https://doi.org/10.22516/25007440.1476

Case report

Primary Biliary Cholangitis Associated with Celiac Disease, Lupus, and Hashimoto's Thyroiditis: A Case Report

Flavia Karoline Gamla Farias,[1] Gabriela Modrak,[1] Lucas Henrique Lopes Mendes de Figueiredo,[2] Nicolle Casas Blanco,[3] Adir Cardoso Gentil Junior,[3] Janaina Sant'Ana Fonseca,[2] Monique Raddatz Reis Vilela,[2] Leonardo de Lucca Schiavon,[4] Janaina Luz Narciso-Schiavon.[4*]

OPEN ACCESS

Citation:
Farias FKG, Modrak G, de Figueiredo LHLM, Blanco NC, Gentil Junior AC, Fonseca JS, Vilela MRR, Schiavon LL, Narciso-Schiavon JL. Primary Biliary Cholangitis Associated with Celiac Disease, Lupus, and Hashimoto's Thyroiditis: A Case Report. Revista. colomb. Gastroenterol. 2026;41(2):250-254.
https://doi.org/10.22516/25007440.1476

[1] Hepatology Resident, PHospital Universitario Profesor Polydoro Ernani de São Thiago, FUniversidad Federal de Santa Catarina (HU-UFSC/EBSERH). Florianópolis, Brazil.
[2] Hepatologist, Hospital Universitario Profesor Polydoro Ernani de São Thiago, Universidad Federal de Santa Catarina (HU-UFSC/EBSERH). Florianópolis, Brazil.
[3] Gastroenterology Resident, Hospital Universitario Profesor Polydoro Ernani de São Thiago, Universidad Federal de Santa Catarina (HU-UFSC/EBSERH). Florianópolis, Brazil.
[4] PhD in Gastroenterology, Universidad Federal de São Paulo. Professor of Gastroenterology, Department of Internal Medicine, Universidad Federal de Santa Catarina. Gastroenterologist and Hepatologist, Hospital Universitario Profesor Polydoro Ernani de São Thiago, Universidad Federal de Santa Catarina (HU-UFSC/EBSERH). Florianópolis, Brazil.

***Correspondence:** Janaina Luz Narciso-Schiavon.
janaina.narciso@ufsc.br

Received: 04/11/2025
Accepted: 23/01/2026

Abstract

Introduction: The coexistence of two or more autoimmune diseases defines multiple autoimmune syndrome. Primary biliary cholangitis (PBC) may occur in association with other immune-mediated conditions. A case of PBC associated with systemic lupus erythematosus (SLE), celiac disease (CD), and Hashimoto's thyroiditis (HT) is described. **Case report:** A 45-year-old woman presented with cholestatic liver enzyme abnormalities and positive autoantibodies. She had a history of HT and a family history of CD. Serology showed positive anti-endomysial antibodies, anti–tissue transglutaminase IgA 117 U/mL, positive AMA-M2, ANA 1:320, positive anti-dsDNA, and decreased C3/C4. Duodenal biopsy revealed villous atrophy, and liver biopsy demonstrated granulomas, bile duct injury, and portal inflammation with portal fibrosis, confirming PBC. A gluten-free diet, ursodeoxycholic acid (15 mg/kg/day), hydroxychloroquine (400 mg/day), prednisone (0.5 mg/kg with taper), and azathioprine were initiated. The patient showed normalization of liver biochemistry and clinical improvement. **Discussion:** Polyautoimmunity in PBC is well recognized and commonly involves thyroid disorders, SLE, and CD. This case illustrates the need for targeted screening for associated autoimmune diseases and multidisciplinary management. The presence of multiple autoantibodies and characteristic histological findings guided diagnosis and treatment. **Conclusion:** In patients with PBC, concomitant autoimmune diagnoses should be considered; early detection and comprehensive management optimize outcomes.

Keywords

Primary biliary cholangitis; systemic lupus erythematosus; celiac disease; Hashimoto's thyroiditis.

INTRODUCTION

Primary biliary cholangitis (PBC) is a chronic cholestatic cholangiopathy of autoimmune origin that predominantly affects middle-aged women(1). The coexistence of autoimmune diseases is common in PBC and may be part of the so-called multiple autoimmune syndrome or polyautoimmunity(2). Polyautoimmunity is defined as the presence of two or more autoimmune diseases in the same patient(3). In this context, the most common extrahepatic autoimmune conditions associated with PBC are, in order of frequency, Sjögren's syndrome (affecting approximately one-third of patients), Raynaud's phenomenon, Hashimoto's thyroiditis (and, less frequently, Graves' disease), scleroderma/CREST

© 2026 Asociación Colombiana de Gastroenterología

syndrome, rheumatoid arthritis, systemic lupus erythematosus (SLE), celiac disease, autoimmune skin diseases (e.g., lichen planus), and vasculitis. These associations appear to reflect shared immunopathogenic mechanisms and a clear female predominance, although, overall, they do not appear to significantly affect survival compared with patients with PBC without autoimmune comorbidities[4]. Recognizing these associations is essential for timely diagnosis, risk stratification, and comprehensive management.

In celiac disease, the autoimmune disorders most frequently associated are type 1 diabetes *mellitus* and autoimmune thyroid diseases (Hashimoto's thyroiditis and, less frequently, Graves' disease). Autoimmune liver diseases have also been described, particularly autoimmune hepatitis and PBC, in addition to Sjögren's syndrome and SLE. This spectrum reinforces the need for targeted surveillance in celiac disease, especially during the first years after diagnosis, as well as confirmation of celiac disease through positive anti-endomysial antibodies (EmA) and/or anti-tissue transglutaminase antibodies (tTG), followed by duodenal biopsy demonstrating typical histologic findings. Furthermore, it underscores the importance of strict gluten avoidance, since more rapid normalization and sustained low tTG levels are associated with a lower subsequent risk of developing new autoimmune diseases[5]. Despite the above, the simultaneous coexistence of all four conditions (Hashimoto's thyroiditis, celiac disease, SLE, and PBC) is uncommon. This rarity gives the present case particular clinical and academic relevance, highlighting the need for an integrative diagnostic approach and interdisciplinary management in the setting of polyautoimmunity.

METHOD

Retrospective descriptive study based on medical record review. Approved by the CEPSH/UFSC. Opinion No. 7.670.068.

CASE

A 45-year-old woman presented with persistent elevation of liver biochemical tests. Overall, she remained asymptomatic and reported no jaundice, pruritus, or abdominal pain (chief complaint), except for the presence of arthralgias. In the history of present illness, she reported laboratory abnormalities detected several months earlier, without identifiable triggers, and denied the use of herbal products, anabolic agents, or cholestatic drugs, as well as alcohol consumption. She denied fever, weight loss, choluria, or acholia. Her comorbidity consisted of treated Hashimoto's thyroiditis, with euthyroid status. Her past medical history was negative for abdominal surgeries, previous hepatitis, cholelithiasis, or known biliary disease. Family history was positive for celiac disease in a first-degree relative. Regarding lifestyle habits, she was a non-smoker, followed an omnivorous diet, engaged in irregular physical activity, and denied recreational drug use. On physical examination, she was in good general condition, afebrile, and hemodynamically stable, without mucocutaneous stigmata of cholestasis or signs of advanced liver disease. The abdomen was flat, soft, and non-tender, with no palpable visceromegaly, clinical jaundice, or lymphadenopathy.

Laboratory tests (**Table 1**) showed a cholestatic pattern, with elevated alkaline phosphatase and γ-glutamyltransferase, mildly increased alanine aminotransferase (ALT) and aspartate aminotransferase (AST), normal bilirubin, and preserved synthetic function (albumin and coagulation tests within normal range). The immunologic profile revealed positive EmA, tTG IgA: 117 U/mL, positive antimitochondrial antibodies type M2 (AMA-M2), antinuclear antibody: 1:320 reticular speckled pattern, positive anti-DNA antibodies, and reduced C3/C4 levels; serum IgA was within the normal range. Viral hepatitis serologies were negative. Endoscopic imaging studies and intestinal histology demonstrated that upper endoscopy with duodenal biopsy showed Marsh 3 villous atrophy consistent with celiac disease. Liver biopsy revealed granulomas, bile duct injury, portal infiltrate, and portal fibrosis, findings consistent with PBC, with mild to moderate histologic activity. Concurrently, she was being followed by Rheumatology, which established the diagnosis of SLE based on a presentation of polyarthralgia.

Table 1. Laboratory Tests Throughout Clinical Follow-up*

Date	AST (RV <37)	ALT (RV <56)	ALP (RV <136)	GGT (RV <55)
Aug/09	**38**	**60**	**197**	**97**
Nov/09	**41**	**61**	**213**	**112**
Jan/12	33	52	**171**	**102**
Feb/15	22	29	**141**	35
Sep/16	29	30	105	37
Aug/18	36	40	133	53
Dec/20	31	27	98	30
Sep/22	20	25	70	25
Feb/25	20	24	73	27

*Values in bold correspond to results above the reference value for each test. ALT: alanine aminotransferase; AST: aspartate aminotransferase; ALP: alkaline phosphatase; GGT: γ-glutamyltransferase; RV: reference value. Author's own research.

Based on the integrated clinical, serologic, and histologic findings, a gluten-free diet, ursodeoxycholic acid 15 mg/kg/day, hydroxychloroquine 400 mg/day, prednisone 0.5 mg/kg with gradual tapering, and azathioprine as a steroid-sparing agent were initiated. During follow-up, progressive improvement in liver biochemistry was documented, culminating in normalization of liver enzymes, along with sustained clinical improvement during follow-up visits through 2025 (**Table 1**). During clinical follow-up, negativization of EmA and tTG autoantibodies was also observed, as well as normalization of the duodenal biopsy (Marsh 0).

DISCUSSION

In the present case, the presence of AMA-M2 and the characteristic histologic findings established the diagnosis of PBC, while the systemic autoantibodies and clinical manifestations supported concomitant SLE. Villous atrophy together with positive EmA and tTG confirmed celiac disease. According to the classical classification of autoimmune polyglandular syndromes, this constellation of diseases corresponds to APS-III (MAS-3), specifically within subgroups IIIb (which include the association of autoimmune thyroiditis with gastrointestinal/hepatobiliary disease) and IIId (characterized by the coexistence of autoimmune thyroiditis with systemic rheumatologic diseases such as SLE). In light of the contemporary association-network analysis proposed by Pham-Dobor and colleagues, these combinations align with the clusters centered on Hashimoto's thyroiditis, in which gastrointestinal, hepatobiliary, and systemic manifestations converge. This integrated approach underscores the importance of early recognition of these patterns of polyautoimmunity in order to anticipate new manifestations, optimize clinical follow-up, and ensure timely interventions[6].

This case reflects the complexity of polyautoimmunity, given that the vast majority of patients with autoimmune polyglandular syndromes present with two and, less frequently, three manifestations. Endocrine diseases are the most common, followed by gastrointestinal disorders and, thirdly, systemic conditions such as rheumatoid arthritis (RA), Sjögren's syndrome (SS), and SLE[6]. In this context, the simultaneous coexistence of four autoimmune diseases (Hashimoto's thyroiditis, celiac disease, PBC, and SLE) constitutes an exceptional finding that broadens the clinical spectrum described in the literature.

Celiac disease is a systemic immune-mediated disorder triggered by gluten in genetically predisposed individuals and is associated with a broad spectrum of extraintestinal manifestations and an increased risk of other autoimmune diseases. Evidence suggests that early diagnosis and treatment are associated with a lower subsequent development of autoimmunity, whereas unrecognized or untreated celiac disease is linked to a greater occurrence of autoimmune and liver disorders over time[7].

At the intersection between celiac disease and PBC, population-based studies have reported elevated bidirectional prevalences. In a United Kingdom cohort, approximately 3% of patients with celiac disease had PBC, and nearly 6% of individuals with PBC had celiac disease[8]. Furthermore, Irish series reported that celiac disease in patients with PBC was at least 10 times more frequent than in the general population, while Scandinavian registries demonstrated very high relative risks of PBC in celiac disease (incidence ratios on the order of approximately 25–28)[9]. Although negative findings have been reported in some series (Sweden, Italy, and Greece), the overall body of evidence supports a clinically relevant association between these two entities[10–13]. These findings justify active screening for celiac disease in patients with PBC and marked autoimmunity and, conversely, hepatologic surveillance in individuals with celiac disease[14].

In this regard, metabolomic analyses by nuclear magnetic resonance of serum and urine demonstrated that PBC exhibits a distinctive metabolic fingerprint compared with healthy controls and celiac disease, with higher serum levels of pyruvate, citrate, glutamate, glutamine, serine, tyrosine, phenylalanine, and lactate, as well as lower urinary levels of hippurate and trigonelline. These findings suggest alterations in energy metabolism and possible intestinal dysbiosis. Furthermore, the profiles allowed discrimination between PBC and celiac disease with high accuracy (approximately 82%–92% in serum, depending on the experiment), supporting the notion that, despite their clinical association, PBC and celiac disease exhibit different metabolic signatures that may provide pathogenic insights and future therapeutic targets[15].

In this setting, it is crucial to differentiate "pure" PBC from a PBC-autoimmune hepatitis (AIH) overlap syndrome, since the presence of systemic autoantibodies related to SLE may complicate interpretation. The Paris criteria propose ALT/IgG thresholds and hepatocellular histologic features to define overlap[16]. In our case, the mildly elevated transaminases, positive AMA-M2, and typical cholangiopathic histology supported PBC without significant overlap, reserving immunosuppression for the management of SLE rather than as a specific strategy for PBC.

From a therapeutic perspective, the cornerstone of treatment remains ursodeoxycholic acid (UDCA 13-15 mg/kg/day), with assessment of biochemical response using validated criteria (Barcelona, Paris I/II, Toronto)[17]. A strict gluten-free diet is mandatory in confirmed celiac disease and may optimize liver parameters in certain subgroups, but it does not replace UDCA as the standard of

care in PBC. Hydroxychloroquine, tapering prednisone, and azathioprine were directed toward the control of SLE; any improvement in liver enzymes under these agents should be interpreted within the context of the primary response to UDCA.

CONCLUSION

This case illustrates how polyautoimmunity may mask or mimic overlap syndromes, requiring a disciplined diagnostic algorithm and the integration of serology, histology, and clinical context. In PBC, complete response to UDCA remains the central prognostic determinant. Concurrently, timely screening and treatment of celiac disease, as well as appropriate control of SLE, contribute decisively to clinical and biochemical improvement. In light of contemporary classifications of autoimmune polyglandular syndromes, this case exemplifies a phenotype of multiple polyautoimmunity centered on Hashimoto's thyroiditis, with hepatobiliary, intestinal, and systemic involvement. Early identification of these associations not only allows anticipation of new autoimmune manifestations, but also optimizes longitudinal follow-up and ensures timely therapeutic interventions, reinforcing the clinical and academic relevance of this case within the spectrum of diseases requiring early detection and comprehensive management.

Conflict of Interest

The authors declare that there are no conflicts of interest related to this manuscript.

Funding Sources

This research received no specific support from public-sector agencies, commercial entities, or non-profit organizations.

Use of Artificial Intelligence

Artificial intelligence-assisted technologies (ChatGPT) were used exclusively to support drafting, style standardization, and linguistic review. All scientific decisions, data analysis and interpretation, and drafting of substantive content were performed by the authors. Artificial intelligence was not used for data analysis or image generation.

REFERENCES

1. Ma D, Ma J, Zhao C, Tai W. Reasons why women are more likely to develop primary biliary cholangitis. Heliyon. 2024;10(4):e25634. https://doi.org/10.1016/j.heliyon.2024.e25634
2. Anaya JM, Rojas-Villarraga A, García-Carrasco M. The autoimmune tautology: from polyautoimmunity and familial autoimmunity to the autoimmune genes. Autoimmune Dis. 2012;2012:297193. https://doi.org/10.1155/2012/297193
3. Anaya JM, Corena R, Castiblanco J, Rojas-Villarraga A, Shoenfeld Y. The kaleidoscope of autoimmunity: multiple autoimmune syndromes and familial autoimmunity. Expert Rev Clin Immunol. 2007;3(4):623-35. https://doi.org/10.1586/1744666X.3.4.623
4. Floreani A, Franceschet I, Cazzagon N, Spinazzè A, Buja A, Furlan P, et al. Extrahepatic autoimmune conditions associated with primary biliary cirrhosis. Clin Rev Allergy Immunol. 2015;48(2-3):192-7. https://doi.org/10.1007/s12016-014-8427-x
5. Abu Hanna F, Sirkin M, Ilovich BS, Egbarieh R, Tatour S, Lahad A, et al. Parameters associated with the development of autoimmune diseases in pediatric onset celiac disease. Eur J Pediatr. 2025;184(3):199. https://doi.org/10.1007/s00431-025-06028-5
6. Pham-Dobor G, Kaltenecker P, Temesfoi V, Bajnok L, Nemes O, Bodis B, et al. Systematic Analysis and Network Mapping of Disease Associations in Autoimmune Polyglandular Syndrome. J Clin Endocrinol Metab. 2025;110(6):1716-1728. https://doi.org/10.1210/clinem/dgae701
7. Chaudrey KH. ACG Guideline: Diagnosis and Management of Celiac Disease. Am J Gastroenterol. 2023;118(1):23. https://doi.org/10.14309/ajg.0000000000002111
8. Kingham JG, Parker DR. The association between primary biliary cirrhosis and coeliac disease: a study of relative prevalences. Gut 1998;42(1):120-122. https://doi.org/10.1136/gut.42.1.120
9. Sorensen HT, Thulstrup AM, Blomqvist P, Nørgaard B, Fonager K, Ekbom A. Risk of primary biliary liver cirrhosis in patients with coeliac disease: Danish and Swedish cohort data. Gut 1999;44(5):736-738. https://doi.org/10.1136/gut.44.5.736
10. Sjöberg K, Lindgren S, Eriksson S. Frequent occurrence of non-specific gliadin antibodies in chronic liver disease. Endomysial but not gliadin antibodies predict coeliac disease in patients with chronic liver disease. Scand J Gastroenterol 1997;32(11):1162-7. https://doi.org/10.3109/00365529709002997
11. Volta U, De Franceschi L, Molinaro N, Cassani F, Muratori L, Lenzi M, et al. Frequency and significance of anti-gliadin and anti-endomysial antibodies in autoimmune hepatitis.

Dig Dis Sci. 1998;43(10):2190-2195. https://doi.org/10.1023/A:1026650118759
12. Bardella MT, Quatrini M, Zuin M, Podda M, Cesarini L, Velio P, et al. Screening patients with celiac disease for primary biliary cirrhosis and vice versa. Am J Gastroenterol. 1997;92(9):1524-1526.
13. Chatzicostas C, Roussomoustakaki M, Drygiannakis D, Niniraki M, Tzardi M, Koulentaki M, et al. Primary biliary cirrhosis and autoimmune cholangitis are not associated with coeliac disease in Crete. BMC Gastroenterol. 2002;2:5. https://doi.org/10.1186/1471-230X-2-5
14. Narciso-Schiavon JL, Schiavon LL. To screen or not to screen? Celiac antibodies in liver diseases. World J Gastroenterol. 2017;23(5):776-791. https://doi.org/10.3748/wjg.v23.i5.776
15. Vignoli A, Orlandini B, Tenori L, Biagini MR, Milani S, Renzi D, et al. Metabolic Signature of Primary Biliary Cholangitis and Its Comparison with Celiac Disease. J Proteome Res. 2019;18(3):1228-1236. https://doi.org/10.1021/acs.jproteome.8b00849
16. Kuiper EM, Zondervan PE, van Buuren HR. Paris criteria are effective in diagnosis of primary biliary cirrhosis and autoimmune hepatitis overlap syndrome. Clin Gastroenterol Hepatol. 2010;8(6):530-4. https://doi.org/10.1016/j.cgh.2010.03.004
17. European Association for the Study of the Liver. EASL Clinical Practice Guidelines: The diagnosis and management of patients with primary biliary cholangitis. J Hepatol. 2017;67(1):145-172. https://doi.org/10.1016/j.jhep.2017.03.022