The clinical features of primary biliary cirrhosis (PBC) are quite diverse, and a considerable number of PBC patients remain asymptomatic at the time of diagnosis. When clinical symptoms or signs are initially detected or recognized, a majority are general malaise or pruritus. In some patients, ascites or bleeding esophageal varices are a first clinical manifestation (1, 2). In addition, recent studies in Japan have shown that some patients of PBC can initially present acute hepatitis-like features with marked elevation of serum transaminases and even transient jaundice at a relatively early histologic stage (3, 4). Histologically, such patients reveal features resembling acute hepatitis with evident interface and even lobular hepatitis. To date, the precise incidence of such presentation and also its significance in PBC remain unclarified. Follow-up or closer examinations of such patients has shown that PBC is finally proven. That is, chronic non-suppurative destructive cholangitis (CNSDC) is histologically found, and serologically, antimitochondrial antibodies (AMA) are found to be positive and the serum level of IgM is elevated. Such patients reacted well to ursodeoxycholic acid (UDCA) as in usual PBC, or AIH features disappeared spontaneously. To date, such presentation of PBC at an early stage is poorly recognized and has been rarely reported, particularly in English journals.

In this issue, Sohda et al (3) report such a case who presented with apparently rapid-onset, drug-induced hepatitis, clinically. Their case had a history of drug-ingestion (diet produs) and the liver injury therefore was initially thought as drug-induced, but subsequent studies showed that AMA was positive, and the serum level of IgM was elevated. Interestingly, antinuclear antibodies (ANA) were also positive. Histologically, CNSDC with significant portal and interface hepatitis was affirmed. Eventually, a diagnosis of PBC stage 2 was made.

What do such cases of PBC with acute hepatitis-like onset mean? Histologically, in PBC, the interlobular bile ducts are primarily and selectively affected, showing CNSDC. Eventually, almost all of the interlobular bile ducts disappear from the liver, followed by chronic cholestasis, and ultimately biliary fibrosis or cirrhosis (5). In addition, some proportion of PBC patients is known to simultaneously present clinical, serological and histological features of autoimmune hepatitis (AIH), transiently or continuously. Such patients are termed as overlapping syndrome of AIH and PBC or a hepatic form of PBC (6). Prominent interface hepatitis and lobular hepatitis, even zonal hepatic necrosis, are encountered in such cases. In this context, it seems plausible to speculate that in PBC patients with acute hepatitis-like onset, AIH or prominent hepatitis might have overlapped at an early stage of asymptomatic PBC. Interestingly, ANA were also positive in the reported cases (3, 4), supporting the above-mentioned speculation. Acute onset of AIH with features of acute hepatitis and minimal or mild hepatic fibrosis is also well known.

Pregnancy or delivery is known to occasionally induce or manifest clinical symptoms or signs of PBC in asymptomatic PBC patients. To date, the trigger for induction of significant interface and lobular hepatitis in PBC patients remains speculative. Recently, Ohba et al (7) reported that AIH flared up in classical PBC after delivery, suggesting that AIH features may become evident or flare-up after some triggering factor(s) including delivery. Pregnancy or delivery is known to affect the immune conditions of the patient such as rheumatoid arthritis and multiple sclerosis and this may be a trigger for flare-up of hepatitic features or AIH hepatitis in PBC. Drug adverse reaction is also known to significantly influence immunological conditions and in fact, some drug-induced hepatitis presents with variable immunological disturbances such as ANA in serum and epithelioid granulomas in the liver. In fact, drug-induced hepatitis could be a big clinical challenge in the differentiation of AIH. In this context, drug-ingestion may also influence the induction of histological and serological features of acute hepatitis in PBC patients.

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References


