Diarrhea and Symptomatic Coagulopathy: An Uncommon Presentation of Celiac Disease

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Abstract

A 39 year-old female was admitted to the emergency department due to watery diarrhea and weight loss for 3 weeks. Over the last days she also presented menorrhagia and vomiting. Physical examination revealed skin paleness and slight dehydration.

Laboratory investigation showed microcytic anemia (hemoglobin 10.6 g/dL), multiple nutritional deficiencies and hypertransaminasemia (aspartate aminotransferase 120 UI/L and alanine aminotransferase 201 UI/L). International normalized ratio was greatly increased (11.87: more than 10 times the upper limit of normal) as well as activated partial thromboplastin time (100 seconds). Additional studies were positive for increased antithissus transfuglutaminase (above 300 UA/mL) and attenuation of duodenal villous pattern on upper endoscopy. Duodenal biopsies confirmed celiac disease. Coagulopathy was treated with vitamin K intravenously with normalization of coagulation assays. Following a gluten-free diet the patient became asymptomatic with no bleeding recurrence and achieved laboratory and histological recovery.

Despite being a well-characterized disorder, celiac disease remains underdiagnosed. This case highlights the several manifestations of celiac disease that may trigger the diagnosis. Furthermore, bleeding due to vitamin K malabsorption is a rare complication of the disease and is herein presented.

Keywords: Celiac disease; Coagulopathy; Malabsorption; Hypovitaminosis K

Introduction

Celiac disease is one of the most common lifelong disorders in Europe and United States of America [1,2]. Patients often present with gastrointestinal symptoms including altered bowel habits, abdominal pain and weight loss [3,4]. Extra-intestinal manifestations such as anemia, osteoporosis, short stature or peripheral neuropathy have been increasingly recognized and may dominate clinical presentation in adults [3,5,6]. Hemorrhagic presentations due to coagulopathy are, however, quite rare [5-8]. A patient with bleeding due to severe coagulopathy is presented. Celiac disease was suspected as there was evidence of malabsorption.

Case Report

A 39 year-old female was admitted to the emergency department due to a history of diarrhea, weight loss (7 Kg), progressive fatigue and anorexia for 3 weeks. She reported between 5 to 6 daily episodes of bulky, watery and nonbloody diarrhea. 3 days before the admission she started vomiting and noticed menorrhagia.

She denied abdominal pain, fever, other blood losses namely melena or hematuria, spontaneous bruising or other symptoms. There was no history of recent travels or sick contacts.

Her past medical history was unremarkable. She had a regular diet and denied any medications or alcohol abuse.

Physical examination revealed skin paleness and slight dehydration. There were no bruises, cutaneous stigmata of liver disease, peripheral edema or other relevant findings on examination.

Laboratory investigation showed: hemoglobin 10.6 g/dL (normal: 12-16), mean corpuscular volume 65 fl (normal: 83-101), mean corpuscular hemoglobin 20 pg (normal: 25-35); leucocytes 3700/uL (normal: 4000-10000), platelets 412000/uL (normal: 150000-400000), serum potassium 2.5 mmol/L (N: 3.6-5.1), magnesium 1.3 mg/dL (N: 3.6-5.1), phosphorus 2.7 mg/dL (N: 2.3-4.7), corrected calcium 9 mg/dL (N: 8.8-10); albumin 2.0 g/dL (N: 3.4-4.8), total protein 4.3 g/dL (N: 6.2-8.5), aspartate aminotransferase 120 UI/L (N: 5-34), alanine aminotransferase 201 UI/L (N: 5-55) and protein C-reaction 7 mg/L (N: < 5 mg/L). The prothrombine time (PT) was increased (143,4 seconds; N: 9.4-13; international normalized ratio of 11,87) as well as activated partial thromboplastin time (aPTT) (100 seconds; N: 20-40).

Subsequent analysis revealed: serum iron 20 ug/dL (normal: 40-145), ferritin 11 ng/mL (normal: 15-160), B12 vitamin 166 pg/mL (normal: 200-900), folic acid 1.2 ng/mL (normal: 3-17).

Celiac serology showed antitissue transglutaminase above 300 UA/mL (normal: <15). Other laboratory work-up was unremarkable including bilirubin, alkaline phosphatase, gamma-glutamyl transpeptidase, cholesterol, triglycerides, thyroid function tests.
serology for human immunodeficiency virus, hepatitis serology and liver autoimmune panel. Bleeding time and fibrinogen were also normal. Abdominal ultrasound was unrevealing.

Upper endoscopy evidenced a discrete attenuation of duodenal villous pattern without other findings (Figure 1). Histopathological examination of duodenal biopsies showed near total villous atrophy, increased intraepithelial lymphocytes and lymphocytic infiltration in the lamina propria (Figure 2). These findings were consistent with celiac disease.

Discussion

Celiac disease or gluten-sensitive enteropathy is an autoimmune disorder triggered by dietary gluten that primarily affects the small intestine in subjects with a genetic predisposition [6,9]. It may appear at any age and can present with a wide variety of clinical symptoms or signs [3,9]. This enteropathy is one of the most common causes of malabsorption characterized by diarrhea, steatorrhea, weight loss, failure to thrive or multiple deficiencies of macronutrients and micronutrients. This results from injury to the small intestine with loss of absorptive surface area, reduction of digestive enzymes and consequential impaired absorption [9].

Anemia secondary to malabsorption of iron, folic acid, and/or vitamin B12 is the most common hematologic manifestation of celiac disease, which may also be associated with thrombocytopenia and leukopenia, as in our case. Malabsorption of vitamin K can occur causing a decrease in K vitamin-dependent coagulation factors. This results in prolongation of coagulation assays namely the PT, INR and aPTT [10]. In fact, prolonged TP has been found in up to 20% of untreated adult cases [11]. However, overt bleeding has been rarely described [5-8].

Our case refers to a patient with celiac disease presenting with signs and symptoms of malabsorption as evidenced by multiple nutritional deficits including electrolyte imbalance, low serum iron, vitamin B12, folic acid and reduced serum albumin. Moreover the patient presented with symptomatic coagulopathy in the form of menorrhagia associated with a severe prolongation of PT, INR (more than 10 times the upper limit of normal) and aPTT, which is a rare manifestation of the disease. The abnormality of both the PT and aPTT, as seen in our case, could indicate either abnormalities of multiple coagulation factors or, less commonly, a deficiency or presence of inhibitors of the common pathway factors II, V, X or fibrinogen. Our patient was not taking vitamin K antagonists, denied a “super-warfarin” rodenticide ingestion and had no evidence of liver disease, biliary obstruction or disseminated intravascular coagulation. The association of symptoms and other signs of malabsorption suggested that the mechanism of this coagulopathy was malabsorption of vitamin K. In the majority of cases, hypoprothrombinemia presents with echymosis and hematomas, which were not present in our case [5]. Instead, menorrhagia was noticed causing a decrease in hemoglobin level.

Furthermore, our patient presented hypertransaminasemia, which is the most common liver abnormality in patients with celiac disease [12]. One proposed explanation for hepatic involvement in these patients is that the increased intestinal permeability may ease the entry of toxins, antigens, and inflammatory substances (cytokines and/or autoantibodies) to the portal circulation that, subsequently, play a role in liver injury [13].

The positive serology for celiac disease and the documentation of villous atrophy on histopathological analysis confirmed the clinical suspicion. Marked clinical improvement without recurrence of bleeding associated with normalization of the laboratory abnormalities and histological recovery after gluten withdrawal was consistent with the diagnosis.

The authors present this case as it represents a good clinical picture of celiac disease including symptomatic hypovitaminosis K, which is a rare complication of the disease. This diagnosis must be kept in mind of the clinicians specially if gastrointestinal symptoms coexist.
References


