Japanese Journal of Gastroenterology and Hepatology

Case Report ISSN: 2435-1210 | Volume 8

Primary Biliary Cholangitis and Type 1 Diabetes in A Male Patient: A Case Report

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Received: 13 Dec 2021
Accepted: 21 Dec 2021
Published: 27 Dec 2021
J Short Name: JJGH

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Citation:

Nkhaili A, PPrimary Biliary Cholangitis and Type 1 Diabetes in A Male Patient: A Case Report. Japanese J Gstro Hepato. 2021; V8(1): 1-4

Keywords:

Primary Biliary Cholangitis; Type 1 Diabetes; Antimitochondrial Antibody; Cirrhosis of the Liver; Pruritus

1. Abstract

Primary Biliary Cholangitis (PBC) isa cholestatic disease of autoimmune origin characterized by the destruction of small to medium size intrahepatic bile ducts due to lymphocytic infiltration. The diagnosis is made by the presence of Anti-Mitochondrial Antibodies (AMAs) specific for the disease. PBC typically affects middle-aged women and is often associated with other autoimmune pathologies which are in decreasing order of frequency: Sjogren's syndrome, autoimmune dysthyroidism, scleroderma, rheumatoid arthritis, lupus and celiac diseasewhich are also more common in women. Few clinical studies evaluate the presentation of PBC in men with concomitant type 1 diabetes due to its low incidence compared to the prevalence of PBC in women.This case report presents that of a male patient with type 1 diabetes, admitted for cholestatic jaundice with pruritus, and in whom the diagnosis of PBC was only made late in the cirrhosis stage.

2. Introduction

Primary biliary cholangitis is a chronic destructive non-supportive cholangitis of the liver representing the primary cause of intrahepatic cholestasis. It is a chronic autoimmune disease mediated by T cells causing inflammation and destruction of the intrahepatic bile ducts leading to the onset of cholestasis and possibly cirrhosis of the liver [1]. PBC preferentially affects women between 35 and 60 years of age but can also occur in men. Its prevalence continues to increase globally at a significant rate [2]. Some patients with PBC are also diagnosed with an associated autoimmune disease. We present a case of stage 2 primary biliary cholangitis in a young man with concomitant autoimmune disease (type 1 diabetes).

3. Observation

Patient AA, 47 years old, followed for 20 years for type 1 diabetes on insulin, reports cholesteric mucocutaneous jaundice made up of dark urine, discolored stools, evolving for 2 months, associated with pruritus and asthenia. The physical examination was normal, except for an evident cutaneous mucous jaundice. Biologically, a cholestasis was found, with GGT at 246 (3.4N) and ALP at 479 (3.7N). Total bilirubin was 49.1 iu / l predominantly direct at 44.3 iu / l; associated with a slight cytolysis ALAT at 50u / l (1.1N), ASAT at 56 (1.2N). Laboratory results were negative for hepatitis A, B and C, Epstein-Barr virus (EBV), cytomegalovirus (CMV). The IgG 4 assay was normal. Antinuclear, anti-mitochondrial, anti sp100, anti-smooth muscle, anti-hepatic-renal microsomal, anticytosol and anti SLA antibodies were negative, only anti gp210 antibodies were positive.

An abdominal ultrasound showed a dysmorphic liver with enlarges segment I and atrophy ofits right posterior sector with no focal lesion,with no dilatation of the intrahepatic and extrahepatic bile ducts.

The diagnosis of PBC was made, the patient was put on UDCA 15mg / kg / day. The fibrosis was estimated at F4 on the fibroscan, the endoscopy revealedsmall varices and no red signs, the patient was thus placed on beta-blocker after ruling out contraindications. As part of the screening for other autoimmune diseases, the serology of celiac disease was normal, the thyroid workup did not reveal any abnormalities. The bone densitometry was normal, the fat-soluble vitamin dosage showed a vitamin D deficiency, thus vitamin D supplementation was started (Figure 1).

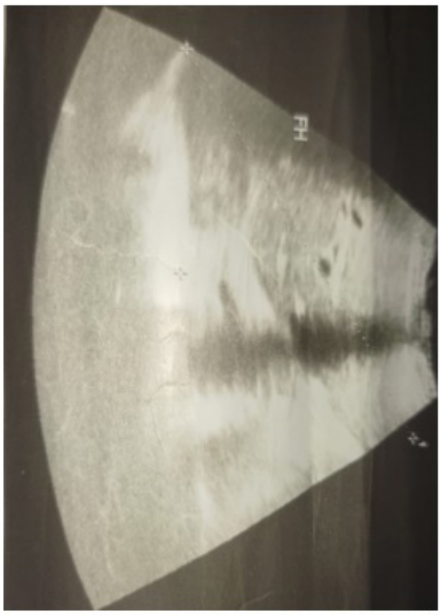

Figure 1: An abdominal ultrasound showed a dysmorphic liver with enlarges segment I and atrophy of its right posterior sector with no focal lesion.

4. Discussion

Primary Biliary Cirrhosis (PBC) is a chronic cholesteric disease of autoimmune origin, the prevalence per million people is 654 for women and 121 for men. It is most often detected in women aged between 30 and 60 years, the sex ratio of this disease would be 9 women for a man [3, 4, 5].

PBC is characterized by small bile duct destruction associated with lymphocyte infiltration. The pathophysiology of PBC is still vague in both women and men, several factors are implicated in the occurrence of PBC such as genetics, sex hormones, microorganisms and the environment. The exact etiology and pathophysiology involving PBC in men and women remains unclear [6]. Usually, autoimmune diseases are mainly mediated by T cells. A study was performed to compare T lymphocytes and antigen presenting cells (APCs) between males and females; The higher incidence of autoimmune diseases seen in women is explained by the higher increase in the number of CD4 T lymphocytes, thus promoting the immune response. There is also the role played by testosterone in reducing the production of immunoglobulins by peripheral blood cells [7].

Due to its pathogenesis, primary Biliary Cirrhosis (PBC) is frequently associated with other autoimmune diseases, such as Sjogren syndrome, dysthyroidism, scleroderma, rheumatoid arthritis, systemic lupus erythematosus, celiac disease and diabetes mellitus [8].

This explains the current trend towards systematic screening. Research is quite limited on how type 1 diabetes plays a role in the occurrence of PBC; however, recent studies suggest that their connection is due to a similar pathway involving protein compounds with hydrodynamic properties of endogenous human retroviruses [9].

Pruritus remains the most often revealing sign of PBC, sometimes associated with asthenia [10]. Patients with PBC can be asymptomatic and the diagnosis is made when liver tests are disturbed, in particular transaminases and cholestasis tests, in other situations, the diagnosis is made during the management of another autoimmune disease or at the stage of cirrhosis in 10% of cases, as is the case in our patient [11].

The detection of Anti-Mitochondria Antibodies (AMA) is the key element for the diagnosis of PBC with a sensitivity of 90% and a specificity of 95%, the anti-mitochondria type M2 antibodies have a specificity of 100% [12]. If the search for anti-mitochondria antibodies is negative, it will be necessary to search for the specific antinuclear antibodies of CBP: the antigp210 and anti-sp100 antibodies, as in the case of our patient. Other immunological abnormalities have been described, in particular the detection of antinuclear antibodies and the increase in immunoglobulins (IGM) [13].

The diagnosis of PBC can be made if at least 2 of the following criteria are present: 1) biochemical signs of cholestasis based primarily on serum PAL activity; 2) presence of AMA; 3) lesions of destructive non-suppurative cholangitis of the interlobular bile ducts [14]. The liver biopsy is not obligatory for the diagnosis of PBC [15], but mainly allows to stage the disease and to show lesions characteristic of this affection on the histology, namely a non-suppurative cholangitis affecting the interlobular bile ducts and septas. The inflammatory infiltrate is mainly composed of lymphocytes and mononuclear cells in direct contact with the basal membrane of cholangiocytes undergoing necrosis. Portal inflammation may appear as epithelioid granulomas [15]. The combination of intrahepatic cholestasis and the positivity of specific antibodies (anti-mitochondria or anti gp-210 or anti-sp100) is sufficient to make the diagnosis of PBC.

In men, PBC is a more aggressive disease than in women. Male sex does not appear to be associated with any sign of disease progression. It is possible that the older age of men at diagnosis simply reflects late diagnosis and therefore more advanced disease [13, 16].

Regarding comorbidity with diabetes, a study was performed to reveal the influence of diabetes mellitus on the natural progression of PBC using non-invasive scores to predict fibrosis. Non-invasive scores were higher in patients with PBC and diabetes mellitus with a fibrosis-4 score of 4.08 compared to a fibrosis-4 score of 3.21 in patients with PBC alone [17] . Patients with PBC and comorbid diabetes mellitus developed cirrhosis at an increased rate (62.2%) compared to 42% in patients with only PBC. Based on these statistics, it can be proposed that effective diabetes control may slow the progression of PBC to cirrhosis [17].

Treatment for primary biliary cholangitis involves preventing disease progression and managing symptoms and complications associated with chronic cholestasis [18]

The only drug approved by the Food and Drug Administration for the treatment of primary biliary cholangitis is ursodeoxycholic acid (UDCA). It is a hydrophilic bile salt, which stabilizes hepatocyte membranes against toxic bile salts and inhibits apoptosis and fibro-

sis. The recommended dose is 13 to 15 mg / kg per day. Patients benefit most when UDCA is started at an earlier stage, which has been shown to delay disease progression and the development of cirrhosis. UDCA also leads to histological improvement [19].

In patients who do not respond to UDCA, obeticholic acid (OBCA) may be given with UDCA. OBCA is a farnesoid X receptor agonist, which helps reduce the levels of ALP, GGT, and transaminases due to its antifibrotic and choleretic properties. However, it does not improve survival or disease symptoms [20]. Treatment also involves relieving pruritus using drugs such as cholestyramine, correcting deficiencies in fat-soluble vitamins due to cholestasis, especially vitamin D which can lead to osteoporosis [13] (Figure 2).

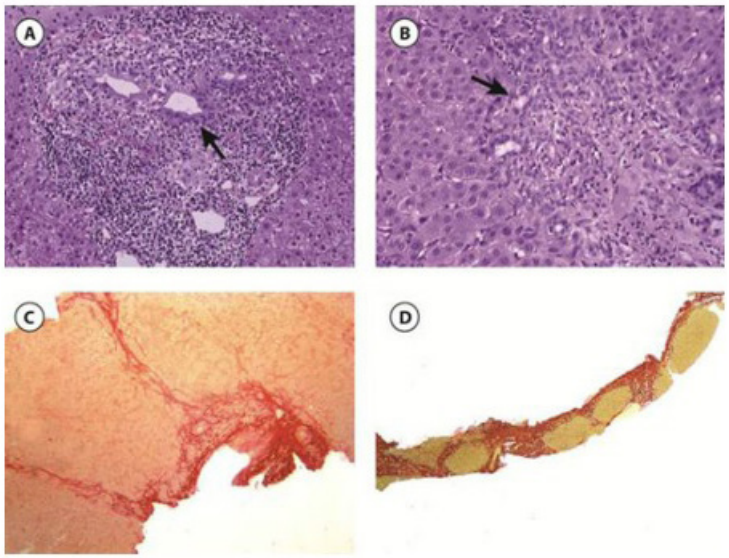

Figure 2: The 4 histological stages of PBC according to the Scheuer classification[13]:

A. Stage 1 with granulomatous destructive cholangitis lesion

B. Stage 2 with periportal ductular reaction

C. Stage 3 with extensive septal fibrosis without cirrhosis.

D. Stage 4 corresponding to cirrhosis

5. Conclusion

The low incidence rates of men with PBC, especially with a diagnosis of type 1 diabetes, have led to poor understanding of the clinical course of the disease, especially in this population group. PBC is frequently associated with other autoimmune diseases, which should be screened for routinely. Conversely, screening for primary biliary cholangitis systematically in patients with other autoimmune diseases is necessary in order to initiate treatment at the early stages, thus improving the prognosis of this pathology.

Reference

1. Maamouri N, Ben Romdhane S, Chouaib S, Ben Hariz F, Belkahla N, Ouerghi H et al., Primary biliary cirrhosis, Retrospective study: Apropos of 43 cases. Rev Med Int. 2008; 03: 328.
2. Smyk DS, Rigopoulou EI, Pares A, Billinis C, Burroughs AK, Muratori L, et al., Gender differences associated with primary biliary cirrhosis. Clin Dev Immunol. 2012; 2012: 610504.
3. McGee EE, Castro FA, Engels EA, Freedman ND, Pfeiffer RM, Nogueira L, et al., Associations between autoimmune conditions and hepatobiliary cancer risk among elderly US adults. Int J Cancer. 2019; 144: 707-17.
4. Arés A, Albillos A, Andrade RJ, Berenguer M, Crespo J, Romero-Gómez M, et al., Primary biliary cholangitis in Spain. Results of a Delphi study of epidemiology, diagnosis, follow-up and treatment. Rev Esp Enferm Dig. 2018; 110: 641-9.
5. Isayama H, Tazuma S, Kokudo N, Tanaka A, Tsuyuguchi T, Nakazawa T, et al., PSC guideline committee Members: Ministry of Health, Labor and Welfare (Japan) Research Project, The Intractable Hepatobiliary Disease Study Group. Clinical guidelines for primary sclerosing cholangitis 2017. J Gastroenterol. 2018; 53: 1006-34.
6. Younossi ZM, Bernstein D, Shiffman ML, Kwo P, Kim WR, Kowdley KV, et al., Diagnosis and management of primary biliary cholangitis. Am J Gastroenterol. 2019; 114: 48–63.
7. Weinstein Y, Ran S, Segal S. Sex-associated differences in the regulation of immune responses controlled by the MHC of the mouse. Immunol. 1984; 132: 656–61.
8. Mahmoudi N, Mustapha B, Serghini, Béjaoui, Fekih S, Matri L, et al., Autoimmune diseases associated with primary biliary cirrhosis The Journal of Internal Medicine. 2014; 35: 160.
9. Levet S, Charvet B, Bertin A, Deschaumes A, Perron H, Hober D. Endogenous human retroviruses and type 1 diabetes. Representative Curr Diab. 2019; 19: 141.
10. European Association for the Study of the Liver. Electronic address, European Association for the Study of the L. EASL Clinical Practice Guidelines: The diagnosis and management of patients with primary biliary cholangitis. J Hepatol 2017; 67: 145-72.
11. Poupon R. Primary biliary cirrhosis; EM consults. http://www.em-consulte.com/article/260239. Accessed 20th February 2014.
12. Leff JA, Ready JB, Repetto C, Goff JS, Schwarz MI. Coexistence of primary biliary cirrhosis and sarcoidosis. The Western Journal of Medicine. 1990; 153: 439–41.
13. Sara Lemoinne. Primary biliary cholangitis; Department of Hepatology, Reference Center for Inflammatory Biliary Diseases, Hôpital Saint-Antoine, Paris, Postu2018.
14. EASL EAftSotL. EASL Clinical Practice Guidelines: management of cholestatic liver diseases. J Hepatol. 2009; 51: 237-67.
15. Lindor KD, Gershwin ME, Poupon R, Kaplan M, et al., Primary biliary cirrhosis. Hepatology (Baltimore, Md). 2009; 50: 291–308.

16. Muratori P, Granito A, Pappas G, Muratori L, Lenzi M, Bianchi FB. Clinical and serological profile of primary biliary cirrhosis in men. QJM My J Assoc Physicians. 2008; 101: 505-6.

17. Liu X, Xu H, Zhan M, Niu J. Potential effects of diabetes mellitus on hepatic fibrosis in patients with primary biliary cholangitis. Med Sci Monit. 2019; 25: 6174-80.

18. Khanna A, Jopson L, Howel D, Bryant A, Blamire A, Newton JL, et al., Rituximab is ineffective for the treatment of fatigue in primary biliary cholangitis: a phase 2 randomized controlled trial. Hepatology. 2019; 70: 1646-57.

19. Carbone M, Nardi A, Flack S, Carpino G, Varvaropoulou N, Gavrila C, et al., Italian PBC Study Group and UK-PBC Consortium. Pretreatment prediction of the response to ursodeoxycholic acid in primary biliary cholangitis: development and validation of the UDCA response score. Lancet Gastroenterol Hepatol. 2018; 3: 626-63.

20. Vetter M, Kremer AE. Primary biliary cholangitis established and new therapies. Internist (Berl). 2018; 59: 544-50.