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Research Article

Primary biliary cholangitis (PBC) - autoimmune hepatitis (HAI) overlap syndrome (OS)

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Abstracts: The AIH-PBC overlap syndrome is the most common form of OS. ***The aim:*** to study the clinical and paraclinical characteristics of the overlap syndrome and to specify the therapeutic and evolutionary characteristics. ***Methods:*** The medical data of 42 PBC patients were evaluated for associated autoimmune hepatitis. ***Results:*** Among the 42 cases of PBC, we retained 16 cases of OS (37%). All female the association of diagnostic criteria for PBC and HAI was simultaneous in 80%. Treatment with AUDC, corticosteroid and Azathioprine was started in the majority of our patients. The course was marked by a complete (10 cases) or incomplete (n = 6) response. ***Conclusion:*** OS should be considered in the presence of any mixed cytolytic and cholestatic liver disease. Its recognition is essential in order to adapt treatment and prevent progression to cirrhosis and its complications.
Keywords: Primary biliary cholangitis, autoimmune hepatitis, overlap syndrome.

INTRODUCTION

Overlap syndrome (OS) is a variant of autoimmune liver disease that combines simultaneously or consecutively characteristic signs of HAI and PBC. It poses diagnostic and therapeutic difficulties (Czaja, A. J. 1996).

The aim of our study was to determine the clinical and paraclinical characteristics of the overlap syndrome and to specify the therapeutic and evolutionary characteristics.

PATIENTS AND METHODS

It is a retrospective study of all cases of CBP-HAI overlap syndrome followed at our hepato-gastroenterology Department over a period of 8 years (January 2012 and December 2019). The diagnosis was based on the Paris criteria recommended by EASL and AASLD.

RESULTS

Among the 42 cases of PBC, we retained 16 cases of OS (37%). All our patients were female. The average age was 46 years old. The association of diagnostic criteria for PBC and AIH was simultaneous in 80%. The diagnosis of OS was made consecutively in 4 patients. The most common circumstance of discovery was generalized pruritus (84%), associated in 68% of cases with jaundice. The biological assessment revealed cholestasis associated with cytolysis in all our patients. Anti-mitochondria antibodies were positive in 87%. Anti-smooth muscle antibodies were positive in 38%. Histologic lesions in OS are associated to varying degrees with histologic signs of PBC and HAI. In our series, liver biopsies performed in patients with OS showed the simultaneous presence of hepatocytic necrosis lesions and cholangiolar lesions in 60%.

Treatment with AUDC, corticosteroid and Azathioprine was started in the majority of our patients. The course was marked by a complete (10 cases) or incomplete (n = 6) response.

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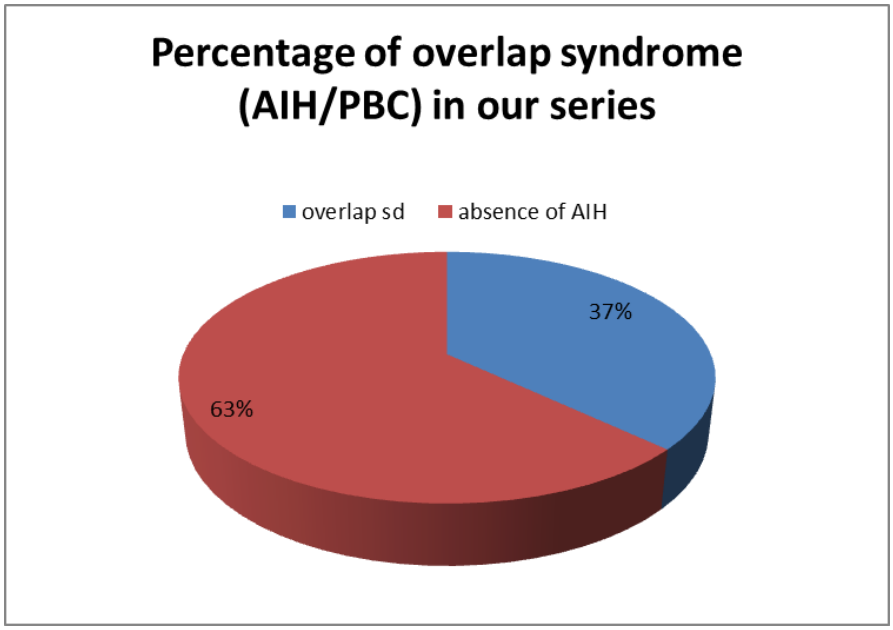

Figure 1: percentage of overlap syndrome (AIH/PBC) in our series

DISCUSSION

The term "overlap syndrome" is used to describe variant forms of autoimmune hepatitis (AIH) which present with characteristics of AIH and primary biliary cholangitis (PBC) or primary sclerosing cholangitis (Czaja, A. J. 1996; & Poupon, R. 2003).

PBC and AIH are the most frequent autoimmune hepatopathies and female gender predominates in both of them (Kim, W. R. *et al.*, 2000; & Prince, M. I., & James, O. F. 2003). Usually, they are easily distinguished. However, the characteristic elements of both diseases may be present in the same subject. It is now well established that an AIH can associate with a PBC either simultaneously or consecutively.

It is important to note that there are no consensual criteria for the diagnosis of overlap syndrome between PBC and HIA. Due to the potential therapeutic implications, however, it is recommended that this diagnosis be ruled out as soon as that of PBC has been established. The original, revised or simplified AIH diagnostic scores are not appropriate. The Paris diagnostic criteria (Czaja, A.J. 2013) based on the presence of at least 2 AIH criteria have been recommended by EASL (European Association for the Study of the Liver. 2017) and AASLD (Lindor, K.D. *et al.*, 2018).

Table 1 (Czaja, A.J. 2013**)** Diagnostic features of the overlap syndromes of autoimmune hepatitis (AIH)

Overlap syndrome	Laboratory features	Serological features	Histological features	Cholangiographic findings
AIH-PBC	Consistent with Paris criteria* Mild forms may have AP ≤2×ULN	AMA positive	Interface hepatitis Destructive cholangitis (florid duct lesions)	Normal
AIH-PSC	AST/ALT>ULN γ-globulin and IgG >ULN AP or GGT>ULN	AMA negative	Interface hepatitis Ductopenia Portal edema or fibrous Obliterative fibrous cholangitis (rare)	Bile duct strictures
AIH-cholestatic syndrome	AST/ALT>ULN γ-globulin and IgG >ULN AP or GGT >ULN	AMA negative	Interface hepatitis Destructive cholangitis or bile duct loss	Normal

**Paris criteria endorsed by the European Association for the Study of the Liver require interface hepatitis and either serum alanine aminotransferase (ALT) level ≥5-fold upper limit of normal range (ULN), serum immunoglobulin G (IgG) level ≥2-fold ULN or smooth muscle antibodies, and two of three features of primary biliary cirrhosis (PBC) including serum alkaline phosphatase (AP) level ≥2-fold ULN or serum gamma glutamyl transferase (GGT) ≥5-fold ULN, antimitochondrial antibodies (AMA) and destructive cholangitis. AST Serum aspartate aminotransferase level; PSC Primary sclerosing cholangitis*

Diagnosing an overlap syndrome has therapeutic implications. Immunosuppression is considered as standard effective therapy for AIH and UDCA is recommended to slow down the progression of PBC (Prince, M. I., & James, O. F. 2003). A complete clinical and biochemical response is achieved in patients after using combination therapy of UDCA and corticosteroids (Chazouillères, O. *et al.*, 1998; & Joshi, S. *et al.*, 2002).

Overlap syndromes should be searched in patients who have inadequate response with therapy employed for any autoimmune liver disease. The diagnosis of an OS could have a significant impact in the treatment of these patients, leading to overall improvement of survival and decrease the need of liver transplantation (Silveira, M.G. 2013).

One study has suggested that OS (PBC/AIH) progress rapidly to cirrhosis and liver failure (Chazouillères, O. *et al.*, 1998). Whereas, another study found that patients with OS were more likely to develop esophageal varices, ascites, liver failure compared to patients with typical PBC (Silveira, M.G. 2013). In our study population, we observed both the findings. Study of more cases is required to find whether these groups have different natural history and response to treatment.

CONCLUSION

OS should be considered in the presence of any mixed cytolytic and cholestatic liver disease. Its recognition is essential in order to adapt treatment and prevent progression to cirrhosis and its complications.

REFERENCES

1. Chazouillères, O., Wendum, D., Serfaty, L., Montembault, S., Rosmorduc, O., & Poupon, R. (1998). Primary biliary cirrhosis–autoimmune hepatitis overlap syndrome: clinical features and response to therapy. *Hepatology*, *28*(2), 296-301.
2. Czaja, A. J. (1996). The variant forms of autoimmune hepatitis. *Annals of internal medicine*, *125*(7), 588-598.
3. Czaja, A.J. (2013). Diagnosis and management of the overlap syndromes of autoimmune hepatitis. *Can J Gastroenterol*, *27*(7), 417-423. doi:10.1155/2013/198070
4. European Association for the Study of the Liver. (2017). EASL Clinical Practice Guidelines: The diagnosis and management of patients with primary biliary cholangitis. *Journal of hepatology*, *67*(1), 145-172.
5. Joshi, S., Cauch-Dudek, K., Wanless, I. R., Lindor, K. D., Jorgensen, R., Batts, K., & Heathcote, E. J. (2002). Primary biliary cirrhosis with additional features of autoimmune hepatitis: response to therapy with ursodeoxycholic acid. *Hepatology*, *35*(2), 409-413.
6. Kim, W. R., Lindor, K. D., Locke III, G. R., Therneau, T. M., Homburger, H. A., Batts, K. P., ... & Dickson, E. R. (2000). Epidemiology and natural history of primary biliary cirrhosis in a US community. *Gastroenterology*, *119*(6), 1631-1636.
7. Lindor, K.D., Bowlus, C.L., Boyer, J., Levy, C., & Mayo, M. (2018). Primary Biliary Cholangitis: 2018 Practice Guidance from the American Association for the Study of Liver Diseases. Hepatology. 2018 Nov 6;hep.30145.
8. Poupon, R. (2003). Autoimmune overlapping syndromes. *Clinics in liver disease*, *7*(4), 865-878.
9. Prince, M. I., & James, O. F. (2003). The epidemiology of primary biliary cirrhosis. *Clinics in liver disease*, *7*(4), 795-819.
10. Silveira, M.G. (2013). Overlap syndromes of autoimmune liver disease. J Clin Cell Immunnol. 2013; 4:4.