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

Uncommon Association of Primary Biliary Cholangitis and Ulcerative Colitis in a Male Patient, Cirrhosis as a Presenting Feature: A Case Report

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

[1]Department of Gastroenterology, CHU Mohammed VI Marrakech, Morocco
[2]Laboratory of physiology, Faculty of medicine and pharmacy of Marrakech, Morocco

DOI: https://doi.org/10.36347/sjmcr.2024.v12i12.046 | **Received:** 19.11.2024 | **Accepted:** 24.12.2024 | **Published:** 28.12.2024

***Corresponding author:** Semlali R
Department of Gastroenterology, CHU Mohammed VI Marrakech, Morocco

Abstract **Case Report**

Primary biliary cholangitis (PBC) is a chronic autoimmune cholangitis characterized by progressive destruction of the small intrahepatic bile ducts, leading to cholestasis and, potentially, liver cirrhosis. While its clinical and biological manifestations are well-documented, its association with inflammatory bowel disease (IBD) remains rare. Inflammatory bowel disease, particularly ulcerative colitis (UC), is frequently linked to hepatobiliary disorders, most notably primary sclerosing cholangitis (PSC). However, the co-occurrence of PBC and UC is highly uncommon and poorly understood. We report a rare case of a male patient in whom PBC and UC coexisted, with cirrhosis being the initial presentation. This case highlights the need for heightened clinical suspicion of atypical hepatobiliary associations in IBD patients and underscores the importance of early recognition and management.

Keywords: Primary Biliary Cholangitis (PBC), Ulcerative Colitis (UC), Inflammatory Bowel Disease (IBD), Autoimmune Disease, Liver Cirrhosis.

INTRODUCTION

Inflammatory bowel diseases (IBD), encompassing Crohn's disease (CD) and ulcerative colitis (UC), are frequently linked to hepatobiliary disorders, with primary sclerosing cholangitis (PSC) being the most common association, likely due to shared pathogenic pathways [1, 2]. In contrast, the coexistence of IBD and primary biliary cholangitis (PBC) is exceptionally rare and largely confined to isolated case reports [1].

Primary biliary cholangitis (PBC), previously referred to as primary biliary cirrhosis, is a chronic autoimmune liver disease characterized by chronic cholestasis and histopathological evidence of non-suppurative destructive cholangitis [3]. The clinical presentation of PBC is often asymptomatic or marked by nonspecific symptoms such as fatigue and pruritus.

Diagnosis is primarily established through the detection of anti-mitochondrial antibodies (AMA), which are highly specific to the disease [4]. Liver function tests typically demonstrate a cholestatic profile, with elevations in gamma-glutamyl transferase (GGT) and alkaline phosphatase (ALP). Prognosis has greatly improved with ursodeoxycholic acid (UDCA), which delays disease progression and reduces the need for transplantation in responders [5].

PBC often coexists with other autoimmune diseases, such as Hashimoto's thyroiditis, Sjögren's syndrome, rheumatoid arthritis, and celiac disease [6]. However, unlike PSC, which has a clear association with IBD, the overlap between PBC and IBD is exceedingly uncommon and mainly observed in anecdotal cases. Notably, PBC predominantly affects women, further differentiating it from PSC [3].

Here, we report a rare case of this association in a male patient.

CASE REPORT

Patient A.A aged 62, presented to our hospital following the onset of an abdominal distension progressing for one month, with a generalized jaundice. The patient history reveals a history of intermittent bloody diarrhea for the past year. Physical examination revealed massive ascites causing the abdominal

distension, lower limb bilateral edema and diffuse abdominal tenderness.

Diagnostic paracentesis followed with ascitic fluid analysis were performed, finding a serum-ascites albumin gradient > 11g/l (highly evocative of portal hypertension) and a neutrophil count of 120/ mm3, ruling out spontaneous bacterial peritonitis.

Labortatory tests revealed normocytic anemia, moderate thrombocytopenia and slightly decreased prothrombin levels.

Liver enzymes were elevated: SGOT and SGPT were 4.5x and 2.6x the normal value, respectively.

GGT were 7x the normal value, and ALP were even more elevated, at 10 times the normal value. Total bilirubin was slightly elevated, at 25.8 mg/l, with a predominance of conjugated bilirubin.

Albumin levels were markedly low at 23g/l and CRP was slightly elevated at 12.4 mg/l.
Other biological parameters were normal.

Abdominal CT-scan revealed a cirrhotic liver, with portal hypertension signs: Splenomegaly, dilated portal vein and ascites. No biliary anomaly that would explain the elevated liver enzymes was found.

Esophagogastroduodenoscopy was performed, revealing grade II oesophagal varices and portal hypertensive gastropathy with no signs of bleeding.

The diagnosis of liver cirrhosis was made on this set of clinical, biological, radiological and endoscopic findings.

Viral hepatitis was ruled out as the aetiology of the patient's cirrhosis and auto-immune tests were performed which came back positive to anti-M2 and anti-sp 100 **(Figure 1).**

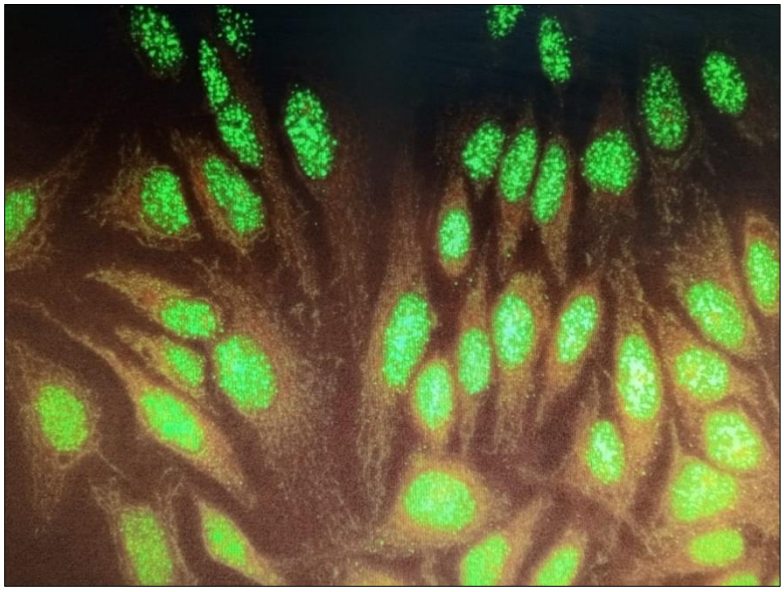

Figure 1: Antimitochondrial antibodies (AMA) found.

The diagnosis of primary biliary cholangitis was confirmed on these criteria: Biological cholestasis and positivity of specific antibodies and treatment with ursodesoxycholic acid (UDCA) was started. Evolution under UDCA was favourable, marked by the resolution of the jaundice and the decrease of liver enzymes. Paris-I score was used one year after the start of UDCA to assess treatment efficacy, and all the response criteria were filled, signalling the treatment success.

Furthermore, during the follow-up period under treatment, the patient's cirrhosis did not advance, with notably no variceal bleeding and no ascitic reccurence, which constitutes another argument pointing towards treatment efficacy.

Regarding the bloody diarrhea, stool coproparasitology was negative and a colonoscopy was performed revealing edematous and erythematous mucosa, with friability, loss of vascular visibility and few shallow ulcers. These lesions were uniform and continuous from the rectum to the promixal part of the descending colon with a clear cut line between the normal and inflammatory mucosa which was already highly evocative of ulcerative colitis (UC) **(Figure 2)**. The transverse colon, right colon, caecum and distal ileal loop were normal. Biopsies were performed.

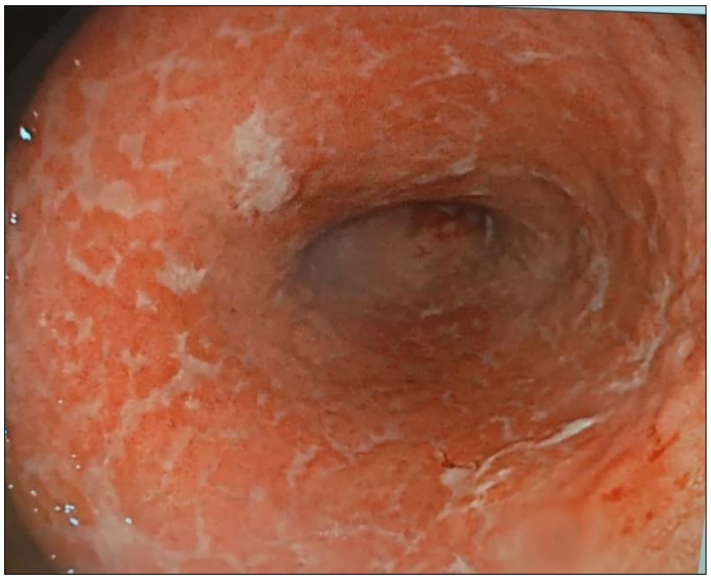

Figure 2: Endoscopic aspect of our patient's colonic mucosa.

Histology found evidence of chronic active colitis with cryptitis, cryptic abscesses, a decrease in mucosecretion, architectural distorsion and basal lymphoplasmocytosis. No granuloma was found.

Based on the aforementioned findings, the diagnosis of non-severe left-sided ulcerative colitis was made and treatment with mesalazine started at the dose of 3g orally and 1g rectal enema every other day. Treatment outcome was positive, with the resolution of diarrhea after a few weeks and the normalization of inflammatory markers after 3 months. Follow-up colonoscopy was performed a year later, finding no lesion in areas previously affected. Biopsies were also negative, showing no signs of active inflammation.

DISCUSSION

Primary biliary cholangitis (PBC) affects individuals across all sexes, races, and ethnicities. Historical data from case-finding studies indicated a median female-to-male ratio of approximately 10:1 [7]. However, more recent studies have revealed that while PBC remains predominantly a disease of females, its prevalence in males is higher than previously reported, with a revised female-to-male ratio ranging from 4:1 to 6:1 [8].

PBC in males is frequently diagnosed later in life and often at a more advanced stage of disease. Furthermore, males with PBC tend to exhibit poorer biochemical responses to ursodeoxycholic acid (UDCA), a cornerstone of PBC management. This suboptimal response is associated with a greater likelihood of progression to cirrhosis, higher rates of liver-related mortality or the need for transplantation, and an elevated risk of hepatocellular carcinoma [9].

A diagnostic of PBC is made in patients with a chronic cholestatic biochemical profile and positive AMA, which are highly specific. Extra-hepatic causes for cholestasis must be ruled out beforehand by imaging. In suspected cases of PBC with negative AMA, antinuclear antibodies (ANA), specifically anti-sp 100 and anti-gp 210 levels should be measured.

Current guidelines highlight that AMA seropositivity in patients with cholestasis is now sufficient to confirm a diagnosis of PBC without the need for liver biopsy. Histological assessment should be reserved for cases where specific antibodies are absent or when overlap syndromes, such as autoimmune hepatitis, are clinically suspected.

Most patients are asymptomatic at diagnosis though the majority will develop symptoms within 20 years. Fatigue is the most reported one, in nearly 80% during the disease course, closely followed by pruritus. Other symptoms include, among others, jaundice, hepatomegaly and abdominal pain. Furthermore, patients with PBC, due to chronic cholestasis, have a significantly higher risk of developing metabolic bone disease, dyslipidaemia, and lipo-soluble vitamin deficiencies [10].

Primary biliary cholangitis (PBC) is frequently associated with a spectrum of other autoimmune conditions, including autoimmune hepatitis, Sjögren's syndrome, rheumatoid arthritis, hypothyroidism, and scleroderma [11]. These comorbidities highlight the systemic nature of autoimmune dysregulation in patients with PBC. Given the significant overlap, routine screening for these associated conditions is recommended in individuals diagnosed with PBC. Early identification and management of coexisting autoimmune disorders can mitigate complications and optimize patient outcomes.

UDCA is the cornerstone for the treatment of PBC. It has helped reshape the prognosis of the disease. The natural history of untreated PBC is marked by a progressive decline in transplant-free survival, with estimated rates of 79%, 59%, and 32% at 5, 10, and 15 years, respectively. However, treatment with UDCA has been shown to significantly improve outcomes, with survival rates increasing to 90%, 78%, and 66% at the same intervals [5].

These findings underscore the critical role of UDCA in altering the disease trajectory of PBC, highlighting its efficacy in delaying liver-related morbidity and the need for transplantation. It should therefore be prescribed as early as possible following diagnosis. Early initiation of treatment maximizes therapeutic benefits, delays disease progression, and improves long-term outcomes.

The association of primary biliary cholangitis (PBC) with ulcerative colitis (UC) is exceptionally rare, with only a limited number of cases described in the medical literature. The largest series reported to date, a retrospective analysis by Liberal *et al*., [12], identified six cases of PBC associated with inflammatory bowel disease, three of which involved patients with UC.

Other reports suggested that PBC in the context of IBD appears to affect a higher proportion of males, with a reduced female-to-male ratio of approximately 2:1. Additionally, these patients are often diagnosed at a younger age compared to those with isolated PBC [13]. In our case, the diagnosis of PBC was established concomitant to that of IBD, contrasting with other reports where PBC seems to develop following the onset of IBD [13].

Beyond conditions that share common pathogenic or pathophysiological mechanisms with inflammatory bowel disease (IBD), hepatic involvement can also emerge as a complication of pharmacologic treatments routinely utilized in IBD management.

Drugs such as thiopurines, methotrexate, biologics, and corticosteroids, frequently used to control IBD, have been implicated in a range of hepatotoxic effects, including hepatocellular injury, cholestasis, and drug-induced liver injury (DILI).

Medications such as thiopurines, methotrexate, biologics, and corticosteroids, widely prescribed to control IBD activity, have been implicated in a spectrum of hepatotoxic effects, including hepatocellular injury, cholestasis, and drug-induced liver injury (DILI). Notably, anti-tumor necrosis factor (anti-TNF) agents have been linked to the onset of autoimmune diseases, including autoimmune liver disorders. Emerging evidence suggests that anti-TNF therapy can trigger immune dysregulation, potentially triggering conditions such as autoimmune hepatitis or other hepatic disorders with autoimmune features [14].

The management of patients with concomitant primary biliary cholangitis (PBC) and ulcerative colitis (UC) presents unique challenges, particularly with regard to bone health. Osteoporosis is a well-documented complication in PBC, and the risk is further compounded in patients with active UC requiring corticosteroid therapy. The combination of chronic cholestatic liver disease, systemic inflammation, and glucocorticoid use significantly increases the likelihood of severe osteoporosis, leading to an elevated risk of fractures.

IBD in patients with PBC is typically mild and can often be effectively managed with aminosalicylates [15]. Unlike PSC, there is no evidence to suggest an increased risk of colorectal cancer in this population. As a result, colonoscopy screening should follow standard guidelines for UC management rather than the more intensive surveillance protocols recommended for patients with PSC.

CONCLUSION

The association of primary biliary cholangitis with inflammatory bowel disease, though rare, presents unique challenges in clinical management. Careful attention to liver function and autoimmune comorbidities is essential, particularly given the risk of complications such as osteoporosis and potential hepatotoxicity from IBD therapies.

Fortunately, IBD in these patients is generally mild and amenable to treatment with aminosalicylates, without the heightened colorectal cancer risk seen in primary sclerosing cholangitis. Standard ulcerative colitis screening protocols can be applied, avoiding unnecessary surveillance burden.

Effective management requires a multidisciplinary approach to address the complexities of concomitant autoimmune diseases, optimize liver and gastrointestinal outcomes, and enhance quality of life for affected patients. Early recognition, regular monitoring, and individualized therapeutic strategies remain the cornerstone of care for this rare association.

BIBLIOGRAPHY

1. Harbord, M., Annese, V., Vavricka, S. R., Allez, M., Barreiro-de Acosta, M., Boberg, K. M., ... & European Crohn's and Colitis Organisation [ECCO]. (2016). The first European evidence-based consensus on extra-intestinal manifestations in inflammatory bowel disease. *Journal of Crohn's and Colitis*, *10*(3), 239-254.
2. Dyson, J. K., Beuers, U., Jones, D. E., Lohse, A. W., & Hudson, M. (2018). Primary sclerosing cholangitis. *The Lancet*, *391*(10139), 2547-2559.

3. Trivella, J., John, B. V., & Levy, C. (2023). Primary biliary cholangitis: Epidemiology, prognosis, and treatment. *Hepatology communications*, *7*(6), e0179.
4. Gershwin, M. E., Ansari, A. A., Mackay, I. R., Nakanuma, Y., Nishio, A., Rowley, M. J., & Coppel, R. L. (2000). Primary biliary cirrhosis: an orchestrated immune response against epithelial cells. *Immunological reviews*, *174*(1), 210-225.
5. Lammers, W. J., van Buuren, H. R., Hirschfield, G. M., Janssen, H. L., Invernizzi, P., Mason, A. L., ... & Global PBC Study Group. (2014). Levels of alkaline phosphatase and bilirubin are surrogate end points of outcomes of patients with primary biliary cirrhosis: an international follow-up study. *Gastroenterology*, *147*(6), 1338-1349.
6. Kumagi, T., & Heathcote, E. (2008). Primary biliary cirrhosis. *Orphanet journal of rare diseases*, *3*, 1-17.
7. Kaplan, M. M., & Gershwin, M. E. (2005). Primary biliary cirrhosis. *New England Journal of Medicine*, *353*(12), 1261-1273.
8. Lu, M., Zhou, Y., Haller, I. V., Romanelli, R. J., VanWormer, J. J., Rodriguez, C. V., ... & Fibrotic Liver Disease Consortium Investigators. (2018). Increasing prevalence of primary biliary cholangitis and reduced mortality with treatment. *Clinical Gastroenterology and Hepatology*, *16*(8), 1342-1350.
9. John, B. V., Aitcheson, G., Schwartz, K. B., Khakoo, N. S., Dahman, B., Deng, Y., ... & Kaplan, D. E. (2021). Male sex is associated with higher rates of liver-related mortality in primary biliary cholangitis and cirrhosis. *Hepatology*, *74*(2), 879-891.
10. Chalifoux, S. L., Konyn, P. G., Choi, G., & Saab, S. (2017). Extrahepatic manifestations of primary biliary cholangitis. *Gut and liver*, *11*(6), 771.
11. Floreani, A., & Cazzagon, N. (2018). PBC and related extrahepatic diseases. *Best Practice & Research Clinical Gastroenterology*, *34*, 49-54.
12. Liberal, R., Gaspar, R., Lopes, S., & Macedo, G. (2020). Primary biliary cholangitis in patients with inflammatory bowel disease. *Clinics and research in hepatology and gastroenterology*, *44*(1), e5-e9.
13. Gizard, E., Ford, A. C., Bronowicki, J. P., & Peyrin-Biroulet, L. (2014). Systematic review: the epidemiology of the hepatobiliary manifestations in patients with inflammatory bowel disease. *Alimentary pharmacology & therapeutics*, *40*(1), 3-15.
14. Efe, C. (2013). Drug induced autoimmune hepatitis and TNF-α blocking agents: is there a real relationship?. *Autoimmunity reviews*, *12*(3), 337-339.
15. Xiao, W. B., & Liu, Y. L. (2003). Primary biliary cirrhosis and ulcerative colitis: a case report and review of literature. *World journal of gastroenterology: WJG*, *9*(4), 878.