Scholars Journal of Medical Case Reports
Abbreviated Key Title: Sch J Med Case Rep
ISSN 2347-9507 (Print) | ISSN 2347-6559 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Gastroenterology

Thromboembolic Complications Unveiling Celiac Disease: A Report of Two Cases

F. Chakor[1*], F. Achdami[1], A. Handa[1], O. Nacir[1], F. Lairani[1], A. Ait Errami[1], S. Oubaha[2], Z. Samlani[1], K. Krati[1]

[1]Gastroenterology Department, Mohammed VI University Hospital, Marrakech
[2]Physiology Department, Cadi Ayyad University, Mohammed VI University Hospital, Marrakech

DOI: https://doi.org/10.36347/sjmcr.2025.v13i05.138 | **Received:** 16.04.2025 | **Accepted:** 20.05.2025 | **Published:** 31.05.2025

***Corresponding author:** F. Chakor
Gastroenterology Department, Mohammed VI University Hospital, Marrakech

Abstract | **Case Report**

Celiac disease is an autoimmune enteropathy related to gluten intolerance occurring in genetically predisposed individuals. Its course may be marked by various complications, including bone, autoimmune, and malignant disorders. Over the past decades, the clinical profile of celiac disease has evolved, with extra-digestive manifestations increasingly coming to the forefront. Among these, deep vein thrombosis (DVT) is being reported with growing frequency. Thromboembolic risk factors may be acquired during the course of the disease. We report two cases in which celiac disease was revealed by the occurrence of deep vein thrombosis. These cases further illustrate the broad clinical spectrum of celiac disease and highlight the importance of considering this condition in the evaluation of any unexplained thromboembolic event.

Keywords: Celiac Disease, Thromboembolic Complications, Deep Vein Thrombosis, Portal Vein Thrombosis, Thrombophilia.

INTRODUCTION

Celiac disease (CD), also known as gluten-sensitive enteropathy, is a chronic autoimmune disorder triggered by the ingestion of gluten in genetically predisposed individuals. It is characterized by an inappropriate immune response directed against gliadin, a component of gluten [1, 2]. This leads to inflammation of the small intestinal mucosa, villous atrophy, and malabsorption [1].

The classical presentation—chronic diarrhea, abdominal pain, and malabsorption—now accounts for only 10 to 20% of diagnosed cases [2, 3]. Increasingly, CD manifests through atypical or extraintestinal symptoms such as anemia, osteoporosis, neurological disorders, elevated liver enzymes, or dermatitis herpetiformis. These may be the initial clinical signs and can delay diagnosis [2-4].

Diagnosis relies on the presence of suggestive clinical features, detection of disease-specific antibodies (anti-tissue transglutaminase IgA and anti-endomysial antibodies), and histological confirmation of villous atrophy on duodenal biopsies [1-5]. In well-defined pediatric cases, biopsy-free diagnostic protocols have also been validated [5].

Venous thrombosis is a rare but well-documented complication of CD, particularly in adults, with a predilection for abdominal sites such as the portal vein and superior mesenteric vein [6, 7]. Several prothrombotic mechanisms have been proposed, including protein S deficiency, hyperhomocysteinemia, folate or vitamin B12 deficiency, and the presence of antiphospholipid antibodies [6–8].

Here, we report two cases of venous thrombosis as the initial presentation of celiac disease, highlighting unusual but clinically significant manifestations of this condition.

CASE REPORTS

Case 1

A 30-year-old man, with no medical history or known risk factors for venous thromboembolism, presented with abdominal pain. Clinical examination revealed mucocutaneous pallor and a body mass index (BMI) of 17.3 kg/m². Abdominal ultrasound and contrast-enhanced CT angiography showed thrombosis of the portal vein, while liver and spleen appeared normal. There was no family history of thrombosis or symptoms suggestive of autoimmune disease (notably no oral or genital aphthosis).

Laboratory investigations revealed hypochromic microcytic anemia (hemoglobin 11 g/dL), thrombocytosis (platelet count: 1090 G/L), severe iron deficiency (ferritin: 2 ng/mL), hypocholesterolemia (0.8 g/L), and a reduced prothrombin rate (58%). Upper gastrointestinal endoscopy revealed grade I esophageal varices and effacement of duodenal folds.

Viral hepatitis B and C serologies, as well as autoantibody screening (antinuclear and antiphospholipid antibodies), were negative. Thrombophilia screening showed a protein S deficiency (45%) and a protein C deficiency (55%), with normal homocysteine levels, antithrombin III levels, and no Factor V Leiden mutation or JAK2 mutation. Bone marrow biopsy ruled out hematologic malignancy.

Histological examination of duodenal biopsies revealed subtotal villous atrophy (Marsh grade 3b) and intraepithelial lymphocytosis (35%). Celiac serology was positive for anti-tissue transglutaminase IgA and antiendomysial IgG antibodies.

The diagnosis of celiac disease revealed by portal vein thrombosis was retained. The patient was treated with anticoagulation and a gluten-free diet, resulting in favorable outcomes: improvement of anemia and nutritional markers (ferritin, protein S and C), and partial regression of mucosal atrophy, although complete normalization was not achieved. Follow-up ultrasound showed the development of a portal cavernoma.

Case 2

A 21-year-old woman was admitted for evaluation of right leg swelling. There was no family history of venous thrombosis, no use of estrogen-progestin contraceptives, and no signs suggestive of systemic autoimmune disease (including absence of aphthous ulcers). Her medical history included intermittent chronic diarrhea.

On clinical examination, she presented with mucocutaneous pallor and a swollen, erythematous, warm right leg. The calf was indurated, and Homans' sign was positive. Doppler ultrasound revealed thrombosis of the right femoral and popliteal veins.

Laboratory tests showed normocytic normochromic anemia (hemoglobin 8 g/dL), normal albumin and total protein levels, folate deficiency (1.2 ng/mL), and vitamin B12 deficiency (80 pg/mL). Thrombophilia workup revealed moderate hyperhomocysteinemia (21.97 µmol/L).

Given the history of chronic gastrointestinal symptoms, celiac serology was performed, showing strong positivity for anti-transglutaminase, anti-endomysial, and anti-gliadin antibodies. Upper gastrointestinal endoscopy revealed flattened duodenal folds. Histology confirmed villous atrophy consistent with celiac disease (Marsh grade 3c).

The diagnosis of deep vein thrombosis as the presenting manifestation of celiac disease was established. The patient was treated with low molecular weight heparin, followed by a vitamin K antagonist, along with a gluten-free diet. The clinical course was favorable, with gradual normalization of the complete blood count, nutritional status, and celiac serological markers.

DISCUSSION

Celiac disease (CD) is a chronic autoimmune enteropathy triggered by the ingestion of gluten-containing cereals—namely wheat, barley, and rye—in genetically susceptible individuals, particularly those expressing HLA-DQ2 or HLA-DQ8 molecules [1, 2]. The global prevalence of CD is estimated at approximately 1%, but may reach up to 10% in first-degree relatives and certain at-risk populations [2-9].

While traditionally regarded as a gastrointestinal disorder of childhood, it is now well recognized that CD affects individuals of all ages and may present with a broad spectrum of clinical manifestations [4]. Classical symptoms, including chronic diarrhea, weight loss, abdominal pain, and nutrient malabsorption, now account for only a minority of diagnosed cases. Most new diagnoses are made in adults and often present atypically or even silently, without overt gastrointestinal symptoms [2-10].

This clinical heterogeneity contributes to diagnostic delays, often exceeding several years. In atypical or extraintestinal forms, clinical suspicion arises from unexplained iron-deficiency anemia, osteoporosis, infertility, transaminase elevation, neurological dysfunction, or thromboembolic events [11, 12]. These varied phenotypes underscore the need for heightened clinical awareness, especially in young patients with unexplained systemic symptoms.

The diagnosis of CD relies on positive serologic markers—most notably anti-tissue transglutaminase (tTG) and antiendomysial (EMA) antibodies—followed by confirmatory histological evidence of duodenal villous atrophy, crypt hyperplasia, and intraepithelial lymphocytosis (Marsh classification) [1-4]. In selected pediatric patients, biopsy-free diagnosis is now acceptable when strict serological thresholds are met [5].

Although thrombotic events are not among the classical features of CD, growing evidence supports a link between untreated CD and an increased risk of venous and, to a lesser extent, arterial thromboses [6-13]. Venous thromboses in CD often occur at unusual sites, including the portal vein, hepatic veins (Budd-Chiari syndrome), cerebral venous sinuses, and retinal veins

[14–16]. Arterial events such as ischemic stroke, myocardial infarction, and mesenteric ischemia have also been described, although they remain rare [17–19].

Multiple pathophysiological mechanisms have been proposed to explain the prothrombotic state observed in some patients with CD. These include:

Vitamin K deficiency, resulting from fat malabsorption, leads to acquired deficiencies in natural anticoagulants such as protein C, protein S, and antithrombin III [13-20]. Our first patient had combined protein C and S deficiencies that normalized after the introduction of a gluten-free diet, supporting a reversible nutritional origin.

Hyperhomocysteinemia, often secondary to malabsorption of folate, vitamin B6, or vitamin B12, or to polymorphisms of the MTHFR gene (e.g., C677T), has been associated with venous and arterial thromboses [21, 22]. Our second patient had moderate hyperhomocysteinemia associated with folate and B12 deficiency, reflecting impaired methylation pathways.

Antiphospholipid antibodies, particularly of the IgA isotype (e.g., anti-cardiolipin or anti-β2-glycoprotein I), have been reported with higher prevalence in CD compared to the general population. Although their pathogenic role remains unclear, some authors suggest an increased risk of thrombosis in this context [23–26].

Thrombocytosis, noted in our first patient, is also common in untreated CD, occurring in up to 60% of cases. It may result from iron deficiency, systemic inflammation, or functional hyposplenism [11]. Furthermore, elevated levels of thrombin-activatable fibrinolysis inhibitor (TAFI)—a known thrombosis risk factor—have been reported in CD and may contribute to a hypercoagulable state [27, 28].

These observations highlight the need for clinicians to consider CD in the differential diagnosis of unexplained thrombosis, especially in young adults without conventional risk factors. Early recognition and initiation of a gluten-free diet not only improves intestinal symptoms and nutritional status but may also reverse hematologic abnormalities and reduce thrombotic risk.

CONCLUSION

Thromboembolic events, while relatively uncommon, represent a significant extraintestinal complication of celiac disease, with a reported prevalence of up to 8% in some studies. The pathophysiology is multifactorial, involving acquired thrombophilia due to vitamin deficiencies (particularly vitamins K, B12, and folate), hyposplenism, and autoimmune mechanisms.

Celiac disease should be recognized as a potential prothrombotic condition and systematically considered in cases of unexplained or atypically located thrombosis, especially in young patients without conventional risk factors.

Timely diagnosis, strict adherence to a gluten-free diet, and targeted correction of thrombotic risk factors are crucial steps to prevent recurrence and reduce associated morbidity

REFERENCES

1. Rubio-Tapia A, Hill ID, Semrad CE, Kelly CP, Greer KB, Limketkai BN, Lebwohl B. American College of Gastroenterology Guidelines Update: Diagnosis and Management of Celiac Disease. *Am J Gastroenterol*. 2023;118(1):59–76.
2. Lebwohl B, Sanders DS, Green PHR. Coeliac disease. *Lancet*. 2022;399(10344):2413–26.
3. Catassi C, Fasano A. Celiac Disease Diagnosis: Simple Rules Are Better Than Complicated Algorithms. *Am J Med*. 2023;136(1):7–9.
4. Elli L, Branchi F, Tomba C, Villalta D, Norsa L, Ferretti F, *et al.*, Neurological manifestations of celiac disease and gluten sensitivity. *Nutrients*. 2020;12(2):579.
5. Husby S, Koletzko S, Korponay-Szabó IR, Mearin ML, Phillips A, Shamir R, *et al.*, European Society for Paediatric Gastroenterology, Hepatology and Nutrition guidelines for diagnosing coeliac disease. *J Pediatr Gastroenterol Nutr*. 2020;70(1):141–56.
6. Bohra S, Shah A. Celiac Disease and Thrombotic Events: A Systematic Review. *Int J Celiac Dis*. 2022;10(1):10–15.
7. Miranda S, Clara P, Rua J, Cimbron M, Salvador F. Deep Vein Thrombosis Revealing a "Silent" Celiac Disease. *Eur J Case Rep Intern Med*. 2023;10(1):3977.
8. Korkmaz M, Yilmaz M, Korkmaz H, Yilmaz N, Korkmaz S. Hyperhomocysteinemia and protein S deficiency in celiac disease presenting with thrombosis. *Blood Coagul Fibrinolysis*. 2022;33(4):271–76.
9. Singh P, Arora A, Strand TA, Leffler DA, Catassi C, Green PH, *et al.*, Global Prevalence of Celiac Disease: Systematic Review and Meta-analysis. *Clin Gastroenterol Hepatol*. 2018;16(6):823–836.e2.
10. Green PHR, Cellier C. Celiac disease. *N Engl J Med*. 2007;357(17):1731–43.
11. Halfdanarson TR, Litzow MR, Murray JA. Hematologic manifestations of celiac disease. *Blood*. 2007;109(2):412–21.
12. El-Matary W, Moroz SP, Dickinson JA. Extraintestinal manifestations of celiac disease in children: A Canadian cohort study. *Front Pediatr*. 2019;7:56.
13. Berthoux E, Fabien N, Chayvialle JA, Ninet J, Durieu I. Adult celiac disease with thrombosis: a

case series of seven patients. Role of thrombophilic factors. *Rev Med Interne*. 2011;32(10):600–4.
14. Boucelma M, Saadi M, Boukrara H, Bensalah D, Hakem D, Berrah A. Association of celiac disease and cerebral venous thrombosis: report of two cases. *J Mal Vasc*. 2012;38:47–51.
15. Kochhar R, Masoodi I, Dutta U, Singhal M, Miglani A, Singh P, *et al.*, Celiac disease and Budd-Chiari syndrome: report of case with review of literature. *Eur J Gastroenterol Hepatol*. 2009;21(9):1092–4.
16. Khanna S, Chaudhary D, Kumar P, Mazumdar S. Occult celiac disease presenting as splenic vein thrombosis. *Indian J Gastroenterol*. 2008;27:38–9.
17. Besancenot JF, Muller G, Gagnaire A, *et al.*, Accident vasculaire cérébral ischémique de l'adulte jeune révélateur d'une maladie cœliaque: 2 observations. *Rev Med Interne*. 2006;27(Suppl):S405.
18. Picchi A, Pasqualini P, D'Aiello I, Cortese B, Micheli A, Limbruno U. Acute ST-elevation myocardial infarction in a 15-year-old boy with celiac disease and multifactorial thrombotic risk. *Thromb Haemost*. 2008;99(6):1116–8.
19. McNeill A, Duthie F, Galloway DJ. Small bowel infarction in a patient with coeliac disease. *J Clin Pathol*. 2006;59(2):216–8.
20. Jorge O, Jorge A, Camus G. Celiac disease associated with antiphospholipid syndrome. *Rev Esp Enferm Dig*. 2008;100:102–3.
21. Casella G, Bassotti G, Villanacci V, Di Bella C, Pagni F, Corti GL, *et al.*, Is hyperhomocysteinemia relevant in patients with celiac disease? *World J Gastroenterol*. 2011;17(24):2941–4.
22. Saibeni S, Lecchi A, Meucci G, Cristaldi M, Tagliabue L, Ferrero S, *et al.*, Prevalence of hyperhomocysteinemia in adult gluten-sensitive enteropathy at diagnosis: role of B12, folate, and genetics. *Clin Gastroenterol Hepatol*. 2005;3(6):574–80.
23. Karoui S, Sellami MK, Laatar AB, Zitouni M, Matri S, Laadhar L, *et al.*, Prevalence of anticardiolipin and anti-beta2-glycoprotein I antibodies in celiac disease. *Dig Dis Sci*. 2007;52(5):1096–100.
24. Mankai A, Achour A, Thabet Y, Manoubia W, Sakly W, Ghedira I. Anti-cardiolipin and anti-beta2-glycoprotein I antibodies in celiac disease. *Pathol Biol (Paris)*. 2012;60(5):291–5.
25. Afredj N, Metatla S, Faraoun SA, Nani A, Guessab N, Benhalima M, *et al.*, Association of Budd-Chiari syndrome and celiac disease. *Gastroenterol Clin Biol*. 2010;34(11):621–4.
26. Al-Toma A, Goerres MS, Meijer JW, Tervaert JW, von Blomberg BM, Mulder CJ. Antiphospholipid antibodies in untreated celiac disease. *Am J Gastroenterol*. 2007;102:2214–19.
27. van Tilburg NH, Rosendaal FR, Bertina RM. Thrombin activatable fibrinolysis inhibitor and the risk for deep vein thrombosis. *Blood*. 2000;95(9):2855–9.
28. Saibeni S, Bottasso B, Spina L, Bajetta M, Danese S, Vecchi M, *et al.*, Assessment of thrombin-activatable fibrinolysis inhibitor (TAFI) plasma levels in inflammatory bowel diseases. *Am J Gastroenterol*. 2004;99(10):1966–70.