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CASE REPORT

Marked coagulopathy without liver disease or anticoagulation therapy

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KEYWORDS
Coagulopathy;
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Liver

Summary Symptomatic coagulopathies in celiac disease (CD) are rare. Here, we report a profound case of coagulopathy in a celiac. A 66-year old female without liver disease or anticoagulation therapy presented with multiple ecchymoses, guaiac positive melanic stool, and a recent 4.5 kg weight loss. Laboratory values included hemoglobin, 3.8 g/dL; MCV, 66 fL; serum iron, 17 μg/dL; platelet count, 580 K/μL; white count, 14.2 K/μL, and vitamin D, < 5.0 ng/mL. Additional values included partial thromboplastin time (PTT), > 200 s; prothrombin time (PT), > 150 s; INR, 20.5, putting her at extreme risk of bleeding. Vitamin K deficiency was assumed. The patient was given two units of fresh frozen plasma, packed red cells, and vitamin K intravenously. Endoscopy and biopsies demonstrated duodenal mucosal atrophy with cobblestoning, erosive gastritis, flattened duodenal villi and numerous intraepithelial lymphocytes. Transglutaminase serology demonstrated IgA TTG > 100 U/mL (normal < 3 U/mL), confirming a diagnosis of CD. The patient's coagulopathy resolved within two days following admission. This case underscores the importance of CD testing in all patients with coagulopathies of unknown origin. Although coagulopathy is an uncommon presentation of CD, in extreme cases such as this, it has the potential to be life-threatening.

Introduction

Celiac disease (CD) is a chronic immune-mediated enteropathy against dietary gluten in genetically predisposed individuals [1]. The reaction can lead to enterocyte destruction and villous atrophy causing gastrointestinal symptoms including abdominal pain, diarrhea, and weight loss [2,3]. It is reported to affect approximately 1% of the general

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population in Europe and North America [4,5], and it is speculated that 80% of patients with CD are not properly diagnosed as many are subclinical or present with extra-intestinal manifestations [6]. Secondary symptoms are frequently the consequence of malabsorption and can include coagulopathies, anemia, hyperparathyroidism, and osteomalacia. Often it is these secondary symptoms that present as the primary issue, thus complicating the diagnostic process. [2,3,7]. Here, we report a profound case of coagulopathy in a celiac patient as a means of highlighting the importance of CD testing in all patients with coagulopathies of unknown origin.

Case report

A 66-year-old female presented to the emergency department with progressive weakness and dizziness. She reported dark stools one day prior, anorexia, and a recent 4.5 kg weight loss. She was recently diagnosed with osteoporosis and six vertebral compression fractures. Prior to the diagnosis of her fractures, the patient was taking Excedrin for analgesia. Upon diagnosis, she began taking vitamin D, calcium supplementation, and Ibuprofen. She reported taking Naproxen one-week prior which resulted in nausea and vomiting without hematemesis. The patient's medical history was significant for anemia due to a peptic ulcer found nearly 20 years previous that required transfusion therapy.

On exam, the patient appeared cachectic with a moderately distended and tympanitic abdomen. Assessment showed multiple ecchymoses, guaiac positive melanic stool, and pertinent laboratory values as follows (Table 1):

- hemoglobin, 3.8 g/dL;
- MCV, 66 fL;
- serum iron, 17 μg/dL;
- platelet count, 580 K/μL;
- white count, 14.2 K/μL;
- partial thromboplastin time (PTT), > 200 s;
- prothrombin time (PT), > 150 s;
- INR, 20.5;
- vitamin D, < 5.0 ng/mL.

She denied use of anticoagulants. Vitamin K deficiency was assumed. She was given two units of fresh frozen plasma, packed red cells, and vitamin K intravenously.

Upper endoscopy demonstrated duodenal mucosal atrophy with cobblestoning and erosive gastritis (Fig. 1a). Duodenal biopsies revealed flattened villi and numerous intraepithelial lymphocytes (Fig. 1b). Transglutaminase serology demonstrated IgA TTG > 100 U/mL (normal < 3 U/mL), confirming a diagnosis of CD. Her coagulopathy resolved within two days following admission.

Discussion

Symptomatic coagulopathies complicated by hemorrhagic events in CD are rare [8,9]. The pathogenic mechanism relates to malabsorption of vitamin K, leading to impaired hepatic synthesis of coagulation factors II, VII, IX, and X. Clinically, the resulting deficiencies can be detected as prolongation of coagulation assays [8,10].

To the best of our knowledge this case demonstrates the most severe coagulopathy documented from CD. Therapeutic INR ranges from 2.0—3.0, with an INR > 5.0 resulting in a significantly increased likelihood of adverse bleeding events [11,12]. Our patient presented with an INR of 20.5 and a PTT > 200 s. Marked elevation in both the INR and PTT suggests a deficiency or inhibitor in both the intrinsic and extrinsic coagulation pathways or complications with the common pathway [13]. Differential diagnostic consideration includes liver disease, malabsorption, and disseminated intravascular coagulopathy [14,15]. Additionally, consideration can be given to congenital deficiency or acquired inhibitors in the common pathway and amyloidosis leading to factor X deficiency, although these cases are extremely rare [16,17]. Due to our patient's low vitamin D, vitamin A, and iron parameters, malabsorption resulting in vitamin K deficiency was suspected and vitamin K supplementation resulted in reversal of the coagulopathy.

CD can be suspected in many cases, but the diagnosis is most often discovered by histopathological examination of duodenal biopsies [18]. Mucosal injury is most often found in the proximal segments of the small bowel, which demonstrates atrophic flattening of the villi, an increased number of lymphocytes, and crypt hyperplasia [3,18,19]. Serologically, the presence of anti-endomysium, anti-transglutaminase, or anti-deamidated gliadin peptide antibodies can aid in the diagnosis of the disease; yet, it is important to note that in 2%—3% of individuals that have confirmed CD, these serological tests may produce a false negative [3,18]. In our patient, serology along with histopathological analysis confirmed the clinical suspicion of CD.

Classical symptoms of CD are often of gastrointestinal origin and include but are not limited to bloating, diarrhea, constipation, abdominal pain, and weight loss [2,18]. Not all gastrointestinal symptoms may be evident and can present instead as nutritional deficiencies. Iron deficiency is the most prevalent, but patients may also demonstrate deficiencies in folate, vitamin B12, zinc, and vitamin D [20]. These deficiencies can lead to anemia, weakness, osteoporosis, and compression fractures, all of which were experienced by our patient. After two months of strict adherence to a gluten free diet, nearly all of our patient's serological testing was within normal limits.

This profound case of coagulopathy underscores the importance of CD testing in all patients with coagulopathies of unknown origin. Although coagulopathy is an uncommon presentation of CD, in extreme cases such as this, it has the potential to be life-threatening.

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Specific author contributions

L.J.H. served as the attending doctor for the patient. All authors made substantial contributions to analysis and interpretation of data and drafting and revising the manuscript. All authors approved the final draft to be submitted.

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Table 1 Laboratory data, pre- and post-treatment.

Measure	Diagnosis	Post treatment (2-day)	Follow up (2 month)	Reference range
Partial thromboplastin time, s	> 200	35	28	20–37
Prothrombin time, s	> 150	13.9	14.1	11.9–14.5
INR	20.5	1.0	1.1	0.9–1.1
Fibrinogen, mg/dL	440			200–400
Iron panel				
Ferritin, ng/ml	16.4		264.6	30–400
Serum iron, μg/dL	17		101	37–145
Unsaturated iron binding capacity, μg/dL	208		208	112–346
Total iron binding capacity, μg/dL	225		309	228–428
% Transferrin saturation	7		32	15–50%
CBC				
WBC, K/μL	14.2	10.8	6.6	4.5–11.0
RBC, M/μL	1.80	3.30	4.42	4.00–5.20
Hemoglobin, g/dL	3.8	9.4	12.9	12.0–15.0
Hematocrit, %	11.9	27.6	39.3	36.0–48.0
Mean cell volume, fL	66.0	83.7	88.9	80.0–100.0
Mean corpuscular hemoglobin concentration, (g/dL)	32.1	34.1	32.7	31.0–36.0
Red Cell Distribution Width, %	19.4	23.8	19.6	11.5–14.5
Platelet Count, K/μL	580	418	512	140–440
Granulocytes, %	81.0	71.4	59.0	38.0–78.0
Lymphocyte, %	8.6	12.0	24.1	15.5–49.0
Monocyte, %	9.7	14.5	11.4	1.0–12.0
Eosinophil, %	0.4	1.9	4.6	0.0–7.0
Basophil, %	0.3	0.2	0.9	0.0–2.0
Granulocyte #, K/μL	11.5	7.7	3.9	1.8–8.0
Lymphocyte #, K/μL	1.2	1.3	1.6	1.5–4.8
Monocyte #, K/μL	1.4	1.6	0.7	0.1–0.9
Eosinophil #, K/μL	0.1	0.2	0.3	0.0–0.7
Basophil #, K/μL	0.0	0.0	0.1	0.0–0.3
Celiac disease complete panel				
Tissue transglutaminase antibody IGG, U/mL	7.0			
Tissue transglutaminase antibody IGA, U/mL	> 100		2.0	
Immunoglobulin A, mg/dL	241.9		168	70.0–400.0
CMP				
Glucose, mg/dL	141	96	81	70–105
BUN, Serum, mg/dL	25	8	13	8–23
Creatinine, Serum, mg/dL	0.6	0.3	0.3	0.6–1.1
Sodium, mmol/L	132	139	137	133–145
Potassium, mmol/L	2.6	3.4	5.6	3.3–5.1
Chloride, mmol/L	94	104	105	96–108
Carbon dioxide, mmol/L	20	22	21	22–30
Anion gap	18.0	13.0	11.0	8–16
Calcium, mg/dL	6.2	6.6	7.2	8.6–10.4
Total protein, mg/dL	4.9	5.0	6.3	5.9–8.4
Albumin, mg/dL	2.7	2.6	4.0	3.2–5.2
Globulin, g/dL	2.2	2.4	2.3	2.2–3.7
Albumin/Globulin ratio	1.2	1.1	1.7	1.0–2.3
Bilirubin, Total, mg/dL	0.3	0.7	0.2	0.0–1.0
AST (SGOT), U/L	20.0	24	40	0–37
ALT (SGPT), U/L	12	12	51	0–40
ALP, U/L	180	212	226	39–117
GFR	95	119	119	
GGT, U/L	10	26		5–36
LDH, U/L	241	253		94–250
Triglycerides, mg/dL	251	219		< 150

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Table 1 (*Continued*)

Measure	Diagnosis	Post treatment (2-day)	Follow up (2 month)	Reference range
Vitamins				
Vitamin A, μg/dL	20		63	38—98
Vitamin D, 25—hydroxy, ng/mL	< 5.0		15.9	≥ 30
Vitamin B9, Folate, ng/mL			5.1	> 5.9
Vitamin B12, pg/ml	534.8			243—894

INR: international normalized ratio; CBC: complete blood count; WBC: white blood cells; RBC: red blood cells; CMP: comprehensive metabolic panel; BUN: blood urea nitrogen; AST (SGOT): aspartate aminotransferase (serum glutamic-oxaloacetic transaminase); ALT (SGPT): alanine aminotransferase (serum glutamic pyruvic transaminase); ALP: alkaline phosphatase; GFR: glomerular filtration rate; GGT: gamma-glutamyl transferase; LDH: lactate dehydrogenase.

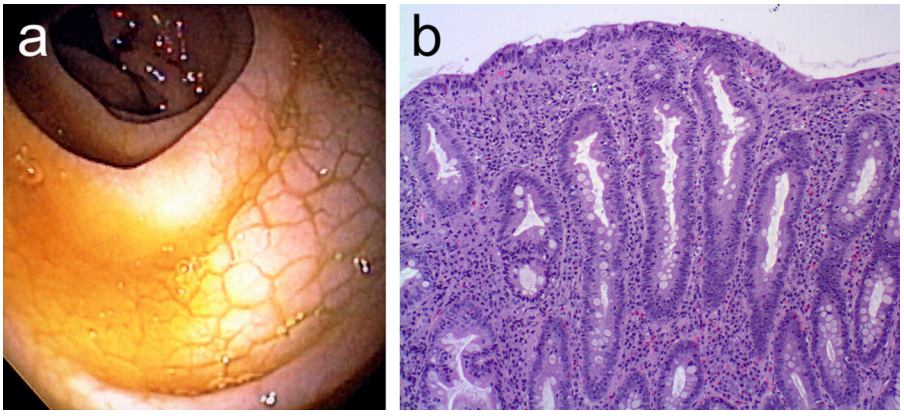

Figure 1 Abnormal endoscopy and histopathological examination of the duodenum revealing findings consistent with celiac disease. (a) Upper endoscopy demonstrating mucosal atrophy with cobblestoning. (b) Duodenal biopsy demonstrating marked mucosal atrophy with total villous blunting and increased intraepithelial lymphocytes (hematoxylin and eosin stain, original magnification × 40).

Ethics

Informed consent to publish this work was obtained from the patient. The University of Idaho Institutional Review Board (IRB) has reviewed this case report and determined that IRB approval is not required for publication.

Disclosure of interest

The authors declare that they have no competing interests.

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