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Severe Coagulopathy as a Rare Feature of Celiac Crisis in a Patient Previously Diagnosed with Celiac Disease

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Conflict of interest: None declared

Patient: Male, 76
Final Diagnosis: Celiac crisis
Symptoms: Abdominal pain • bleeding • diarrhea • weakness • weight loss
Medication: —
Clinical Procedure: Esophagogastroduodenoscopy • Colonoscopy
Specialty: Gastroenterology and Hepatology

Objective: Rare disease

Background: Celiac crisis is an uncommon but critical complication of celiac disease (CD) manifesting with copious diarrhea, dehydration, and severe metabolic imbalances. Celiac crisis occurring in individuals who have been formerly diagnosed with CD and displaying severe coagulopathy is tremendously rare.

Case Report: We report a case of a 76-year-old male, previously diagnosed with CD and non-compliant with gluten free diet, who presented with severe coagulopathy manifesting as gastrointestinal bleeding in addition to other features of celiac crisis, including severe diarrhea, dehydration, metabolic acidosis, electrolyte disturbances, and renal dysfunction. Esophagogastroduodenoscopy revealed flattened mucosa and mucosal nodularity in the duodenum. Duodenal biopsies exhibited active chronic inflammation with intraepithelial lymphocytosis and subtotal villous blunting. The patient was diagnosed with celiac crisis and treatment with vitamin K, parenteral nutrition, and steroids was commenced. After initial clinical improvement, a gluten-free diet was implemented with complete resolution of symptoms.

Conclusions: Though celiac crisis typically presents in patients with undiagnosed CD, it should be considered in patients who have been previously diagnosed CD but who are non-compliant with gluten free diet. Severe coagulopathy, though extremely rare, can be a feature of celiac crisis and should be consider when encountered in a patient with history of steatorrhea and gastrointestinal bleeding.

MeSH Keywords: Celiac Disease • Dehydration • Malnutrition • Vitamin K Deficiency Bleeding • Weight Loss

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Background

Celiac disease (CD) is a chronic, small intestinal, immune-mediated enteropathy that is triggered and perpetuated by exposure to dietary gluten in genetically predisposed individuals [1,2]. Most adult patients will have an indolent course with mild gastrointestinal symptoms, anemia, and/or nutritional deficiencies [2,3]. Celiac crisis is an uncommon, life-threatening form of CD that commonly presents in patients with undiagnosed CD [4] Common presentation includes profuse diarrhea, dehydration, and severe metabolic disturbances [2,5]. Celiac crisis occurring in individuals who have been formerly diagnosed with CD and displaying severe coagulopathy is extremely rare [6–8]. We report a case of a patient formerly diagnosed with celiac crisis and preceding diagnosis of CD who presented with severe coagulopathy evident by gastrointestinal bleeding.

Case Report

A 76-year-old Caucasian male was admitted to the hospital with a 4-day history of bloody diarrhea about 6 times per day, intermittent abdominal pain, vomiting, dizziness, and generalized weakness. He had been experiencing watery foul-smelling diarrhea, generalized weakness, and weight loss in the preceding 3 months. He had CD, diagnosed 5 years earlier on serological studies and duodenal biopsy. He was initially on a gluten-free diet but became non-compliant 4 months before presentation. He reported no traveling outside the United States. On arrival, he was afebrile but tachycardic and severely hypotensive. Also, he was evidently cachectic, severely dehydrated with hyperactive bowel sounds and diffuse abdominal tenderness.

Laboratory studies after initial resuscitation revealed microcytic hypochromic anemia, metabolic acidosis, hypoalbuminemia, hypokalemia, acute renal failure, and severe coagulopathy (Table 1). Initial differential diagnoses included septic shock due to gastrointestinal infection, hemolytic uremic syndrome, gastrointestinal malignancy and ischemic colitis. Blood, urine and stool cultures were obtained. Computed tomography (CT) of abdomen and pelvis without contrast reported no acute intraabdominal process. He was admitted to medical intensive care unit (MICU) and treated at first with intravenous fluids, antibiotics (vancomycin and piperacillin-tazobactam), sodium bicarbonate drip, fresh frozen plasma, electrolyte supplementation, and emergent hemodialysis. Hypotension, anion-gap metabolic acidosis, ARF and severe coagulopathy rapidly improved within 24 hours.

Additional laboratory studies showed ferritin level of 49.9 ng/mL (22–322 ng/mL), low serum iron of 24 ug/dL (65–175 ug/dL), normal total iron-binding capacity of 256 ug/dL (228–460 ug/dL) and low iron saturation of 9.38% (25–35%) consistent with iron deficiency anemia. Thyrotropin, vitamin B12, and folate levels were within normal limits. Total bilirubin, lactate dehydrogenase, and peripheral blood smear were within normal limits. Blood, urine, and stool cultures, fecal leukocytes, *Clostridium difficile* toxin polymerase chain reaction (PCR) assay, and ova and parasites were negative. Intravenous antibiotics were discontinued after 2 days due to lack of signs/symptoms of an acute infectious process and negative cultures.

Table 1. Laboratory results.

Laboratory tests	Results	Normal values
White blood count	10.5×10^3/uL	$4.5–11.0\times10^3$/uL
Hemoglobin	10.2 g/dL	13.5–17.7 g/dL
PT	>110.0 s	11–13.5 s
INR	>10	0.8–1.1
aPTT	38 s	25–35 s
Potassium	3.1 mmol/L	3.5–5.1 mmol/L
Magnesium	1.2 mg/dL	1.7–2.7 mg/dL
pH	6.93	7.35–7.45
Lactic acid	3.0 mmol/L	0.5–2.0 mmol/L
Creatinine	4.41 mg/dL	0.50–1.50 mg/dL
Glomerular filtration rate	13 mL/min	60–240 mL/min
Albumin	2 g/L	3.5–5.0 g/dL

PT – prothrombin time; INR – international normalized ratio; aPTT – activated partial thromboplastin time.

Due to persistent diarrhea, we performed a colonoscopy followed by an esophagogastroduodenoscopy (EGD). The colonoscopy showed normal colonic and rectal mucosa. The EGD revealed flattened mucosa and areas of mucosal nodularity in the second part of the duodenum (Figure 1). Duodenal biopsies exhibited active chronic inflammation with intraepithelial lymphocytosis and subtotal villous blunting (Figure 2). He was diagnosed with celiac crisis and treatment with intravenous vitamin K, parenteral nutrition, and methylprednisolone (80 mg, every 8 hours) commenced. Following clinical improvement, he was transferred from the MICU to the general medicine floor and a gluten-free diet initiated as well as treatment with oral budesonide (9 mg, every 24 hours).

After 10 days, oral steroid was discontinued, and the patient was discharged on a gluten-free diet. At follow-up, substantial improvement of malabsorptive symptoms were noted. The patient remained adherent to a gluten-free diet and asymptomatic at 12-month follow-up.

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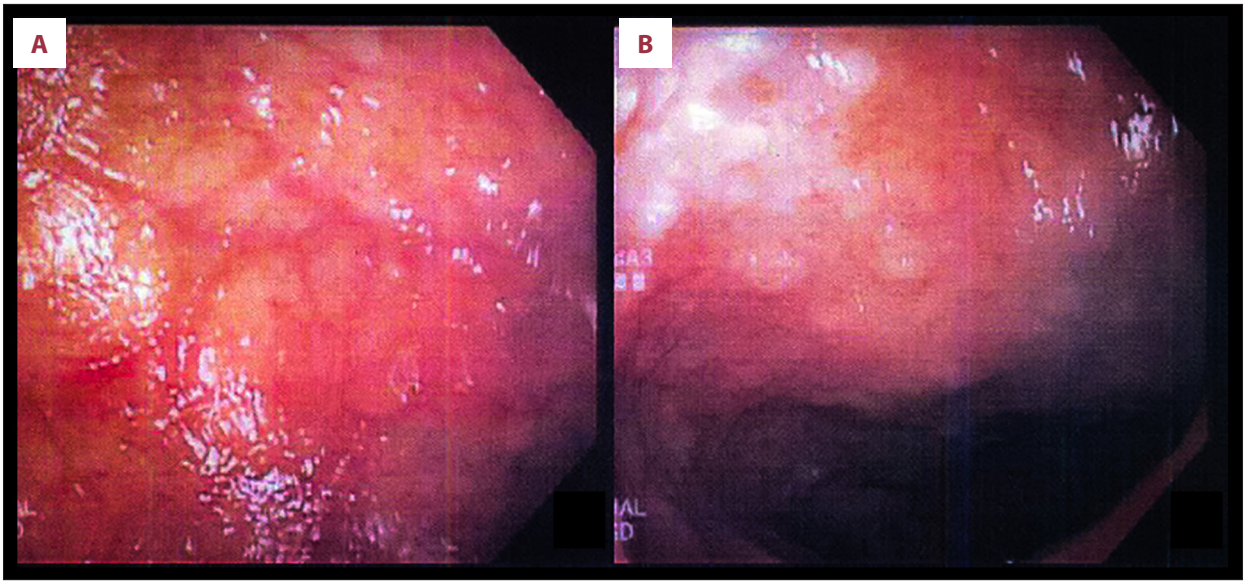

Figure 1. (**A**) Duodenum displaying loss of mucosal folds and atrophy on endoscopy. (**B**) Duodenum showing mucosal nodularity on endoscopy.

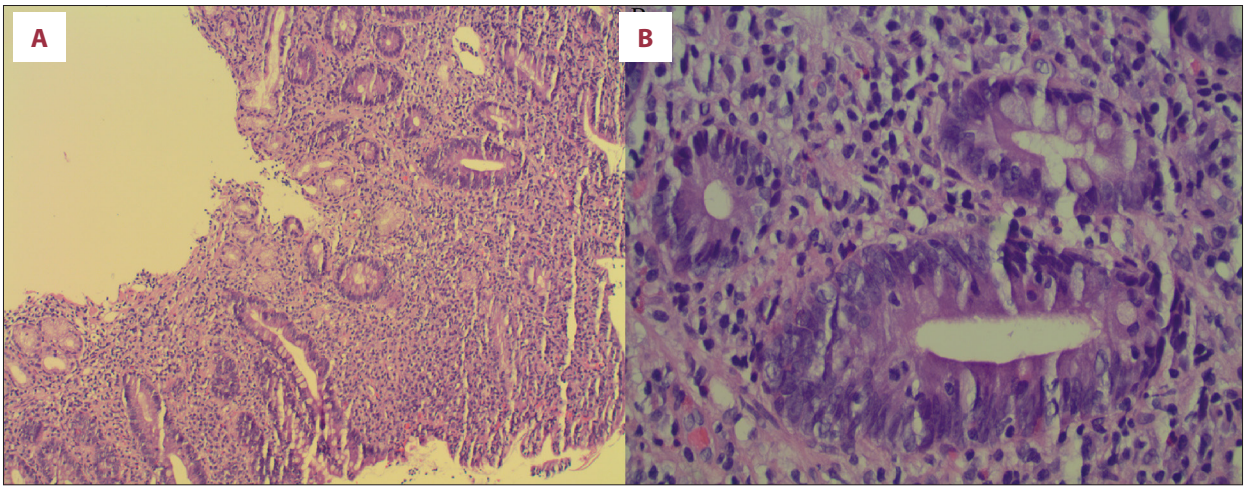

Figure 2. (**A**) Duodenal biopsy revealing subtotal villous blunting and hypoplasia. (**B**) Duodenal biopsy demonstrating intraepithelial lymphocytosis.

Discussion

The term celiac crisis was initially used in 1950s by Anderson and di Sant'Agnese to describe an acute fulminant form of celiac disease [4,6]. It has been documented to date in fewer than 30 adults [9]. The majority of reported cases have been in patients with no preexisting diagnosis of CD [4–6,9,10]. Proposed diagnosis criteria for celiac crisis requires acute onset or rapid progression of gastrointestinal symptoms attributable to CD requiring hospitalization and/or parenteral nutrition along with at least 2 of the following: signs of severe dehydration including hemodynamic instability and/or orthostatic hypotension; neurologic dysfunction; creatinine >2 g/dL; metabolic acidosis defined as pH <7.35; albumin <3.0 g/L; abnormal electrolyte levels including hyper/hyponatremia, hypocalcemia, hypokalemia or hypomagnesemia; and weight loss >4.5 kg (10 lbs) [4,9]. The index patient had all the features required for the diagnosis of celiac crisis. Unlike the majority of the reported cases, our patient developed celiac crisis following CD diagnosis due to non-compliance.

While asymptomatic mild coagulopathy is relatively common in celiac crisis, severe coagulopathy with clinical evidence of bleeding has rarely been described. A study showed that 18.5% of patients with CD had an international normalized ratio (INR) greater than 1.4 [11]. A case report by da Costa Becker et al. described a patient who presented with celiac crisis, coagulopathy, and upper gastrointestinal bleeding as initial presentation

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of CD [6]. While the biologic mechanism responsible for the development of celiac crisis remains unclear, previously described triggering factors include surgery, pregnancy, immunosuppressive therapy, infections, among others [4]. The presumptive mechanism includes a combination of severe mucosal inflammation, immune activation, and disruption of normal patterns of motility [4,10]. Coagulopathy develops from severe vitamin K malabsorption in the small intestine resulting in impaired activation of vitamin K dependent clotting factors such as factor II, VII, IX, and X [7].

Importantly, the diagnosis of celiac crisis requires the exclusion of other causes of diarrhea and malabsorption including infectious diarrhea, tropical sprue, intestinal lymphoma, eosinophilic gastroenteritis, among others [3]. These diagnoses were excluded in our patient. Due to its high morbidity, celiac crisis demands immediate recognition and treatment involving intravenous hydration, electrolyte repletion, and initiation of a gluten-free diet [5]. In patients who are extremely sick or who do not respond promptly to the aforementioned interventions, intravenous corticosteroids and/or total parenteral nutrition have been effective [4]. In the current patient, intravenous corticosteroids and total parenteral nutrition were initiated due to the severity of the presentation, resulting in an initial improvement. Complete symptom resolution occurred over months of a gluten free diet.

Conclusions

Although cases of severe symptomatic coagulopathy are a rare manifestation of celiac crisis, it is important to consider this diagnosis when confronted with a patient with gastrointestinal bleeding and a history of steatorrhea [8]. Furthermore, education regarding compliance with a gluten-free diet and appropriate follow-up is important to prevent this rare complication.

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