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Case Report

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Primary Biliary Cholangitis Related Hepatocellular Carcinoma on the Background of Decompensated Liver Cirrhosis: A Case Report and Review of Literature

Ahmed Lutful Moben[1], Rokshana Begum[2], Sheikh Mohammad Noor E Alam[3], Md. Abdur Rahim[4], Bishnu Pada Dey[5], Sheikh Mohammad Fazle Akbar[6] and Mamun Al Mahtab[7*]

[1]*Department of Hepatology, Kurmitola General Hospital, Dhaka, Bangladesh*

[2]*Department of Hepatology, Shaheed Suhrawardy Medical College, Dhaka, Bangladesh*

[3]*Department of Hepatology, Bangladesh Medical University, Dhaka, Bangladesh*

[4]*Department of Hepatology, International Medical College, Gazipur, Bangladesh*

[5]*Department of Pathology, Bangladesh Medical University, Dhaka, Bangladesh*

[6]*Ehime University, Ehime, Japan, Oita University, Oita, Japan and Miyakawa Memorial Research Foundation, Tokyo, Japan*

[7]*Interventional Hepatology Division, Bangladesh Medical University, Dhaka, Bangladesh*

[*]Corresponding author

Mamun Al Mahtab, Head, Interventional Hepatology Division, Bangladesh Medical University, Dhaka, Bangladesh.

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ABSTRACT

Primary biliary cholangitis is a relatively less common chronic autoimmune liver disease more commonly seen in females and has the potential of progression to liver cirrhosis and hepatocellular carcinoma. More common in the West, it is increasingly being recognized in the Asian Pacific region and there is a gradual shift of gender predominance from females in the recent decades. There are significant advances in the pharmologic management of the disease in recent times. Diagnosis of primary biliary cholangitis therefore has to be considered in appropriate cases, as early diagnosis can ensure liver transplant-free survival.

Keywords: Primary Biliary Cholangitis, Liver Cirrhosis, Hepatocellular Carcinoma

Introduction

Primary biliary cirrhosis, now renamed as primary biliary cholangitis (PBC) is a slowly progressive chronic, cholestatic, autoimmune liver disease that can lead to liver cirrhosis [1]. The entity was first described by Addison and Gull in 1851 and the terminology primary biliary cirrhosis adopted in 1949, although not all patients with PBC go on to develop liver cirrhosis [2]. The incidence of PBC is 1.76/100,000 population and prevalence 14.6/100,000 population [3]. Compared to the Asia-Pacific region, the incidence and prevalence of PBC is higher in Europe and in North America, where it has however plateaued after 2000. In contrast, the incidence and prevalence are on the rise in the Asia-Pacific region [1,3]. PBC is more often encountered in women than in men, peaking between 60-79 years of age [3]. Over the last two decades, there has been change in gender distribution of PBC, with female to male ration changing from 9:1 to 4:1 [4]. Prognosis is poorer in men who usually present with advanced disease and have higher incidence of hepatocellular carcinoma (HCC) [5]. Improved survival in PBC has been attributed to early diagnosis and long-term use of ursodeoxycholic acid (UDCA) [6].

Case Report

The 53-year-old, male patient presented in critically ill condition. He had deep jaundice and ascites, with recent history of undergoing treatment with undefined herbal medicines by a non-qualified herbal medical practitioner. There was no family history of jaundice or liver disease.

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His hemoglobin was 9.0 gm/dL, total white blood cell count 6000/cumm, platelet count 130,000/cumm, serum bilirubin 17.5 mg/dL (indirect serum bilirubin 4.6 mg/dL), serum alanine aminotransferase (ALT) 230 U/L, aspartate aminotransferase (AST) 380 U/L, gamma -glutamyl transferase (ϒ-GT) 296 U/L, serum alkaline phosphatase (ALP) 559 U/L, serum albumin 2.0 gm/dL, international normalized ratio (INR) 1.52, α-feto protein (AFP) 2 ngm/mL, serum creatinine 0.78 mg/dL, serum ceruloplasmin 210 mg/dL, urinary copper 45 µgm per 24 hours. No Kayser-Fleischer (KF) ring was present on slit lamp ocular examination.

He tested negative for hepatitis A (anti-HAV IgM negative), hepatitis E (anti-HEV negative), hepatitis B (HBsAg and anti HBc IgM negative) and hepatitis C viruses (anti-HCV negative). He had no history of alcoholism. He also tested negative for anti-nuclear (ANA), anti-smooth muscle (ASMA), anti-liver kidney microsomal-1 (anti-LKM 1) and anti-mitochondrial (AMA) antibodies.

Magnetic resonance cholangiopancreatograpy (MRCP) and abdominal computed tomography (CT) showed mild hepato-splenomegaly, contracted gall bladder and normal main pancreatic duct and normal intra- and extra-hepatic biliary channels and huge ascites. There was a 5.2 x 3.9 cm space occupying lesion in his left hepatic lobe. On fibroscan, his continued attenuation parameter (CAP) was 185 i.e. less than 4% hepatic steatosis.

Endoscopy of upper gastrointestinal tract revealed features of severe portal hypertensive gastropathy and antral erosive gastritis.

Diagnostic aspiration of ascitic fluid showed light yellow coloured fluid containing red blood cells (RBC) 10-15/HFF, total white blood cell (WBC) counts 380 cells/dL with 20% lymphocytes, albumin 0.5 gm/dL, adenosine deaminase (ADA) 13 U/L and no malignant cells.

A 2.0 x 0.2 cm linear piece of liver tissue was obtained at percutaneous liver biopsy with Tru-Cut biopsy needle (Becton Dickenson and Co., Franklin Lakes, NJ, USA). Microscopic examination revealed diffuse distortion of the lobular architecture with nodule formation and marked cholestasis. The regenerative hepatocyte nodules were separated by bridging fibrous septa. The nodules and septa showed infiltration of brown/black pigment containing liver parenchymal cells. Marked ductular proliferation and infiltration of pigment containing liver parenchymal cells were also seen. Diffuse disruption in architecture and bridging fibrous septa with irregular, jigsaw puzzle shaped parenchymal nodules of regenerating hepatocytes with peripheral pale halo i.e. peripheral septal oedema, loose packed fibrous tissue and chronic cholestasis of periseptal hepatocytes leading to feathery degeneration were present (Figure 1). As per Laennec scoring system, fibrosis was 4B i.e. moderate cirrhosis with at least 2 broad septa. No malignancy was seen. Diagnosis was PBC related liver cirrhosis was thus attained.

We also did fine needle aspiration from the hepatic space occupying lesion (SOL) for cytology, which revealed atypical epithelial cells in tiny aggregates and singly. The cells had hyperchromatic nuclei and eosinophilic nucleoli. They were moderately pleomorphic. Occasionally large cells were present. The background showed inflammatory cells and blood. Findings were suggestive of moderately differentiated (grade 2) HCC.

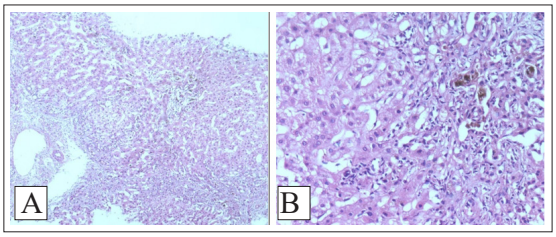

Figure 1: A.H&E100x, B.H&E200x: Microscopic examination of liver biopsy specimen showing diffuse distortion of lobular architecture with nodule formation and marked cholestasis. The regenerative hepatocyte nodules are separated by bridging fibrous septa. The nodules and septa show infiltration of brownish bill pigment containing liver parenchymal cells.

So, our final diagnosis was primary HCC on the background of PBC related decompensated liver cirrhosis with drug induced liver injury (DILI).

Discussion

Pathogenesis of PBC involves both genetic factors as well as environmental triggers. Immune dysregulation of T cells, B cells and other lymphocytes and biliary epithelial cells (BEC) are important in the pathogenesis. Loss of tolerance to the autoantigen PDC-E2 is key to PBC development, as anti-mitochondrial antibody primarily targets lipoyl domain of PDC-E2. Besides, the presence of granuloma implies role of innate immunity in the pathogenesis of PBC [7]. There is increase in innate immune cells like natural killer cells and myeloid derived suppressor cells in PBC [8-13].

Genetic variations in HLA and non-HLA loci are associated with susceptibility to developing PBC. These include HLA-DRB6, HLA-DQA2 and HLA-DRB1 [14]. Non-HLA alleles that are associated with risk of PBC development vary geographically and include IL-12A and IL-12 RB2 in North America, CCL20 and IL-12B in Europe, TNFSF15, POU2AF1 and PRKCB in Japan, IL-21, IL-21R, STAT4, CD28/CTLA4/ICOS, CD58, ARID3A and IL-16 in China and ID2, TMEM163, PRDM1, CCR6, ETS1 and FAM177A1 in Europe and China [15-20]. Arid 3a is a PBC risk gene, which promotes cholestasis [13].

Oestrogen stimulation of the immune system has been postulated for the female predominance of PBC. Oestrogen receptors are expressed in T cells, B cells, innate immune cell and also cholangiocytes in PBC [21,22]. Besides, FOXP3 locus on X-chromosome, which is important in regulatory T cell development and function, may also contribute to the gender inequality of PBC [23].

Several environmental factors like cigarette smoking, nail polish, hair dye, urinary tract infection and E. coli have been implicated to increase the risk of PBC development [24-30]. In elderly, unhygienic living conditions may trigger PBC [30]. Alterations of gut microbiota have also been implicated. Increase in Enterobacteriaceae, Pseudomonas, Veillonella and

Suterella and decrease in Oscillospiracae and Faecalibacterium are all responsible [31-33]. Altered gut microbiota alters serum and fecal bile acid profiles with decreased conversion of primary bile acids to secondary bile acids [34, 35].

Diagnosis of PBC requires fulfillment of two out of the three criteria namely, biochemical evidence of chronic cholestasis, positive anti-mitochondrial antibody (AMA) and histological features compatible with PBC [36,37]. Diagnosis can be confirmed without liver biopsy if AMA is positive and serum ALP is raised. Positive PBC-specific antinuclear antibody (ANA) namely anti-gp210 or anti-sp100 are as good as positive AMA for the diagnosis of PBC. Liver biopsy is needed to confirm the diagnosis in AMA-negative PBC and in AMA-positive PBC with normal serum ALP. ϒ-GT may also be raised and persistently elevated ϒ-GT may be the earliest biochemical change in PBC [38]. Raised serum bilirubin in PBC results from ductopenia, hepatocellular cholestasis and biliary ductular reaction, while SGPT and SGOT may become elevated due to lobular and periportal inflammation and necrosis. Hypercholesterolemia and raised IgM are useful biochemical markers for PBC diagnosis. Ultrasonography of hepato-biliary system and/or magnetic resonance cholangiopancreatography (MRCP) is important to rule out biliary obstruction on histopathology, the characteristic lesion in PBC is chronic non-suppurative destructive cholangitis leading to ductopenia and adjacent epithelioid cell granulomas [7].

PBC patients typically present with fatigue, which is seen in more than 50% cases and results from sleep disturbance, autonomic dysfunction and depression [38,39]. Pruritus is also common, seen in 20-80% patients, resulting from cholestasis [40]. Hypercholesterolemia is present in 80%, while there is more than 3-fold increased risk of PBC patients developing osteoporosis due to decreased bone formation [41,42]. The risk of developing HCC is 3.4-3.6/1000 patient years with male gender, alcohol consumption, overweight, diabetes mellitus, advanced disease and cirrhosis being the risk factors [43-46].

UDCA remains the standard of care for PBC to date. In PBC, 10-year liver transplant-free survival is 79.7% in patients taking UDCA against 60.7%, who do not take the medicine [47]. Both Asian Pacific Association for the Liver (APASL) and American Association for the Study of Liver Diseases (AASLD) recommend UDCA (13-15 mg/kg body weight/day) for PBC management [36,37]. Obeticholic acid (OCA), which is an agonist of intranuclear bile acid farnesoid X receptor (FXR), has been conditionally approved by the United States Food and Drug Administration (USFDA) as a second -line therapy for PBC [7]. OCA is associated with longer liver transplant-free survival in PBC; however, it's use has been subsequently restricted by USFDA in PBC patients with decompensated liver cirrhosis or with compensated liver cirrhosis with portal hypertension due to safety concerns. The European Medicines Agency has recommended revoking the conditional approval of OCA in PBC in 2024 [48].

Several peroxisome proliferator-activated receptor (PPAR) agonists have been evaluated for PBC management. Bezafibrate, a PPR-α, β and δ agonist, has shown to improve liver biochemistry and stiffness and in combination with UDCA, reduce liver transplantation and liver related deaths in PBC [49,50]. However, it's use in PBC is discouraged due to safety concerns like hepatotoxicity, renal toxicity and rhabdomyolysis [51]. Elafibranor, a PPR-α/δ agonist, in combination with UDCA, has been found to be safe and reduces serum ALP in PBC patients who show incomplete response to UDCA alone [52]. Seladelpar is a PPR-α agonist, which has also shown to be effective in serum ALP normalization with no safety concerns [53,54]. The fourth drug of this family, saroglitazar, a PPR-α and ϒ agonist, is also showing promising results in normalizing serum ALP in combination with UDCA [55]. Although PBC is an autoimmune disease, the use of steroids like budesonide has not been found to be beneficial [56].

It is important to identify patients who are at risk of disease progression. Young patients below 45 years of age with advanced fibrosis, those positive for anti-gp210 and anti-sp100 autoantibodies, high LSM values and high splenic stiffness values are the ones having poorer prognosis in PBC [57,58].

We reviewed the literature for reports of PBC from Bangladesh. We found three previous reports. The first case of PBC was reported from Bangladesh by our group in 2010 [59]. The patient was an elderly female presenting with complaints of itching for 2 years. She had raised serum ALP and tested positive for AMA. The second patient, who was AMA-negative middle-aged female, had elevated serum ALP. She had complaints of fatigue and the diagnosis was confirmed at liver biopsy. The case was reported by our group in 2015 [60]. The third case was a 52-year-old male who had pruritus. He was AMA positive with elevated serum ALP [61].

Conclusion

This is fourth case report of PBC from Bangladesh. Important learning points from this study is that the patient was a decompensated cirrhotic with HCC, initially thought to be cryptogeic. Since the gender distribution of PBC is shifting and the disease is becoming more prevalent in the Asia-Pacific region, it is therefore important to consider PBC as a probable diagnosis in relevant patients.

References

1. Lleo A, Wang GQ, Gershwin ME, Hirschfield GM. Primary biliary cholangitis. Lancet 2020. 396: 1915-1926.
2. Addison T, Gull W. On a certain affection of the skinvitiligoidea-á-plana â-tuberosa. Guys Hosp Rept. 1851. 7: 265-277.
3. Lv T, Chen S, Li M, Zhang D, Kong Y, et al. regional variation and temporal trend of primary biliary cholangitis epidemiology: a systematic review and meta-analysis. J Gastroenterol Hepatol. 2021. 36: 1423-1434.
4. Colapietro F, Bertazzoni A, Lleo A. Contemporary epidemiology of primary biliary cholangitis. Clin Liver Dis. 2022. 26: 555-570.
5. Lindor KD, Bowlus CL, Boyer J, Levy C, Mayo M. Primary biliary cholangitis: 2018 practice guidance from the American Association for the Study of Liver Diseases. Hepatology. 2019. 69: 394-419.
6. Murillo Perez CF, Goet JC, Lammers WJ, Gulamhusein A, van Buuren HR, et al. Milder disease stage in patients with primary biliary cholangitis over a 44-year period: a changing natural history. Hepatology. 2018. 67: 1920-1930.

7. Tanaka A, Ma X, Takahashi A, Vierling JM. Primary biliary cholangitis. Lancet. 2024. 404: 1053-1066.
8. Chuang YH, Lian ZX, Tsuneyama K, Chiang BL, Ansari AA, et al. Increased killing activity and decreased cytokine production in NK cells in patients with primary biliary cirrhosis. Journal of autoimmunity. 2006. 26: 232-40.
9. Shimoda S, Harada K, Niiro H, Shirabe K, Taketomi A, et al. Interaction between Toll-like receptors and natural killer cells in the destruction of bile ducts in primary biliary cirrhosis. Hepatology 2011. 53: 1270-1281.
10. Shimoda S, Hisamoto S, Harada K, Iwasaka S, Chong Y, et al. Natural killer cells regulate T cell immune responses in primary biliary cirrhosis. Hepatology. 2015. 62: 1817-1827.
11. Zhang H, Lian M, Zhang J, Bian Z, Tang R, et al. A functional characteristic of cysteine-rich protein 61: modulation of myeloid-derived suppressor cells in liver inflammation. Hepatology 2018. 67: 232-246.
12. Chen R, Huang B, Lian M, Wei Y, Miao Q, et al. A+ T rich interaction domain protein 3a (Arid3a) impairs Mertk-mediated efferocytosis in cholestasis. Journal of Hepatology2023. 79: 1478-1490.
13. Cho M, Dho SH, Shin S, Lee Y, Kim Y, et al. Caspase-10 affects the pathogenesis of primary biliary cholangitis by regulating inflammatory cell death. Journal of Autoimmunity. 2022. 133: 102940.
14. Hitomi Y, Nakamura M. The genetics of primary biliary cholangitis: a GWAS and post-GWAS update. Genes. 2023.14: 405.
15. Cordell HJ, Han Y, Mells GF, Li Y, Hirschfield GM, et al. international genome-wide meta-analysis identifies new primary biliary cirrhosis risk loci and targetable pathogenic pathways. Nature communications. Nat Commun. 2015. 6: 8019.
16. Hirschfield GM, Liu X, Xu C, Lu Y, Xie G. Primary biliary cirrhosis associated with HLA, IL12A, and IL12RB2 variants. N Engl J Med. 2009. 360: 2544-55.
17. Kawashima M, Hitomi Y, Aiba Y, Nishida N, Kojima K. Genome-wide association studies identify PRKCB as a novel genetic susceptibility locus for primary biliary cholangitis in the Japanese population. Hum Mol Genet. 2017. 26: 650-659.
18. Nakamura M, Nishida N, Kawashima M, Aiba Y, Tanaka A. Genome-wide association study identifies TNFSF15 and POU2AF1 as susceptibility loci for primary biliary cirrhosis in the Japanese population. Am J Hum Genet. 2012. 91: 721-728.
19. Qiu F, Tang R, Zuo X, Shi X, Wei Y. A genome-wide association study identifies six novel risk loci for primary biliary cholangitis. Nat Commun. 2017. 8: 14828.
20. Cordell HJ, Fryett JJ, Ueno K, Darlay R, Aiba Y. An international genome-wide meta-analysis of primary biliary cholangitis: novel risk loci and candidate drugs. J Hepatol. 2021. 75: 572-581.
21. Gerussi A, Cristoferi L, Carbone M, Asselta R, Invernizzi P. The immunobiology of female predominance in primary biliary cholangitis. J Autoimmun. 2018. 95: 124-132.
22. Alvaro D, Invernizzi P, Onori P, Franchitto A, De Santis. Estrogen receptors in cholangiocytes and the progression of primary biliary cirrhosis. J Hepatol. 2004. 41: 905-912.
23. Asselta R, Paraboschi EM, Gerussi A, Cordell HJ, Mells GF. X chromosome contribution to the genetic architecture of primary biliary cholangitis. Gastroenterology 2021. 160: 2483-2495.
24. Howel D, Fischbacher CM, Bhopal RS, Gray J, Metcalf JV. An exploratory population-based case-control study of primary biliary cirrhosis. Hepatology. 2000. 31: 1055-1060.
25. Parikh-Patel A, Gold EB, Worman H, Krivy KE, Gershwin ME. Risk factors for primary biliary cirrhosis in a cohort of patients from the United States. Hepatology. 2001. 33: 16-21.
26. Gershwin ME, Selmi C, Worman HJ, Gold EB, Watnik M. Risk factors and comorbidities in primary biliary cirrhosis: a controlled interview-based study of 1032 patients. Hepatology 2005. 42: 1194-1202.
27. Prince MI, Ducker SJ, James OF. Case-control studies of risk factors for primary biliary cirrhosis in two United Kingdom populations. Gut. 2010. 59: 508-512.
28. Corpechot C, Chrétien Y, Chazouillères O. Demographic, lifestyle, medical and familial factors associated with primary biliary cirrhosis. J Hepatol. 2010. 53: 162-169.
29. Kim KA, Kim YS, Park SH, Chung WJ, Choi DH. Environmental risk factors and comorbidities of primary biliary cholangitis in Korea: a case-control study. Korean J Intern Med. 2021. 36: 313-321.
30. Matsumoto K, Ohfuji S, Abe M, Komori A, Takahashi A. Environmental factors, medical and family history, and comorbidities associated with primary biliary cholangitis in Japan: a multicenter case-control study. J Gastroenterol. 2022. 57: 19-29.
31. Gulamhusein AF, Hirschfield GM. Primary biliary cholangitis: pathogenesis and therapeutic opportunities. Nat Rev Gastroenterol Hepatol. 2020. 17: 93-110.
32. Tang R, Wei Y, Li Y, Chen W, Chen H. Gut microbial profile is altered in primary biliary cholangitis and partially restored after UDCA therapy. Gut. 2018. 67: 534-541.
33. Zhou YJ, Ying GX, Dong SL, Xiang B, Jin QF. Gut microbial profile of treatment-naive patients with primary biliary cholangitis. Front Immunol. 2023. 14: 1126117.
34. Chen W, Wei Y, Xiong A, Li Y, Guan H. Comprehensive analysis of serum and fecal bile acid profiles and interaction with gut microbiota in primary biliary cholangitis. Clin Rev Allergy Immunol. 2020. 58: 2-38.
35. Martinez-Gili L, Pechlivanis A, McDonald JAK, Begum S, Badrock J. Bacterial and metabolic phenotypes associated with inadequate response to ursodeoxycholic acid treatment in primary biliary cholangitis. Gut Microbes. 2023. 15: 2208501.
36. Hirschfield GM, Beuers U, Corpechot C, Invernizzi P, Jones D. EASL Clinical Practice Guidelines: the diagnosis and management of patients with primary biliary cholangitis. J Hepatol. 2017. 67: 145-72.
37. You H, Ma X, Efe C, Invernizzi P, Jones D. APASL clinical practice guidance: the diagnosis and management of patients with primary biliary cholangitis. Hepatol Int. 2022. 16: 1-23.
38. Terziroli Beretta-Piccoli B, Stirnimann G, Mertens J, Semela D, Zen Y. Primary biliary cholangitis with normal alkaline phosphatase: a neglected clinical entity challenging current guidelines. J Autoimmun. 2021. 116: 102578.
39. Lynch EN, Campani C, Innocenti T, Dragoni G, Biagini MR. Understanding fatigue in primary biliary cholangitis: from pathophysiology to treatment perspectives. World J Hepatol. 2022. 14: 1111-1119.

40. Beuers U, Kremer AE, Bolier R, Elferink RP. Pruritus in cholestasis: facts and fiction. Hepatology. 2014. 60: 399-407.
41. Sorokin A, Brown JL, Thompson PD. Primary biliary cirrhosis, hyperlipidemia, and atherosclerotic risk: a systematic review. Atherosclerosis. 2007. 194: 293-99.
42. Liao CY, Chung CH, Chu P, Wei KY, Feng TM. Increased risk of osteoporosis in patients with primary biliary cirrhosis. PLoS One. 2018. 13.
43. Cavazza A, Caballería L, Floreani A, Farinati F, Bruguera M. Incidence, risk factors, and survival of hepatocellular carcinoma in primary biliary cirrhosis: comparative analysis from two centers. Hepatology. 2009. 50: 1162-1168.
44. Harada K, Hirohara J, Ueno Y, Nakano T, Kakuda Y. Incidence of and risk factors for hepatocellular carcinoma in primary biliary cirrhosis: national data from Japan. Hepatology. 2013. 57: 1942-1949.
45. Trivedi PJ, Lammers WJ, van Buuren HR, Parés A, Floreani A. Stratification of hepatocellular carcinoma risk in primary biliary cirrhosis: a multicentre international study. Gut. 2016. 65: 321-329.
46. Rong G, Wang H, Bowlus CL, Wang C, Lu Y. Incidence and risk factors for hepatocellular carcinoma in primary biliary cirrhosis. Clin Rev Allergy Immunol. 2015. 48: 132-141.
47. Roberts SB, Ismail M, Kanagalingam G, Mason AL, Swain MG. Real-world effectiveness of obeticholic acid in patients with primary biliary cholangitis. Hepatol Commun. 2020. 4: 1332-1345.
48. Jones DEJ, Beuers U, Bonder A, Carbone M, Culver E. Primary biliary cholangitis drug evaluation and regulatory approval: where do we go from here? Hepatology. 2024.
49. Corpechot C, Chazouillères O, Rousseau A, Le Gruyer A, Habersetzer F. A placebo-controlled trial of bezafibrate in primary biliary cholangitis. N Engl J Med. 2018. 378: 2171-2181.
50. Tanaka A, Hirohara J, Nakano T, Matsumoto K, Chazouillères O. Association of bezafibrate with transplant-free survival in patients with primary biliary cholangitis. J Hepatol. 2021. 75: 565-571.
51. Hosonuma K, Sato K, Yamazaki Y, Yanagisawa M, Hashizume H. A prospective randomized controlled study of long-term combination therapy using ursodeoxycholic acid and bezafibrate in patients with primary biliary cirrhosis and dyslipidemia. Am J Gastroenterol. 2015. 110: 423-431.
52. Kowdley KV, Bowlus CL, Levy C, Akarca U, Alvares-Da-Silva MR. Efficacy and safety of elafibranor in primary biliary cholangitis. N Engl J Med. 2024. 390: 795-805.
53. Hirschfield GM, Bowlus CL, Mayo MJ, Kremer AE, Vierling JM. A phase 3 trial of seladelpar in primary biliary cholangitis. N Engl J Med. 2024. 390: 783-794.
54. Mayo MJ, Vierling JM, Bowlus CL, Levy C, Hirschfield GM. Open-label, clinical trial extension: two-year safety and efficacy results of seladelpar in patients with primary biliary cholangitis. Aliment Pharmacol Ther. 2024. 59: 186-200.
55. Vuppalanchi R, Caldwell SH, Pyrsopoulos N, DeLemos AS, Rossi S. Proof-of-concept study to evaluate the safety and efficacy of saroglitazar in patients with primary biliary cholangitis. J Hepatol. 2022. 76: 75-85.
56. Hirschfield GM, Beuers U, Kupcinskas L, Ott P, Bergquist A. A placebo-controlled randomised trial of budesonide for PBC following an insufficient response to UDCA. J Hepatol. 2021. 74: 321-329.
57. European Association for Study of Liver. EASL-ALEH Clinical Practice Guidelines: non-invasive tests for evaluation of liver disease severity and prognosis. J Hepatol. 2015. 63: 237-264.
58. Matsumoto K, Hirohara J, Takeuchi A, Miura R, Asaoka Y. Determinants of the effectiveness of bezafibrate combined with ursodeoxycholic acid in patients with primary biliary cholangitis. Hepatol Res. 2023. 53: 989-997.
59. Mahtab MA, Uddin K, Rahman S, Khan M, Kamal M. A case of primary biliary cirrhosis: first report from Bangladesh. Clinical & Experimental Medical Journal. 2010. 4: 187-191.
60. Begum R, Mahtab MA, Al Mamun A, Kumar Saha B, Shahadat Hossain SM. A Case of Antimitochondrial Antibody Negative Primary Biliary Cirrhosis from Bangladesh and Review of Literature. Euroasian J Hepatogastroenterol. 2015. 5: 122-126.
61. Afroze S R, Rahim M A, Hasan M M, Afroz F, Haque H F. Primary Biliary Cirrhosis in a Male: A Case Report and Review of Literature. Journal of Medicine. 2015. 16: 128-131.