Case Report

Hypoalbuminemia and generalized edema as an atypical presentation of celiac disease

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Abstract

The clinical presentation of celiac disease has evolved significantly over the last few decades. Previously defined as a malabsorption syndrome in pediatric patients, now it is considered an autoimmune disorder with diverse systemic manifestations among all age groups. We report a case of 56-year-old male presented with pedal edema and gradually progressive abdomen distention for the last 3 months. Serological evaluation and duodenal biopsy reports were suggestive of celiac disease. The patient was advised gluten-free diet, after 12 weeks, the patient became asymptomatic with the resolution of ascites and peripheral edema. According to the literature, there are few reports of protein-losing enteropathy as an initial presentation of celiac disease. The possibility of celiac disease should be considered even in the setting of atypical symptoms.

Keywords: Celiac disease, hypoalbuminemia, edema, protein-losing enteropathy

Introduction

Celiac disease is a chronic autoimmune disease characterized by small intestine malabsorption after the ingestion of gluten. Although previously considered a pediatric disease, nowadays the number of cases diagnosed in adults has increased. A recent meta-analysis showed the global prevalence of celiac disease in adults is 0.5%, which is lower than children (0.9%).[1] There is also a significant change in the symptomatology of celiac disease in past few decades, diarrhea is now reported less often and many patients are now presenting with subtle or unusual symptoms. In many cases, it is possible that celiac disease can present in later life without antecedent illness. Herein we report a 56-year-old male with presenting symptoms of pedal edema and hypoalbuminemia diagnosed as celiac disease. A recent study showed the average delay in diagnosis of celiac disease is ≥3 years, resulting in significant morbidity.[2] There should be a high index of suspicion regarding these subtle and diverse clinical manifestations of celiac disease, in order to improve early diagnosis and prognosis.

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Case Presentation

A 56-year-old male patient presented to us with a history of bilateral pedal edema, abdominal distention and decreased appetite for the last 3 months. There was no history of weight loss, fever, jaundice, diarrhea, or reduced urine output. He denied any history of diabetes, hypertension, alcohol, or other drug abuse. On physical examination, he was afebrile, with a pulse rate of 82/min, blood pressure of 100/68 mm hg. Further examination revealed bilateral pitting pedal edema, shifting dullness on abdomen percussion suggestive of ascites. Laboratory analysis revealed hemoglobin of 13.4 gm/dl, total leukocyte count of 7.02 × 10^9/l, mean corpuscular volume of 89 fL, and platelet count of 486 × 10^9/l. Rest biochemical investigations were normal except total protein of 3.9 g/dl and albumin of 1.86 g/dl [Table 1]. The chest radiograph showed bilateral minimal pleural effusion. Ascitic fluid analysis was transudative in nature with low serum-ascites albumin gradient <1.1 g/dl. A computed

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Table 1: Biochemical and hematological investigations

CBC (complete blood count)	Hb- 13.9 gm/dl, TLC - 7.02 × 10^9 per liter (L), MCV- 89 fL Plt - 461 × 10^9/L
LFT (liver function test)	ALT - 18 U/L, AST - 21 U/L, total protein/albumin - 3.9/1.86 mg/dl
KFT (kidney function test)	Urea - 26 mg/dl, creatinine 0.91 mg/dl
CRP (C-reactive protein)	0.6 mg/L, normal <1.0 mg/L
ESR (erythrocyte sedimentation rate)	12 mm/h, normal <20 mm/h
Serum electrolytes	Sodium - 135 mmol/L, potassium - 3.9 mmol/L
Urinalysis	Sugar-Nil, protein- Trace, RBCs- Nil, Pus cells- Occasional
urine protein creatinine (PCR) ratio	0.18 mg/mg
Viral markers	HIV - negative, HBsAg - negative, Anti HCV - negative
Blood glucose (random)	115 mg/dl
INR (international normalized ratio)	0.94
Serum tissue transglutaminase (tTG) antibody	162.32 units, normal <20 units
Autoimmune profile	ANA - negative
Thyroid function test	T3-0.4 ng/dl, T4-0.9 ng/dl, TSH - 2.9 mIU/L

tomography of the abdomen was normal except moderate ascites. Further evaluation of hypoalbuminemia, urinalysis did not show proteinuria. The initial treatment was consisting of fluid restriction and diuretics. Echocardiography was also done to rule out constrictive pericarditis, which was unremarkable. After excluding, cardiac, renal, and hepatic causes of hypoalbuminemia and edema, additional workup was performed in a view of protein-losing enteropathy (PLE). We did not have the availability of stool alpha-1 antitrypsin assay. Upper gastrointestinal (GI) endoscopy was performed which showed decreased mucosal fold thickness with nodularity in the second part of duodenum. Subsequently, a duodenal biopsy was taken which revealed partial (marked) villous atrophy with increased intraepithelial lymphocytes and crypt hyperplasia (modified marsh stage 3b, [Figure 1a and b]). Serum tissue transglutaminase (tTG) antibody was also elevated (162.32 units, normal < 20 units). We made the final diagnosis of celiac disease on the basis of positive serological and tissue biopsy findings. The patient was advised to follow gluten-free diet, within 2 weeks, patient's general condition was improved significantly with decreased ascites and pedal edema. At 3 months of follow-up, the patient was completely asymptomatic on gluten-free diet (total protein and albumin were 7.4 g/dl and 3.8 g/dl, respectively). The follow-up serology (anti-tTG) at 6th month was also negative.

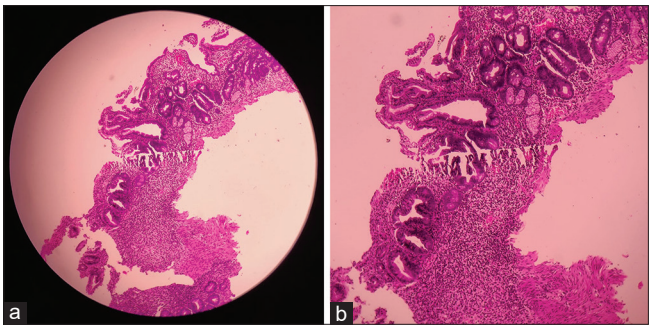

Figure 1: (a, b) Duodenal biopsy showing marked villous atrophy, crypt hyperplasia and increased intraepithelial lymphocytes (modified marsh stage-3b) characteristic of celiac disease

Discussion

Traditionally considered a primary malabsorption disorder with diarrhea as a cardinal presenting symptom, now celiac disease regarded more of a multisystem disorder with predominant nondiarrheal manifestations. A recent report by Singh *et al.*, described the global prevalence of celiac disease is about 1.4% of population.[1] The prevalence of celiac disease in Asia was 0.6% according to the same report. Moreover, the prevalence rate in north Indians is ever increasing, probably related to a much higher rate of wheat consumption.[3] Despite increasing prevalence at recent times, celiac disease is still underdiagnosed.[4] The silent and subtle presentation is largely associated with underdiagnosis of celiac disease. Iron deficiency anemia, osteoporosis, pain abdomen, bloating, amenorrhea are the common nonclassical presentations of celiac disease. A study by PH Green reported silent disease (38%) as the second most common presentation after diarrhea in celiac disease.[5] Celiac disease is no longer to be considered as a disease of malnourished individuals with overweight is found in 8.8% to 20.8% of the cases.[6] Similar to these reports our patient did not have any GI symptoms and presented with pedal edema and ascites.

The other less common presentations are hypoalbuminemia, macroamylasemia, increased erythrocyte sedimentation rate, and neuromuscular symptoms.[7-10] Generalized edema and hypoalbuminemia without gastrointestinal symptoms is unusual in celiac disease. A study by Kuloglu *et al.* reported the prevalence of hypoalbuminemia and peripheral edema is 9.5% and 6.5%, respectively.[11] Both serological test and small intestinal biopsy (regardless of serology results) should be performed in all individuals with high celiac disease probability. However, patients with low probability of celiac disease should undergo serology testing. Those with positive serology should be evaluated subsequently by small bowel biopsy. Despite the increasing prevalence of silent celiac disease, there is inadequate evidence to support population screening in asymptomatic individuals.[12]

PLE should be suspected in every patient with edema and hypoalbuminemia with no alternate cause of protein loss. In PLE, there is abnormal, rapid loss of serum protein from gut lumen. A large group of disorders are associated with PLE

which include diseases with increased lymphatic pressure, erosive gastrointestinal diseases (GI malignancies, infectious diseases, sarcoidosis, ulcerative colitis and Crohn's disease), and diseases without mucosal erosions (including celiac disease, Whipple's disease, and systemic lupus erythematosus (SLE)). In celiac disease, there is a loss of villi and surface epithelium which increases the plasma protein leakage resulting in PLE. The diagnosis of PLE is confirmed by an increase in alpha-1 antitrypsin (αAT) clearance. A report by Levitt *et al.* showed decreased αAT clearance in celiac patients with gluten-free diet.[13] Our patient also showed significant improvement with gluten-free diet with the resolution of peripheral edema and ascites.

Conclusion

The clinical presentation of celiac disease is diverse. The nondiarrheal symptoms are increasingly prevalent in the recent past. These patients with atypical symptoms are likely to present to physicians; thus, early recognition by primary care physicians is vital to prevent significant morbidity in celiac disease.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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