with Lymphocytic Colitis (LC, Figure 1B).

Patient was followed in the OPD setting after one month and showed improvement both clinically and in laboratory parameters with Hb: 9 g/dl, MCV: 73 fl, platelets: 280 x 10^9/L. Purpura disappeared on GFD and repeat cryoglobulin testing was negative; therefore, skin biopsy was deferred. As liver function tests were persistently deranged even on GFD, liver biopsy was performed which was reported as mild portal inflammation and few non-caseating epithelioid granulomas and was consistent with celiac hepatitis with no features of autoimmune hepatitis, primary biliary cirrhosis or fibrosis.

Chest X-ray, computer tomography scan of abdomen and pelvis, serum Angiotensin Converting Enzyme level (ACE) and ESR were performed to rule out common etiologies of granulomata in the liver. All of which negated the presence of malignancy, tuberculosis and sarcoidosis. The patient was on regular follow-up for 3 years now and was symptom-free. The spleen has become impalpable. Her weight has increased to 43 kg.

In view of positive family history, patient's sister was screened and she was also diagnosed as CD with iron deficiency anemia without MC.

**DISCUSSION**

Celiac Disease (CD) is an autoimmune enteropathy characterized by intolerance to gluten in genetically susceptible subjects, with a higher prevalence in females (F/M: 2.5/1). In 15 - 55% of patients with CD, liver damage may range from mild hepatic abnormalities to severe liver disease. The mechanism of liver injury is not been clearly defined. Celiac hepatitis, which is characterized by mild periportal inflammation with Kupffer cell hyperplasia, mononuclear cell infiltration, absence of any clinical features suggesting chronic liver disease, hypergammaglobulinemia, serum autoantibodies, and hepatomegaly, splenomegaly, or both; this form is reversible with consumption of GFD, differentiating it from autoimmune liver disorder.

Hepatic granulomas have been associated with a wide variety of diseases, including sarcoidosis, tuberculosis, primary biliary cirrhosis, and drug reactions, accounting for up to 50 - 75% of hepatic granulomas. The etiology remains undetermined in approximately 36% of reported cases.

In this patient, liver biopsy findings were consistent with celiac hepatitis but repeat biopsy to document the reversal of histological changes on GFD was not performed. We also documented the presence of a few small non-caseating granulomas. The workup for sarcoidosis, tuberculosis, primary biliary cirrhosis and malignancy was carried out and was negative. The granulomas most probably were of idiopathic nature.

LC, along with Collagenous Colitis (CC), is included under the term MC, which have been reported in several series of patients with CD who have persisting symptoms despite GFD. In this patient, MC was diagnosed on preliminary work up due to positive family history with no history of refractory symptoms.

Although splenic atrophy is established as an extra-intestinal manifestation of CD, splenomegaly has been recently reported in association with IPH. IPH is a
combination of PH, splenomegaly, pancytopenia in the absence of histological liver damage or obstruction of the hepatic veins.

To the authors' knowledge, this is first report of CD with splenomegaly with no evidence of IPH (absence of varices, ascites) and no histological evidence of significant portal fibrosis.

This case highlights the phenotypic variability of familial cases of CD and a very rare association of splenomegaly with the disease. The case also provides evidence that MC can occur at early, non-refractory stage of the disease. The other reasons for splenomegaly and MC can be confidently excluded as the patient is symptom-free at 3 years of follow-up. These findings also support our theory that these extra-small intestinal complications are most probably related to CD.

In conclusion, CD can present with a variety of extra-intestinal complications and a thorough investigation is required to exclude other causes of these additional pathologies.

REFERENCES