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Hematologic and bone manifestaions as initial presentation of celiac disease: a case of vitamin K deficiency–related coagulopathy

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ABSTRACT

Celiac disease is a chronic autoimmune enteropathy triggered by gluten, and its atypical presentations often remain underdiagnosed. Among these, coagulopathy related to vitamin K deficiency is an uncommon manifestation associated with fat and fat-soluble vitamin malabsorption. We report the case of a young adult admitted for evaluation of an unexpectedly prolonged prothrombin time without bleeding symptoms. The clinical history was marked by chronic diarrhea, persistent fatigue, and unintentional weight loss. Biological investigations revealed anemia, electrolyte imbalance, low folate levels, and a reduction in vitamin K-dependent coagulation factors. The rapid correction of coagulation abnormalities following vitamin K administration supported a malabsorptive mechanism. Positive celiac serology and duodenal biopsies showing villous atrophy confirmed the diagnosis. Additional assessment identified early metabolic bone involvement. A gluten-free diet along with vitamin supplementation led to clear clinical and biochemical improvement.
This case highlights a rare initial manifestation of celiac disease revealed through isolated coagulation abnormalities, underscoring the importance of including this condition in the differential diagnosis of unexplained clotting disorders. Comprehensive management and systematic evaluation of nutritional complications remain essential to prevent long-term consequences.

KEYWORDS

Celiac disease, Malabsorption, Coagulopathy, Prothrombin time, Osteopenia , Gluten-free die

MAIN ARTICLE

INTRODUCTION

Celiac disease is a chronic autoimmune enteropathy triggered by gluten ingestion in genetically predisposed individuals, characterized by villous atrophy and malabsorption that can lead to a wide range of systemic manifestations [1]. Its prevalence is estimated to be around 1% of the global population, yet the disease remains largely underdiagnosed due to the diversity of its clinical presentations [2].

While classical forms primarily present with digestive symptoms such as chronic diarrhea, abdominal pain, or weight loss, atypical or extra-intestinal forms are increasingly recognized. These include iron-deficiency anemia, metabolic bone disease, elevated liver enzymes, and certain coagulation abnormalities. Coagulopathy related to vitamin K deficiency, resulting from malabsorption of fats and fat-soluble vitamins, represents a rare but documented manifestation of celiac disease [3].

Although a few reports have described inaugural coagulopathy revealing previously unrecognized celiac disease [4], this presentation remains exceptional and may delay diagnosis.

We report here the case of a young adult in whom an isolated prolongation of prothrombin time led to the diagnosis of celiac disease, illustrating an unusual inaugural presentation that may hinder timely management.

CASE PRESENTATION

A 24-year-old single man with no significant past medical history was admitted for investigation of a low prothrombin time (37%) and other symptoms without associated bleeding. His primary care physician had ordered an evaluation for asthenia. The patient reported chronic watery diarrhea, occurring in episodes interspersed with periods of remission, accompanied by atypical periumbilical pain present since adolescence, without other gastrointestinal symptoms. He also reported intermittent muscle cramps, persistent asthenia, and significant (unspecified) weight loss, occurring within a general context of fatigue over several years.

On clinical examination, the patient presented with pallor of the skin and mucous membranes, signs of malnutrition such as muscle weakness, dry and scaly skin, brittle hair, and ecchymoses on the anterior aspect of both legs. Abdominal examination revealed diffuse periumbilical tenderness without guarding or a palpable mass.

Laboratory tests revealed microcytic hypochromic anemia (hemoglobin 10 g/dL), a low prothrombin time (PT) of 37%, and a normal activated partial thromboplastin time (aPTT). Electrolytes, renal function, and liver function tests were normal. Albumin and total protein levels were also normal.

The fibrinogen concentration was slightly elevated at 5 g/L (normal range: 2.5-4.5 g/L), thus ruling out artifactual elongation due to a blood clot in the tubule or congenital or acquired hypofibrinogenemia. The presence of circulating anticoagulants was systematically investigated by calculating the Rosner index (a mixture of the patient's index and a control to normalize the aPTT; a Rosner index of 5% corresponds to a normal value below 15%). Further investigations of hemostasis suggested a vitamin K deficiency with a deficiency of the four vitamin K-dependent factors (factors II, VII, IX and X) (Table *1*) .

Slow intravenous administration of 20 mg of vitamin K resulted in a correction of the prothrombin time (PT to 73.3%) at twelve hours, leading further investigations toward a possible gastrointestinal malabsorption.

Hypocalcemia (77.79 mg/L) was observed, while magnesium levels were normal and vitamin D levels were low. Total cholesterol was decreased to 1.07 g/L, while ferritin (106.83 ng/mL) and vitamin B12 levels were normal, but the folate level was low (2.9 ng/mL) (Table *1*) .

Parameter	Result	Reference range
Hemoglobin	10g/dl	13–17 g/dl
Prothrombin Time	37%	80–100%
Fibrinogen	5 g/l	2.5–4.5 g/l
Calcium	77.79 mg/l	88–102 mg/l
Vit D	12 ng/ml	30–100 ng/ml
Total cholesterol	1.07 g/l	1.5–2.00 g/l
Ferritin	106.83 ng/ml	30–400ng/ml
Vit B12	400 pg/ml	200–900 pg/ml
Folates	2.9 ng/ml	4–20 ng/ml

Table 1: Admission Blood Test Results With Normal Reference Ranges

Celiac disease serology revealed the presence of anti-transglutaminase (IgA 92 and IgG 87) and anti-gliadin (IgA 91 and IgG 90) antibodies, with a normal total IgA level (Table 2).

Parameter	Result	Reference
Ac anti –tTG IgA	92 U/ml	< 10 U/ml
Ac anti –tTG IgG	87 U/ml	< 10 U/ml
Anti – gliadin IgG	90 U/ml	< 20 U/ml
Anti –gliadin IgA	91 U/ml	< 20 U/ml
Total IgA	2.0 g/L	0.7–4.0 g/L

Table 2: Results of celiac serology and total IgA measurement.

Intestinal multiplex PCR showed soft stools with mucus, but no pathogenic bacteria. Endoscopic examination by esophagogastroduodenoscopy showed obliteration of the duodenal folds (Figure 1), while colonoscopy revealed no particular abnormalities.

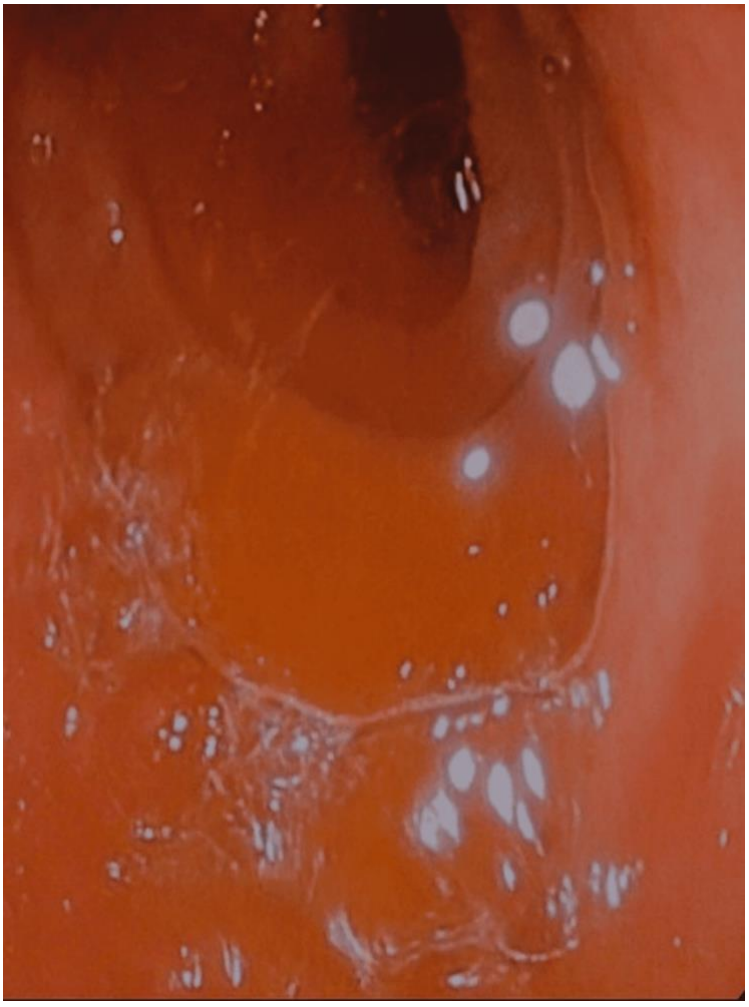

Figure 1: DUODENAL FOLDS EFFECTED

The abdominal and pelvic CT scan was otherwise normal, except for right kidney stones causing minimal left ureterohydronephrosis.

Histopathological examination of the duodenal biopsies revealed partial villous atrophy with 35% intraepithelial lymphocytosis, consistent with a diagnosis of celiac disease (Figure 2).

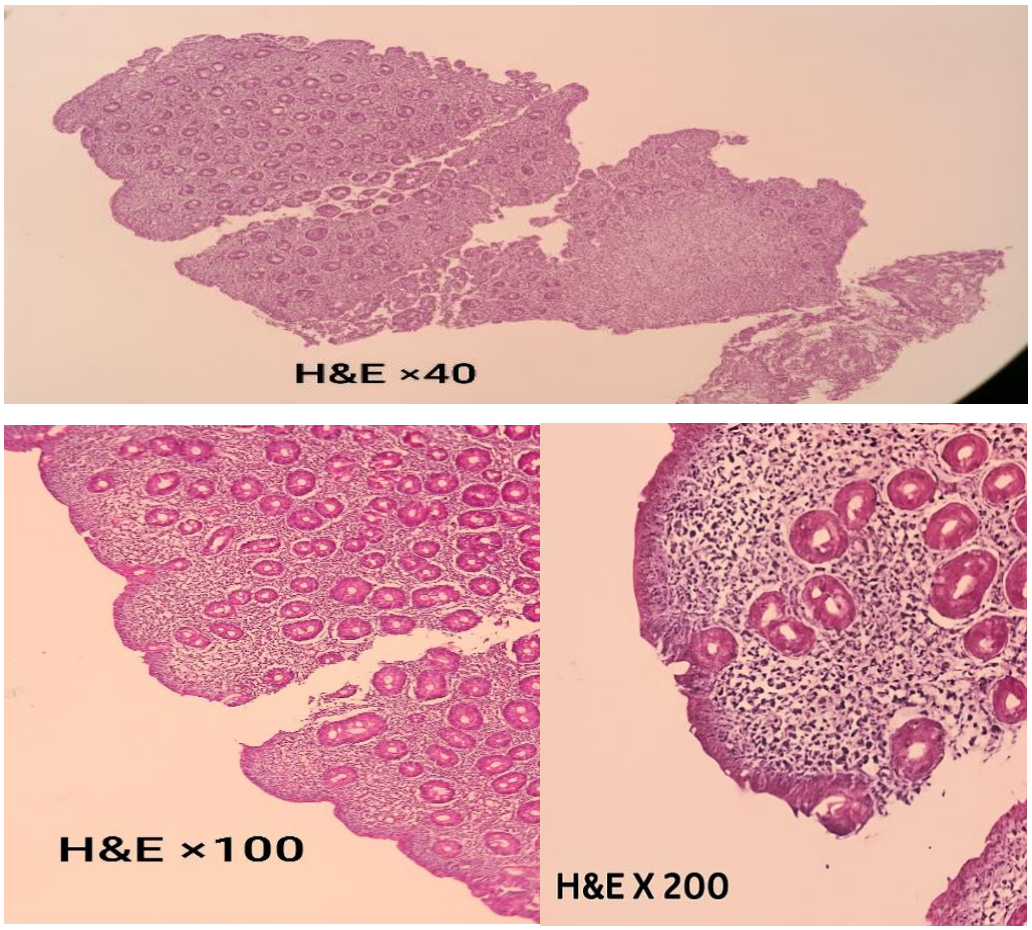

Figure 2: H&E slide photographie of duodenal mucosa showed : Increased intra epithelial lymphocytes (intra epithelial lymphocytosis)complete (Total) villous atrophy and crypt hyperplasia consistant with Marsh type 3C

The search for other autoimmune diseases frequently associated with celiac disease, including fasting plasma glucose (FPG), HbA1c, TSH, and anti-TPO antibodies, was negative, as was the search for lymphoma or squamous cell carcinoma.

A bone densitometry scan revealed osteopenia with a T-score of -2 and a high risk of fracture. Phosphocalcium levels showed secondary hyperparathyroidism with PTH-dependent hypercalciuria. An intravenous infusion of vitamin K normalized the prothrombin time (PT).

Implementation of a strict gluten-free diet led to the gradual resolution of digestive symptoms, weight gain, and normalization of the PT. The patient also received vitamin D supplementation, with specialized follow-up for the management of osteopenia and fracture prevention. Furthermore, calcium supplementation was avoided due to her kidney stones. Regular follow-up with gastroenterologists and nutritionists was initiated to ensure adherence to the diet and the management of associated metabolic complications.

DISCUSSION

Celiac disease is an autoimmune enteropathy triggered by gluten ingestion in genetically predisposed individuals [5]. It leads to villous atrophy of the small intestine, causing a malabsorption syndrome whose clinical manifestations vary from classic forms to mild or even asymptomatic forms. In adults, diagnosis is often delayed, sometimes after age 60, and may be revealed by isolated biological abnormalities or nutritional deficiencies [6].

From a pathophysiological perspective, the gliadin in gluten reacts with tissue transglutaminase, the main autoantigen involved. Diagnosis is based on the following triad: clinical or biological signs of malabsorption, histological villous atrophy, and improvement on a strict gluten-free diet. Serology (anti-transglutaminase and anti-gliadin IgA/IgG antibodies) is an essential screening tool, but its performance may be impaired in the case of selective IgA deficiency [7].

The hematological manifestations of celiac disease are less frequent but clinically important. A prolonged prothrombin time (PT) or activated partial thromboplastin time (aPTT) is observed in approximately 40% of mild cases, often related to vitamin K deficiency secondary to proximal malabsorption. The severity of the coagulation disorder appears to correlate with the extent of mucosal damage.

Cases of celiac disease associated with an abnormal prothrombin time (PT) are rare, but hemorrhagic manifestations, such as muscle hematomas or mucosal bleeding, have been described in severe cases [8]. In our case, the low PT of 37% without clinical signs of hemorrhage suggests the possibility of an isolated biological abnormality. This finding underscores the importance of including celiac disease in the etiological workup of unexplained coagulation abnormalities, even in the absence of suggestive gastrointestinal symptoms.

Bone involvement is a common complication of celiac disease. Osteopenia and osteoporosis are observed in 38% to 72% of patients at the time of diagnosis, including young people. This

risk is primarily related to malabsorption of calcium and vitamin D, which can be exacerbated by factors such as low body weight, menopause, or smoking [9].

Our observation, that the discovery of osteopenia in a young adult illustrates this early risk, justifies the systematic performance of bone densitometry (BD) upon diagnosis [10]. A gluten-free diet allows for partial improvement in bone mineral density, but supplementation with calcium (1,000 to 1,200 mg/day) and vitamin D (800 to 2,000 IU/day) remains essential. In cases of severe osteoporosis or fragility fractures, drug treatment with bisphosphonates or denosumab may be considered depending on digestive tolerance [11].

The management of celiac disease must be comprehensive and multidisciplinary. It relies on a strict gluten-free diet (excluding wheat, barley, and rye) to promote mucosal healing and prevent long-term complications [12], correction of vitamin deficiencies, particularly vitamin K, calcium, and vitamin D, regular blood tests (iron, folate, vitamin B12, coagulation parameters, celiac serology), and monitoring of bone density through periodic bone marrow aspiration.

Intravenous administration of vitamin K allows for rapid correction of prothrombin time (PT) abnormalities and prevents the risk of bleeding. Nutritional education for the patient is essential to ensure good adherence to the diet and avoid cross-contamination [13].

CONCLUSION

Celiac disease can manifest in atypical forms dominated by isolated biological abnormalities, including coagulation disorders or osteopenia. The case presented illustrates the importance of a broad diagnostic approach and multidisciplinary follow-up to correct deficiencies, prevent bone and hemorrhagic complications, and improve the patient's quality of life. Early recognition and comprehensive management are crucial to reduce long-term complications. Moreover, patient education and regular monitoring play a key role in ensuring adherence to dietary and therapeutic measures. Finally, this case highlights the need for clinicians to maintain a high index of suspicion even when classical gastrointestinal symptoms are absent.

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