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SEVERE COAGULOPATHY AND INTRA-ALVEOLAR HAEMORRHAGE DUE TO FAT MALABSORPTION IN CELIAC DISEASE

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ABSTRACT

Celiac disease, a prevalent autoimmune disorder, can present atypically with fat malabsorption and coagulopathy due to vitamin K malabsorption.

A 64-year-old male presented with haemoptysis and severe anaemia (Hb 6 g/dl). Despite normal previous coagulation tests, admission laboratory tests revealed an international normalised ratio (INR) of 7.0 and iron deficiency anaemia. Initial blood products and vitamin K treatment corrected the INR temporarily, but the patient's haemoptysis returned, and his INR values continued to rise. Further investigation revealed celiac disease with fat malabsorption, leading to vitamin K malabsorption and along with a previously prescribed antiplatelet aggregation therapy, this led to diffuse alveolar haemorrhage. A gluten-free diet and vitamin supplementation normalised the patient's INR and stopped the bleeding.

This case highlights the importance of considering celiac disease in unexplained coagulopathies and the effectiveness of dietary management.

KEYWORDS

Celiac disease, coagulopathy, fat malabsorption, vitamin K deficiency, intra-alveolar haemorrhage

LEARNING POINTS

- Celiac disease can cause severe coagulopathy due to fat malabsorption and vitamin K deficiency.
- High suspicion is required for atypical presentations of celiac disease.
- A gluten-free diet is essential for managing celiac disease and normalising coagulation profiles.

INTRODUCTION

Celiac disease is an autoimmune disorder affecting approximately 1.4% of the population[1]. It results from an immune response to ingested gluten, a protein found in wheat, barley and rye. This immune reaction leads to inflammation and damage to the small intestine's mucosa,

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specifically the villi, which are responsible for absorption of nutrients. Celiac disease typically presents with a range of gastrointestinal symptoms, including chronic diarrhoea, abdominal pain, bloating and weight loss. Extraintestinal manifestations may include anaemia, osteoporosis, dermatitis herpetiformis and neurological symptoms such as peripheral neuropathy[2].

Damage to the villi impairs the absorption of fats and fat-soluble vitamins (A, D, E and K)[3]. Vitamin K is particularly crucial for the synthesis of clotting factors II, VII, IX and X. Without adequate vitamin K, the liver cannot produce functional clotting factors, reflected by prolonged prothrombin time and elevated international normalised ratio (INR), leading to coagulopathy and an increased risk of bleeding. Fat malabsorption also leads to deficiencies in vitamins A, D and E, contributing to a wide range of clinical symptoms including osteoporosis, night blindness and neuropathy[4,5].

CASE DESCRIPTION

A 64-year-old male presented at our emergency department with shortness of breath and haemoptysis, which started a day before his admission. He had been on dual antiplatelet therapy with prasugrel and aspirin for a recent acute coronary syndrome six months before admission, leading to percutaneous coronary intervention of his left circumflex artery and an insertion of a drug-eluting stent. He reported non-stop haemoptysis and shortness of breath, which worsened when lying down, and ruled out any recent trauma, change of medications, fever or melaena. He presented a plastic bag with about 100 ml of blood which he brought from home.

On physical examination, he was communicating and pale, with a respiratory rate of 15 breaths per minute, heart rate of 110 beats per minute, blood pressure of 135/70 mmHg and oxygen saturation of 83% on room air. Lung auscultation was significant for diffuse bilateral crackles; no other significant physical examination findings were noted. Initial laboratory tests on admission revealed severe anaemia (Hb: 6.0 g/dl), a significantly prolonged INR of 7.0. and prolonged activated partial thromboplastin time (aPTT). Further tests showed a low reticulocyte production index (0.34), normal platelet count and a normal D-dimer. Chemistry tests were significant for hypocalcaemia, slight hypomagnesaemia and hyponatraemia *(Table 1)*. Iron studies were significant for iron deficiency as indicated by the very low transferrin saturation (7.9%) with normal ferritin levels (228 µg/l), and normal B12 and folic acid levels *(Table 2)*.

A chest computerized tomography (CT) scan with IV contrast demonstrated bilateral emphysema (which was a known finding in previous CT's of this patient) and diffuse alveolar haemorrhage *(Fig. 1)*.

The patient was admitted to the intensive care unit and treated with vitamin K supplementation, blood transfusions and prothrombin complex concentrate, which temporarily normalised his INR. After the cessation of his haemoptysis, his respiratory status and haemodynamics stabilised, and he was transferred to the internal medical ward. Unfortunately, haemoptysis returned a week later with INR prolongation *(Table 3)*, prompting further investigation. Further investigation was negative for antiphospholipid

Test	Result	Normal range
White blood count (10^3/µl)	8.9	4–11
Red blood count (10^6/µl)	2.7 ↓	4.4–5.9
Haemoglobin (g/dl)	6.0 ↓	13.5–17.5
Haematocrit test (%)	18.9 ↓	40–52
Reticulocytes (%)	1.9 ↑	0.5–1.5
Reticulocytes (10^6/µl)	0.05	–
aPTT (sec)	50.5 ↑	25–40
Prothrombin time (sec)	75.60 ↑	10.03–12.43
INR	7.47 ↑	0.97–1.19
Prothrombin time (%)	6 ↓	75–125
D-dimer (mg/l FEU)	0.28	0.05–0.55
Sodium (mmol/l)	132 ↓	135–145
Potassium (mmol/l)	3.7	3.5–5.1
Chloride (mmol/l)	96	96–106
Glucose (mg/dl)	124 ↑	80–115
Urea (mg/dl)	43.1	20–45
Creatinine (mg/dl)	0.78	0.7–1.2
Calcium (mg/dl)	6.9 ↓	8.6–10.3
Magnesium (mg/dl)	1.6 ↓	1.7–2.5

Table 1. Initial laboratory tests.

Test	Result	Normal range
Iron (µg/dl)	19.9	59–158
Transferrin (g/l)	1.8	2–3.6
Transferrin saturation (%)	7.9	15–45
Ferritin (µg/l)	228	30–400
Total iron-binding capacity (µg/dl)	251	250–400
Unsaturated iron-binding capacity (µg/dl)	231	120–470
Vitamin B12 (pg/ml)	616	200–770
Folic acid (ng/ml)	4.6	4.6-18.7

Table 2. Iron studies.

INR values								
Day 0	Day 1	Day 2	Day 3	Day 5	Day 6	Day 7	Day 8	Day 9
7.47	3.47	2.07	2.48	1.19	1.11	1.47	2.35	3.1

Table 3. INR values throughout the first nine days of hospitalisation.

Test	Result	Normal range
Anti-tissue transglutaminase IgA-B (U/ml)	104 ↑	0–10
IgA (celiac)-B	464.2 ↑	70–-400
25 hydroxyvitamin D (ng/ml)	4 (deficiency)	-
Thiamine (vitamin B_1) (mcg/l)	82 ↑	33–1-60.7
Tocopherol (vitamin E) (mg/l)	2 ↓	5–18
Retinol (vitamin A_1) (µg/dl)	6 ↓	30–70

Table 4. Celiac and vitamins studies.

syndrome, ANCA-associated vasculitides and anti-GBM disease. A thromboelastogram showed results consistent with a coagulation factor defect; blood tests revealed hypocalcaemia and low levels of vitamin A, vitamin E and vitamin D, indicating potential fat malabsorption. The faecal elastase test was negative indicating no pancreatic insufficiency, and an abdominal CT imaging scan showed a normal pancreas and biliary tract. Elevated levels of anti-tissue transglutaminase antibodies were detected *(Table 4)*. A duodenal biopsy revealed villous atrophy, increased intraepithelial lymphocytes and crypt hyperplasia, confirming the diagnosis of celiac disease. The combination of fat malabsorption markers, serology, iron deficiency anaemia and the biopsy findings confirmed celiac disease as the underlying cause. The patient was placed on a strict gluten-free diet. Parenteral vitamin K was continued until the coagulopathy was corrected. Over the following days his laboratory tests – including coagulation profiles – normalised, and he experienced no further bleeding episodes.

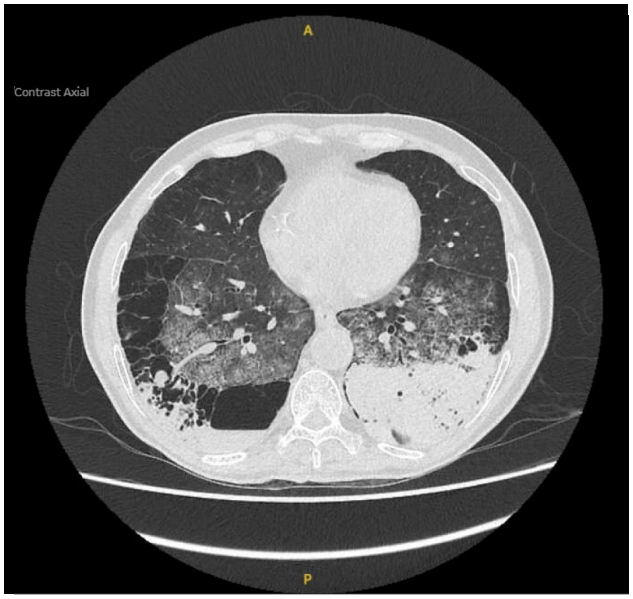

Figure 1. A chest CT showing bilateral emphysemas and signs indicating diffuse alveolar haemorrhage.

DISCUSSION

This case demonstrates an atypical presentation of celiac disease with severe coagulopathy due to impaired fat malabsorption and more specifically vitamin K deficiency. The severe anaemia upon the patient's initial presentation was probably due to the coagulopathy as mentioned, along with the more common finding in celiac disease of iron deficiency anaemia in up to 50% of patients with celiac disease at some point[6]. While gastrointestinal symptoms are common in celiac disease, clinicians should consider celiac disease in patients with unexplained coagulopathies. A gluten-free diet and appropriate supplementation are crucial for management. The response to dietary changes underscores the importance of recognising and treating underlying celiac disease to prevent life-threatening complications.

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APPENDIX

Other test results.

Test	Result	Normal range
Bilirubin total (mg/dl)	0.4	0.2–1.2
ALT (U/l)	45 ↑	4–41
AST (U/l)	33	5–40
LDH (U/l)	215	135–225
ALP (U/l)	173 ↑	40–129
GGT (U/l)	117 ↑	10–55
Total protein (g/dl)	6.7	6.4–8.3
Albumin (g/dl)	3.2 ↓	3.4–4.8
Globulin (g/dl)	3.5	2.2–4
CRP (mg/l)	279 ↑	≤5.0
Cholesterol (mg/dl)	54.1	<200
eGFR (ml/min/1.73m²)	>60	>60
HS troponin T-B (ng/l)	37	≤14
CRP-B (mg/l)	54.1 ↑	≤5.0
Osmolality calculated-B (mOsm/kg)	279 ↓	280–301

Test	Result	Normal range
Cardiolipin IgG (U/ml)	2.7	0–10
ANCA-PR3, Ab-B (U/ml)	2.2	0–10
Cardiolipin IgM (U/ml)	1.2	0–10
Beta2-glycoprotein IgG (U/ml)	2.7	0–5
Beta2-glycoprotein IgM (U/ml)	1.7	0–5
Anti-nuclear Ab (ANA)	Negative	-
ANCA-MPO Ab-B (U/ml)	1.1	0–5

Test	Result	Normal range
RDW (%)	19.8 ↑	12.0–14.7
PDW (fl)	12.2	9.5–15.2
MPV (fl)	10.7	7.3–11.5
PLT (10^3/µl)	400	140–450
NRBC abs. (10^3/µl)	0.0	0.0
NRBC (%)	0.0	0.0
NEU abs. (10^3/µl)	6.2	2–7.7
LYM abs. (10^3/µl)	2.1	1–4
MONO abs. (10^3/µl)	0.5	0.2–1.2
EOS abs. (10^3/µl)	0.1	0.0–0.7
BASO abs. (10^3/µl)	0.0	0.0–0.2
NEU (%)	69.8	50–70
LYM (%)	23.4	18–4
MONO (%)	5.6	2–11
BASO (%)	0.2	0–2
EO (%)	1	0–2
IG (%)	1	0–1
Fibrinogen (mg/dl)	294.3	170–420

Test	Result	Normal range
DRVVT screen (sec)	49.1 ↑	25.7–46.1
DRVVT confirm (sec)	37.4 ↑	25.4–34.6
RVVT ratio	1.31	0–1.4
SCT screen (sec)	58.5 ↑	24–38.8
SCT confirm (sec)	46.5 ↑	24.2–45.5
SCT ratio	1.3	0–1.3

Test	Result (03/12/23 12:40)	Normal range
Citrated kaolin (CK)-R (min)	10.1 ↑	4.6–9.1
Citrated kaolin (CK)-K (min)	1.8	0.8–2.1
Citrated kaolin (CK)-angle (deg)	69.7	63–78
Citrated kaolin (CK)-MA (mm)	69.3 ↑	52–69
Citrated kaolin (CK)-LY30 (%)	0.0	0.0–2.6
Citrated rapid test (CRT)-R (min)	1.5 ↑	0.3–1.1
Citrated rapid test st (CRT)-K (min)	0.9	0.8–2.7
Citrated rapid test (CRT)-angle (deg)	76.2	60–78
Citrated rapid test (CRT)-MA (mm)	70.4 ↑	52–70
Citrated rapid test (CRT)-LY30 (%)	0.0	0.0–2.2
aPTT (sec)	48.6 ↑	25–4
Citrated kaolin heparinase (CKH)-R (min)	13 ↑	4.3–8.3
Citrated kaolin heparinase (CKH)-K (min)	1.3	0.8–1.9
Citrated kaolin heparinase (CKH)-angle (deg)	73.1	64–77
Citrated kaolin heparinase (CKH)-MA (mm)	69.6	52–69
Citrated functional fibrinogen (CFF)-MA (mm)	34.4	15–32
PT-SEC (sec)	26.1 ↑	10.03–12.43
TEG-ACT (sec)	21.9 ↑	82–152