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**Case Report** **Hepato-Gastro-Enterology**

# Budd-Chiari Syndrome Complicating a Coeliac Disease in Adult: Case Report

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## Abstract

Coeliac disease (CD) is an immune mediated enteropathy caused by the ingestion of gluten in genetically predisposed individuals. It is frequently associated with wide spectrum of extra-intestinal manifestations, including thromboembolism events. We report the case of a young woman known with a CD since the age of 6, who says to be compliant to the gluten free diet (GFD), and presented with bloating and anemic syndrome. The endoscopic and anathomopathological examinations revealed no abnormalities. The CT scan revealed incidentally a chronic obstruction of the inferior vena cava (IVC). the etiological work-up for thromboembolic disease was negative, concluding to a Budd-Chiari syndrome complicating her CD. She was managed with anticoagulants, specifically Direct oral anticoagulants (DOACs).

**Keywords:** Coeliac disease, thromboembolism, thrombosis, Budd-chiari syndrome, thrombosis of IVC, DOACs, gluten free diet.



## INTRODUCTION

CD is a common autoimmune condition affecting the small intestine of genetically predisposed individuals, triggered by the consumption of gluten, and leading to symptoms of malabsorption such as weight loss, steatorrhea, diarrhea, and nutritional deficiencies [1]. It can also affect other organs and has been associated with a range of extra-intestinal manifestations, including liver, skin, and neurological disturbances. In recent decades, the clinical presentation tends to be milder with a higher prevalence of extraintestinal symptoms than gastrointestinal ones [2], making the diagnosis of CD more challenging. An increased risk of thromboembolism events has also been described in several studies [3]. Herein, we present a rare association between CD and Budd-Chiari syndrome (BCS), an exceptionally rare condition that involves the obstruction of hepatic venous flow in the vascular space between the hepatic venules and the junction between the IVC and the right atrium.

## CASE REPORT

A 30-year-old north African female with a known case of celiac disease since the age of 6, and compliant to the gluten free diet (GFD) for the past 4 years according to her and her family, presented to our out-patient department with chief complaints of bloating, abdominal pain, diarrhea, palpitations and shortness of breath for one year. A general physical examination revealed pallor, accelerated pulse to 101 beats per minute, no jaundice, and no peripheral oedema. On per abdominal examination, an isolated hepatomegaly was appreciable, without any evidence of ascites. Bowel sounds were normoactive. Rest of the systematic examination was unremarkable. Hematological investigation displayed microcytic hypochromic anemia (hemoglobin level of 5,1g/dl, mean corpuscular volume of 55fL), platelet count of 500000/m3, and WBC count of 3200/µL. Serum ferritin level was <1,98 µg/dL (normal 11–307 µg/dL). Liver function test showed a total bilirubin of 4mg/l, alanine aminotransferase (ALAT) 58 U/L (normal<35UI/L), aspartate aminotransferase (ASAT) 33UI/L (normal<35UI/L), alkaline phosphatase (ALP) 136UI/L (normal 106UI/l), gamma-glutamyl transpeptidase (GGT) 137UI/l (normal

38UI/L), Albumine 44,6g/l, prothrombin time ratio 91% and factor V 116%. Vitamin B12 and folate levels were within normal limits. Fasting lipid profile, thyroid function and kidney tests were within normal limits. Serum anti-tissue transglutaminase antibodies IgA were increased 80UI/ml (normal<10UI/ml) questioning the adherence of patient to the GFD. Upper gastrointestinal endoscopy showed a congestive and erosive bulbitis. Duodenal biopsies revealed 30% intraepithelial hyperlymphocytosis with partial villous atrophy and crypt hyperplasia compatible with March stage IIIa celiac disease, suggesting a non-adherence to the GFD. Beta-2-microglobulin and LDH levels were within normal limits. A contrast-enhanced computed tomography revealed mucosal thickening of the first duodenal portion with mucosal enhancement, dysmorphic liver, hepatic perfusion disorders with inhomogeneous mottled liver, and chronic thrombosis of the IVC extending from the suprahepatic portion to the infrahepatic portion (Figures A-B), with developpement of collateral venous circulation, dilatation of the azygos, hemi-azygos and left renal veins (Figures C-D), as well as a dilatation of portal trunk (Figure A). Hepatic veins were permeable. Hence, the diagnosis of BCS by obstruction of IVC was made.

Further analysis were done to identify the possible causes of the thrombosis and dysmorphic liver. Ag Hbs and hepatitis C antibodies were negative. Serological screening for autoimmune liver diseases (antinuclear antibodies, anti-smooth muscle antibodies, anti-soluble liver antigen antibodies, anti-liver cytosol antibody Type1, anti-liver/kidney microsome antibody Type 1, anti-mitochondria M2 antibodies, anti-sp100 antibodies, anti-GP210 antibodies, anti-neutrophil cytoplasm antibody) showed normal results. No iron overload was noted with a transferrin saturation of 20,86%. Cholangio-MRI revealed no thickening nor dilatation of biliary ducts. Screening for the hypercoagulable state turned out to be insignificant. Specifically, Levels of protein C, protein S and antithrombin III were within reference range. Prothrombin and factor V Leiden mutations were not detectable. Serum homocysteine level was within normal limits. Anticardiolipine, anti Beta2- Glycoprotein, and Lupus anticoagulant antibodies were all negative. Testing for JAK 2 mutation was also negative. Flow cytometry did not reveal decreased CD59 and CD55 expression on either white or red cells, the diagnosis of paroxysmal nocturnal haemoglobinuria was therefore ruled out. Bone marrow examination did not identify any myeloproliferative disorders. Ileo-coloscopy was performed and came back negative for inflammatory bowel disease. The diagnosis of Budd-Chiari Syndrome complicating coeliac disease was thus made, and patient was put on curative anticoagulation with DOACs: Rivaroxaban.

The evolution was marked by the occurrence of 2 episodes of upper gastrointestinal bleeding at 1 month and 6 months from the start of Rivaroxaban anticoagulation. A first EGD revealed bulbar erosions without identification of a hemorrhagic lesion. Ileocoloscopy was normal. An endoscopic videocapsule revealed bleeding from the duodenum without identification of a hemorrhagic lesion. The entero-scanner found no digestive thickening nor hemorragic lesions. After multidisciplinary discussion, it was decided to start the patient on Apixaban, which is less prone to GI bleeding, and to look for complications of her coeliac disease such as refractory sprue or intestinal lymphoma. An EGD with a new series of multiple duodenal biopsies was performed and revealed antral vascular ectasia and grade I oesophageal varices. Anatomopathological study coupled with immunohistochemistry revealed a focal intraepithelial hyperlymphocytosis at 30% corresponding to a Marsh stage I celiac disease, without stigmata of refractory sprue. The petscan performed in search of lymphomatous transformation came back negatif.

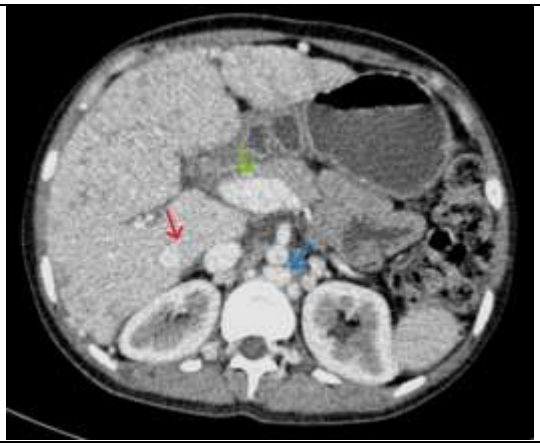

**Figure A: Axial CT section showing inhomogeneous mottled liver, thrombosis of intra-hepatic portion of IVC (Red arrow), dilatation of the portal vein (green arrow), and collateral venous circulation (Blue arrow)**

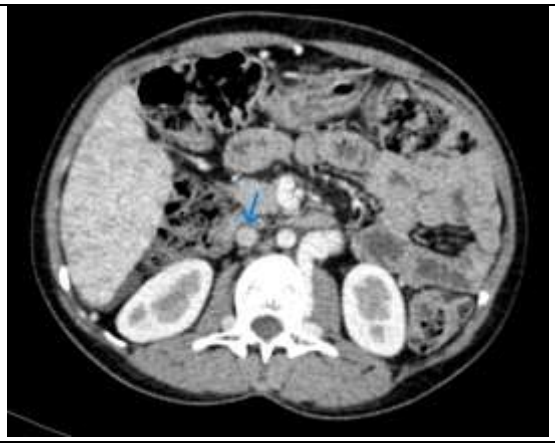

**Figure B: Axial CT section showing thrombosis of infra-hepatic portion of IVC (Blue arrow)**

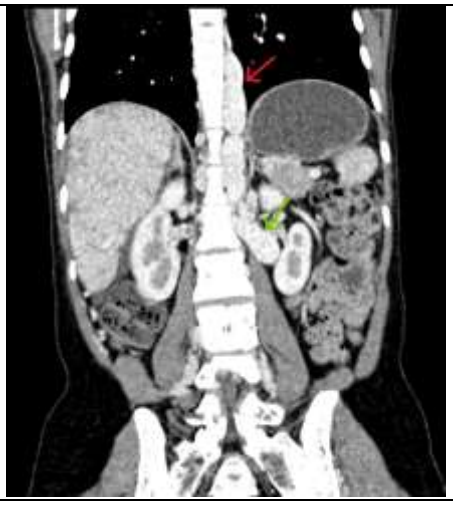

**Figure C: Coronal scan section showing dilatation of hemi-azygos vein (Red arrow) with renal collateral venous circulation (Green arrow)**

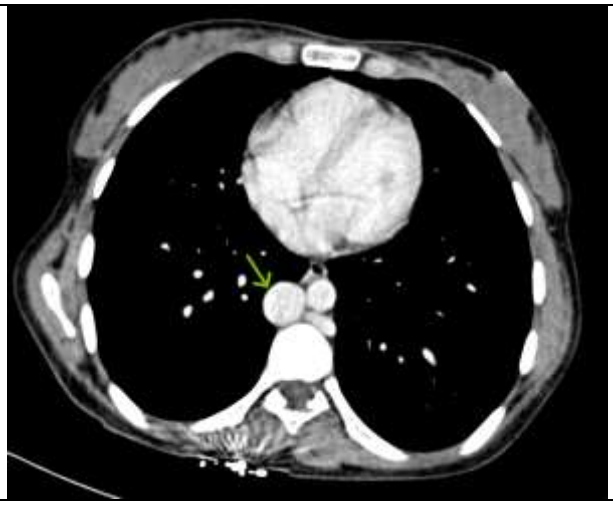

**Figure D: Axial CT section showing dilatation of Azygos vein (Green arrow)**

## DISCUSSION

There is a wide spectrum of extraintestinal manifestations of CD that are sometimes more prominent than readily recognized intestinal symptoms. Thrombo-embolic events have only recently emerged as manifestations of CD [4]. Initially, evidence of hypercoagulability in CD surfaced through case reports and case series (5-6). A recent systematic review uncovered 55 documented cases of thromboembolism associated with CD [4]. The most frequent thrombosis site is recognized to be hepatics veins with almost one third of cases [4].

The occurrence of BCS in CD patients is very rare with an annual incidence of this association being less than 5 per million [7]. The majority of described cases were from North Africa, Middle East, and Southern Europe [8-11]. Reports have attributed this to genetic factors, environmental influences, and dietary components present in the North African diet [12-14]. A multicentric case series revealed that the majority of reported patients were females who presented in their third or fourth decade of life [10]. Similarly, our patient was a female in her second decade of life. The clinical presentation ranged from fulminant and acute to subacute and chronic, with chronic BDS being the most frequent presentation [15]. Our patient was asymptomatic for the BDS which was discovered by chance on the abdominal CT. The occurrence of BDS with CD remains incompletely elucidated. However, multiple theories have been made to explain this association including malabsorption of vitamin K leading to deficiencies in protein C, protein S, and antithrombin III. Additionally, it may involve hyperhomocysteinemia due to folic acid deficiency or methylenetetrahydrofolate reductase (MTHFR) gene mutation, lymphoma, myeloproliferative disorders, magnesium deficiency, thrombocytosis, autoimmune vasculitis, association with serum lupus anticoagulant, and thrombocytopenia secondary to hypersplenism [16-18]. However, in our case, no specific cause for this hypercoagulable state could be identified. 61% of patients with BDS and CD had no identifiable underlying thrombotic cause in a recent study [10].

Strict life-long adherence to a GFD is the mainstay for the treatment of CD, and the prevention of complications, including thrombo-embolic events. The effect of a GFD on the course of BCS in CD has not been frequently reported. In our case, BCS had developed in patient who says to be compliant to the diet but with serological and histological findings not supporting this claim. In a study, 7 out of 9 patients with BCS-CD experienced the resolution of ascites and the formation of collateral porto-systemic circulations after following GFD for six months [19]. In contrast, the two patients who did not adhere to a GFD had persistent ascites and showed progression of thrombosis in the hepatic veins and the IVC. The findings in this study are interesting but the small number of patients does not allow valid conclusions.

The role of anticoagulation in CD, particularly for prophylactic purposes, remains unexplored. Further research is required to evaluate the potential risks and benefits of this therapeutic approach [20]. In a recent review [4], 69% of patients underwent anticoagulation therapy, with vitamin K antagonists being the most frequently used. The findings highlight the critical importance of anticoagulation, as all patients receiving this treatment achieved a 100% survival rate. This underscores the necessity of initiating anticoagulation therapy in all CD patients with thrombosis. However, the optimal duration of treatment remains uncertain and warrants investigation through more rigorous prospective studies.

## CONCLUSION

This case describes the occurrence of BCS in a female patient with known CD and non-adherent to

GFD, in the absence of any known pro-thrombotic factor. Further research is warranted to elucidate the pathological mechanisms underlying the development of this association. We suggest a screening of BCS while evaluating a patient of CD of undetermined liver disease.

## REFERENCES


1. Green PH. The many faces of celiac disease: clinical presentation of celiac disease in the adult population. Gastroenterology. 2005;128(4): S74-S78.
2. Hujoel IA, Reilly NR, Rubio-Tapia A (2019) Celiac disease: clinical features and diagnosis. Gastroenterol Clin N Am 48(1):19–37
3. Lerner A, Blank M (2014) Hypercoagulability in celiac disease– an update. Autoimmun Rev 13(11):1138–1141
4. Pantic, N.; Pantic, I.; Jevtic, D.; Mogulla, V.; Oluic, S.; Durdevic, M.; Nordin, T.; Jecmenica, M.; Milovanovic, T.; Gavrancic, T.; *et al*. Celiac Disease and Thrombotic Events: Systematic Review of Published Cases. Nutrients 2022, 14, 2162.
5. Upadhyay, R.; Park, R.H.; Russell, R.I.; Danesh, B.J.; Lee, F.D. Acute mesenteric ischaemia: A presenting feature of coeliac disease? Br. Med. J. (Clin. Res. Ed.) 1987, 295, 958–959.
6. Marteau, P.; Cadranel, J.F.; Messing, B.; Gargot, D.; Valla, D.; Rambaud, J.C. Association of hepatic vein obstruction and coeliac disease in North African subjects. J. Hepatol. 1994, 20, 650–653
7. Choudhry MS, Zaidi SM, Mohiuddin O, Khan AA, Hanif A. Rare association of Budd-Chiari syndrome with celiac disease: a case report. Cureus. 2020 Oct;12(10).
8. Manzano ML, Garfia C, Manzanares J, *et al*. Celiac disease and Budd-Chiari syndrome: an uncommon association. Gastroenterol Hepatol 2002; 25(3): 159–161.
9. Danalioğlu A, Poturoğlu S, Güngör Güllüoğlu M, *et al*. Budd-Chiari syndrome in a young patient with celiac sprue: a case report. Turk J Gastroenterol 2003; 14(4): 262–265.
10. Jadallah KA, Sarsak EW, Khazaleh YM, *et al*. Budd-Chiari syndrome associated with coeliac disease: case report and literature review. Gastroenterol Rep 2016; 6(4): 308–312.
11. Afredj N, Metatla S, Faraoun SA, *et al*. Association of Budd-Chiari syndrome and celiac disease. Gastroenterol Clin Biol 2010; 34(11): 621–624.
12. Boudhina T, Ghram N, Becher SB, Ayach R, Ghachem KB, Yedes A, Hamza M. [Budd-Chiari syndrome and total villous atrophy in children: apropos of 3 case reports]. Tunis Med. 1990;68:59-62. French.
13. Hamdi A, Ayachi R, Saad H, Gargouri R, Zouari K, Chebbah MS. Hémiplégie révélant un syndrome de Budd-Chiari associé à une maladie coeliaque chez un nourrisson. Presse Med. 1990;19(21):1011-2. French.
14. Maccini DM, Berg JC, Bell GA. Budd-Chiari syndrome and Crohn's disease. An unreported association. Dig Dis Sci. 1989;34:1933-6.
15. Durga Shankar Meena , Vikram Singh Sonwal, Gopal Krishna Bohra, Jitendra Balesa and Amit Kumar Rohila. Celiac disease with Budd–Chiari syndrome: A rare association. SAGE Open Medical Case Reports volume 7: 1–3, 2019
16. Vives MJ, Esteve M, Mariné M, Fernández-Bañares F, Alsina M, Salas A, Loras C, Carrasco A, Almagro P, Viver JM, Rodriguez-Carballeira M. Prevalence and clinical relevance of enteropathy associated with systemic autoimmune diseases. Dig Liver Dis. 2012;44:636-42.
17. Wilcox GM, Mattia AR. Celiac sprue, hyperhomocysteinemia, and MTHFR gene variants. J Clin Gastroenterol. 2006;40:596-601.
18. Durlach J. [Celiac disease, magnesium deficiency and venous thrombosis]. Presse Med. 2001;30(18):904.
19. Afredj N,2Metatla S, Faraoun SA *et al*. Association of Budd- Chiari syndrome and celiac disease. Gastroenterol Clin Biol 2010;34:621–24.
20. Fousekis, F.S.; Beka, E.T.; Mitselos, I.V.; Milionis, H.; Christodoulou, D.K. Thromboembolic complications and cardiovascular events associated with celiac disease. Ir. J. Med. Sci. 2021, 190, 133–141.