# Ulcerative colitis with overlap syndrome of autoimmune hepatitis, primary biliary cholangitis, and primary sclerosing cholangitis: a case report

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Introduction. We discuss a rare case of autoimmune hepatitis- primary biliary cholangitis/ primary sclerosing cholangitis triple overlap syndrome accompanying ulcerative colitis. The patient was a 55-year-old male who was diagnosed with ulcerative colitis 6 years ago. During the follow-up, abnormal liver function was found and overlap syndrome was diagnosed, and glucocorticoid and ursodeoxycholic acid (UDCA) were given combined treatment. In view of the difficulties encountered in the treatment of this case, it is worth discussing together to further improve the level of clinical treatment.

Keywords. Ulcerative colitis; Primary sclerosing cholangitis; Autoimmune hepatitis; Primary biliary cholangitis; Overlap syndrome

## 1. INTRODUCTION

Ulcerative colitis ( UC) is a chronic colonic and proctitis disease related to immune abnormalities, which can be accompanied by multiple other diseases [1]. The relationship between UC and autoimmune hepatopathy overlap syndrome (AHOS) has been reported [2], and autoimmune hepatitis-primary sclerosing cholangitis (AIH-PSC) overlap syndrome is the most common AHOS [3]. Autoimmune hepatitis-primary biliary cholangitis/primary sclerosing cholangitis (AIH-PBC-PSC) triple overlap syndrome is rare. We discuss a case of AIH-PBC-PSC triple overlap syndrome accompanying UC.

## 2. Case Report

A 55-year-old man reported defecating 3 or 4 times a day since June 2016 for unknown reasons, accompanied by mucus and purulent blood. Colonoscopy revealed UC (total colonic type, severe active stage); he was prescribed oral anti-inflammatory

treatment with mesalazine 4 g/day. Initially, the patient's liver function was normal.

However, liver chemical examination results in June 2018 detected abnormal liver function ( Table 1). Despite discontinuing mesalazine and starting hepatoprotective treatment, liver function showed no improvement after 3 years. Upper abdominal magnetic resonance plain scan and retrograde cholangiopancreatography revealed cholecystitis with polyps, gallbladder adenomyosis, mild intrahepatic bile duct dilatation and thickening, intrahepatic cholangitis, mild oedema of the liver tissue in the left inner lobe, splenomegaly, and colonic changes combined with a history of inflammatory bowel disease. Serum immunoglobulin G, immunoglobulin M, and

serum γ-globulin levels were significantly higher than normal. Anti-mitochondrial

antibody ( AMA), antinuclear antibody (ANA), anti-smooth muscle antibody (SMA), and anti-hepatorenal microsomal type I antibody (LKM- 1) were normal. A percutaneous liver biopsy performed in August 2021 revealed a histological autoimmune hepatitis (AIH) score of 5, including interface hepatitis, plasma cell, and Rosette scores of 3, 1, and 1, respectively. Fibrous obstructive cholangitis and typical concentric round collagen deposition (onion skin) were observed around the bile duct in some portal area lobules, which could aid AIH-PBC-PSC overlap syndrome diagnosis (G3S3/ early cirrhosis) (Figure 1). Following treatment with ursodeoxycholic acid (UDCA) and prednisolone, liver function improved significantly (Table 1). Currently, the patient is undergoing glucocorticoid and UDCA treatment.

## 3. DISCUSSION

Some scholars recommend the combined administration of prednisone and UDCA to treat AHOS [3]. Second-line immunosuppressants, such as cyclosporine A and tacrolimus, can induce biochemical remission in 50% of patients who do not respond to initial immunosuppression [4].

The risk of atypical colorectal hyperplasia and colorectal cancer in patients with UC increases with PSC, and UC increases the incidence of cholangiocarcinoma in patients with PSC [5]. Annual colonoscopy and histological examination are recommended for patients with PSC to evaluate colitis. Additionally, patients should undergo imaging examination and CA 19-9 examination every 6−12 months to screen for hepatobiliary malignancies [6]. Abdominal ultrasonography and alpha fetoprotein level measurements should be performed every 6 months in patients with AIH, especially in those with liver cirrhosis, to screen for hepatocellular carcinoma [7].

PBC rarely occurs in ulcerative colitis, and the pathogenesis of the two diseases has not been elucidated. It is often believed that environmental and genetic factors lead to susceptibility to the two diseases, indicating that the two diseases may share a common immune pathogen pathway. Thus, not only should PSC be considered in patients with UC, but also PBC should be considered as a potential concomitant disease. It is suggested that a serum AMA antibody test or an AMA- M2 antibody test should be performed in such patients to screen for PBC [8].

Because of early liver cirrhosis, we cautiously chose prednisone combined with UDCA for the treatment. Thus far, the follow-up after treatment has been ideal. Researchers have suggested that vedolizumab does not improve liver function and may even induce colorectal cancer because of decreased immune surveillance of the gut in patients with inflammatory bowel disease and PSC [9]. Therefore, regular immune surveillance of the gut is required if vedolizumab is used. Moreover, there is a need for interventions that can simultaneously control intestinal and liver diseases. Further, guidelines recommend close monitoring and periodic follow-up of patients to prevent tumour development.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests in this study.

AUTHOR'SCONTRIBUTIONS

J.Z. and X.L.Z. conceived and designed the study. T.Y.L. and Q.S.T. analysed and interpreted the data. P.Y. and Z.H.L. wrote several drafts of the manuscript. T.Y.L. and J.Z. provided critical revision and final approval of the article. All authors read and approved the final manuscript.

## INFORMED CONSENT AND ETHICAL STATEMENT

The patient's data were used with his consent, and the study was reviewed by our institution's Ethics Committee.

## ACKNOWLEDGEMENT

None.

## AVAILABILITY OF DATA AND MATERIALS

To protect the privacy of the patient, the data sets generated and analysed during the current study are not publicly available. However, these may be obtained from the corresponding author on reasonable request.

## REFERENCES

[1] Ott C, Schölmerich J. Extraintestinal manifestations and complications in IBD. Nat Rev Gastroenterol Hepatol 2013; 10 :585-95.

[2] Koskinas J, Raptis I, Manika Z, et al. Overlapping syndrome of autoimmune hepatitis and primary sclerosing cholangitis associated with pyoderma gangrenosum and ulcerative colitis. Eur J Gastroenterol Hepatol 1999; 11 :1421-4.

[3] McNair AN, Moloney M, Portmann BC, Williams R, McFarlane IG. Autoimmune hepatitis overlapping with primary sclerosing cholangitis in five cases. Am J Gastroenterol 1998; 93 :777-84.

[4] Ozaslan E, Efe C, Heurgué–Berlot A, et al. Factors associated with response to therapy and outcome of patients with primary biliary cirrhosis with features of autoimmune hepatitis. Clin Gastroenterol Hepatol 2014; 12: 863-9.

[5] Guerra I, Bujanda L, Castro J, et al. Clinical characteristics, associated malignancies and management of primary sclerosing cholangitis in inflammatory bowel disease patients: a multicentre retrospective cohort study. J Crohns Colitis 2019; 13 :1492-1500.

[6] Chinese Society of Hepatology, Chinese Society of Gastroenterology & Chinese Society of

Infectious Diseases. Chinese consensus on the diagnosis and management

of autoimmune hepatitis (2015). J Dig Dis 2017; 18 :247-64.

[7] Chinese Society of Hepatology, Chinese Medical Association; Chinese Society of Gastroenterology, Chinese Medical Association; Chinese Society of Infectious Diseases, Chinese Medical Association. Consensus on the diagnosis and management of primary sclerosing cholangitis (2015 version). Zhonghua Gan Zang Bing Za Zhi 2016; 24 :14-22.

[8] Polychronopoulou E, Lygoura V, Gatselis NK, et al. Increased cholestatic enzymes in two patients with long-term history of ulcerative colitis: consider primary biliary cholangitis not always primary sclerosing cholangitis. BMJ Case Rep 2017; 2017 :bcr2017220824.

[9] Christensen B, Micic D, Gibson PR, et al. Vedolizumab in patients with concurrent primary sclerosing cholangitis and inflammatory bowel disease does not improve liver biochemistry but is safe and effective for the bowel disease. Aliment Pharmacol Ther 2018; 47 :753-62.

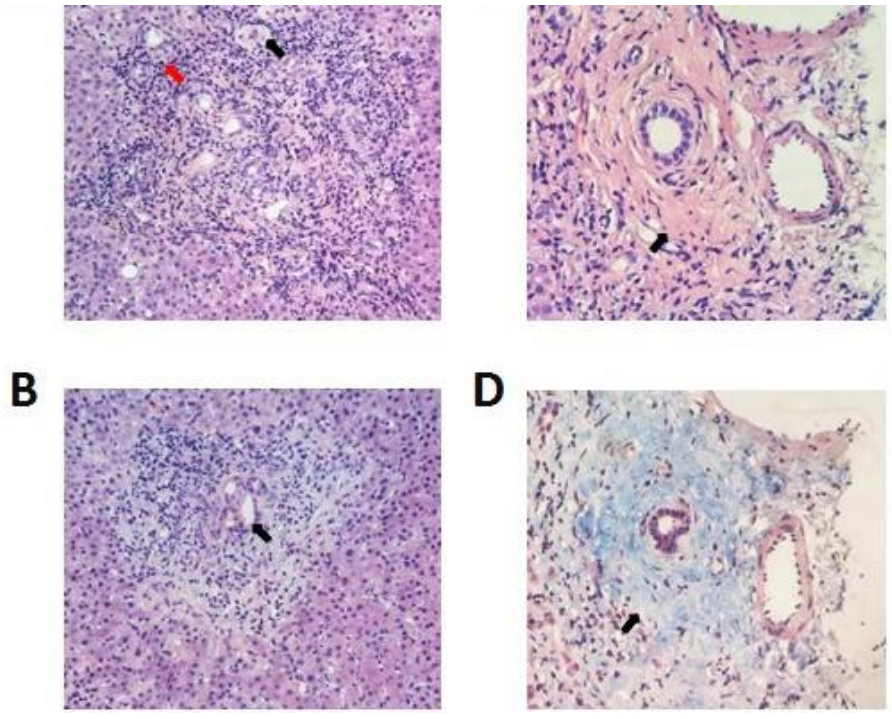
Table 1. Results of liver function tests performed during follow-up

| | June 22, 2018 | July 14, 2020 | August 20, 2021 | October 24, 2021 | April 18, 2022 | September 29, 2022 |
|---|---|---|---|---|---|---|
| ALT | 51 | 45 | 44.5 | 85.9 | 47.99 | 44.02 |
| AST | 46 | 32 | 46.7 | 36 | 42.04 | 31.51 |
| γ-GT | 517.73 | 540 | 440.9 | 255 | 227.26 | 215.29 |
| AKP | 661 | 672 | 1172 | 342 | 431.65 | 608.52 |
| TB | 11.3 | 13.5 | 28 | 14.7 | 12.21 | 20.57 |
| DB | 5.6 | 6.4 | 11.5 | 11.6 | 7.40 | 13.04 |
| ALB | 32.3 | 30.4 | 31.1 | 34.1 | 39.46 | 36.37 |

ALT, glutamic pyruvic transaminase; AST, glutamic oxaloacetic transaminase; γ-GT, γ-glutamyl transpeptidase; AKP, alkaline phosphatase; TB, total bilirubin; DB, direct bilirubin; ALB, serum albumin. Unit is U/L.

FIGURE LEGEND

Figure 1: Ultrasound-guided percutaneous hepatic biopsy findings from 27 August 2021 revealed a histological AIH score of 5. A) Interface hepatitis 3, plasma cell 1 (red arrow), rosette 1 (black arrow), and bile duct injury and destruction, basement membrane incomplete. B) obvious fibrous obstructive cholangitis (black arrow). C) typical concentric round collagen deposition (onion-like, black arrow). D) Masson's trichrome staining further confirmed collagen deposition around the bile duct in some portal lobules (black arrow). (Biopsy specimens shown in panels A, B, and C were stained with haematoxylin–eosin; scale bar = 100 μm).



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