CASE REPORT

A Case of Autoimmune Hepatitis and Primary Biliary Cirrhosis Overlap Syndrome Treated with Chinese Herbs

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Some patients present with overlapping features between disorders within the spectrum of autoimmune liver diseases, i.e., autoimmune hepatitis (AIH), primary biliary cirrhosis (PBC), and primary sclerosing cholangitis (PSC), and are commonly classified as having an "overlap syndrome". The pathophysiological mechanisms underlying AIH-PBC overlap remain unclear. Due to the lack of standardization and variations in the populations under study, the characteristics of these entities vary between studies and there have been few effective medical therapies for overlap syndrome up to now. Here, we report a case of a woman diagnosed as AIH-PBC overlap syndrome who had suboptimal response to single ursodeoxycholic acid (UDCA) or combination with immunosuppressive drug but had optimal response to Chinese herbs.

Case Report

A 53-year-old female patient started to suffer lethargy, anorexia and pruritus in June 2006. She visited our hospital in February 2007, and her laboratory data were as follows: alanine transaminase (ALT) 74 U/L (normal, <40 U/L), aspartate aminotransferase (AST) 103 U/L (normal, <40 U/L), alkaline phosphatase (ALP) 381 U/L (normal, 40–150 U/L), gamma glutamyl transferase (GGT) 413 U/L (normal, 7–32 U/L), total bilirubin 28 μmol/L (normal, <17.1 umol/L), IgG 39 g/L (normal, 7.23–16.60 g/L), IgM 5.7 g/L (normal, 0.63–2.77 g/L), antinuclear antibody (ANA) titer 1/1280 (negative, <1/80), antimitochondrial antibody (AMA) titer 1/640 (negative, <1/80) and AMA-M2 (+). Anti-smooth muscle antibodies and viral serologies (hepatitis A, B, C, E, cytomegalovirus, Epstein-Barr virus and human immunodeficiency virus) were negative and there was no history of drug or alcohol intake. Liver biopsy demonstrated interface hepatitis, plasma cell infiltration and ductal lesion (Figure 1). Both histological and laboratory findings (positive ANA and AMA-M2) were compatible with AIH-PBC overlap syndrome.

The patient was treated with UDCA 15 mg/kg per day in the initial month, however, her serum liver enzymes were persistently rising. Because of specific characteristics of this patient, from the second month, azathiopyrine 50 mg/day was added, but her serum liver enzymes were still rising. Therefore, from the third month, azathiopyrine was stopped and Chinese herbs were medicated as pilot therapy, which was composed of Radix Rubiae 30 g, Radix Salviae Miltiorrhizae 30 g, Radix Gentianae Macrophyllae 20 g, Semen Coicis 30 g, Astragalus membranaceus  Bge 30 g, and Herba Artemisiae scopariae 15 g (experience prescription in our hospital). The drugs were prepared by decocting with water, one dose per day, taking in two parts for a total of 10 days. After that, her liver function was improved, and this medication was taken continuously.

In September 2010, the titer of ANA and

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would be more effective in improving biological indicators for AIH-PBC overlap patients than either UDCA or immunosuppressive therapy administered separately.\(^{(5,7)}\) For patients resistant to combination therapy of UDCA and azathioprine, other agents such as cyclosporine-A and mycophenolate mofetil were used but their efficacy in these patients was not often satisfactory.\(^{(8)}\)

In this report, the patient was not respond to UDCA monotherapy or combination of UDCA and azathiopyrine, but was under control after azathiopyrine was stopped and Chinese herbs were medicated as pilot treatment from the third month.

### DISCUSSION

As a disease entity, Popper and Schaffner first proposed AIH-PBC overlap syndrome in 1970.\(^{(4)}\) In clinic, the presentation of autoimmune liver diseases varies widely, ranging from asymptomatic elevations of serum liver enzymes to massive hepatic necrosis resulting in fulminant hepatic failure, and there are no disease-specific clinical features. Günsar, et al\(^{(5)}\) reported that lethargy was the most common symptom in these patients. Similar to the report, the chief complaint of the present patient is lethargy, which is a subsidiary consideration for the diagnosis excluding other forms of liver diseases.

Though UDCA is not effective in all patients with PBC,\(^{(6)}\) it is generally accepted in America and Europe that patients with this syndrome should continue to receive UDCA. To date, it is unclear if the degree of AIH-PBC overlap of these cases may justify the addition of corticosteroid or immunosuppressive therapy. Some researchers have suggested that UDCA and immunosuppressive combination therapy could be more effective in improving biological indicators for AIH-PBC overlap patients than either UDCA or immunosuppressive therapy administered separately.\(^{(5,7)}\) For patients resistant to combination therapy of UDCA and azathioprine, other agents such as cyclosporine-A and mycophenolate mofetil were used but their efficacy in these patients was not often satisfactory.\(^{(8)}\)

In this report, the patient was not respond to UDCA monotherapy or combination of UDCA and azathiopyrine, but was under control after azathiopyrine was stopped and Chinese herbs were added, which included Radix Rubiae, Radix Gentianae Macrophyllae, and Semen Coicis, etc. The research results showed that these herbs had cholagogic and anti-inflammatory function and regulative function on the whole body. Moreover, they had the effects of decreasing cholestasis and removing dampness, and played important roles in normalizing the hepatic transaminases.\(^{(9,10)}\) Pharmacological studies showed that alkaloids in Radix Rubiae and Radix Gentianae Macrophyllae could reduce inflammation,\(^{(11)}\) which contributed to the remission of AIH, and tanshinone in Radix Salviae Miltiorrhizae could decrease the activity of phosphodiesterase and the growth of fibroblast cells,\(^{(12)}\) which helped to ameliorate the condition of PBC. With the treatment duration, the two positive autoantibodies of the patient eventually converted to negativity and her condition was greatly improved.