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Editorial

Regression of liver cirrhosis: Orthodoxy or paradigm shift?

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Liver fibrosis is a wound-healing process that happens in almost patients with ongoing chronic liver injury. For instance, patients surviving acute liver failure do not undergo scar change despite a plenty of fibrogenic stimuli, unless chronic liver injury follows.[1] Moreover, even liver fibrosis related to certain kind of sustained liver injury is often reversible. The reason for fibrosis reversibility in chronic liver disease is not fully understood, but may be associated with the balance of matrix-degrading enzymes and their inhibitors, in addition to the relative range of collagen cross-linking. Complications of end stage liver disease are related to the underlying fibrotic response. Therefore, fibrosis is harmful both by its indirect mechanical role to increased portal resistance and by its direct damages on cellular function. Ultimately, liver fibrosis leads to the end stage of liver fibrosis, cirrhosis, characterized by architectural distortion, abnormal hepatocyte regeneration, nodular change, vascular alterations and organ contraction.[2]

Cirrhosis significantly increases the risk of cirrhotic complications, hepatocellular carcinoma, and death.[3,4] Therefore it is important to exactly predict the rate of liver fibrosis progression in patients with chronic viral hepatitis, which has important clinical impact in terms of prognostic and treatment implications. The exact moment when liver fibrosis becomes irreversible is still not known, in terms of either a histological marker or a specific change in the matrix content or composition. Dense cirrhosis, with regenerating nodule formation and portal hypertension, is usually considered irreversible, but several studies have demonstrated that prolonged antiviral therapy improves liver histology and even reverses cirrhosis in patients with chronic hepatitis B (CHB).[5]

However, the evidences existing so far is based on limited number of patients, especially in case of advanced liver fibrosis or cirrhosis.[5] Moreover, there is a possibility of bias due to selection of patients undergoing repeat biopsy and the important concern of the right staining for elastic fibers in liver biopsies.[5] Indeed, mostly in existence of high grade of necroinflammation, there is a parenchymal collapse mimicking septa, and in these cases collagen stains including Sirius Red and Masson's Trichrome could lead to a misdiagnosis of liver cirrhosis which disappeared in the successive liver biopsies.[5] Since the amount of liver fibrosis could be decreased by a switching off of necroinflammation, liver stiffness which is mainly associated with fibrosis is also affected by alanine aminotransferase (ALT) level.

In this issue, Yo et al reported the factors associated with longitudinal change of liver stiffness in patients with CHB.[6] In this

Abbreviations:
CHB, chronic hepatitis B; ALT, alanine aminotransferase

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study, they excluded patients with an ALT level >80 IU/mL to prevent ALT values affecting results and found that a higher initial liver stiffness value was associated with liver stiffness improvement in patients with CHB with antiviral therapy and in patients with stable disease state for about 2 years. Although they excluded patients with an ALT level >80 IU/mL, the enrollment of patients with ALT level between 40 and 80 IU/mL could affect overestimated liver stiffness due to the existence of low grade inflammation in this study. Moreover, coincidental metabolic syndrome,[7] edema, and vascular congestion which also could influence liver stiffness were not totally excluded in this study. Therefore, it is possible that a high initial liver stiffness value might be the result of mildly elevated necroinflammatory activity or the presence of metabolic syndrome, edema and/or vascular congestion, and more significant reductions in liver stiffness values were observed in the patients with an initial high liver stiffness value after the improvement of inflammatory activity, metabolic syndrome, edema and/or vascular congestion both in patients with CHB with antiviral therapy and in patients with stable disease state. Moreover, there was no significant difference in the rate of improvement of liver stiffness between the antiviral therapy (+) group and the antiviral therapy (–) group in this study.

The significance of the reversal of cirrhosis is still a subject of debate because neither the histological scoring systems nor noninvasive markers to evaluate the reversal of cirrhosis have been validated.[8] Therefore, further studies are warranted to validate the findings of Yo's work in larger liver biopsy-based study population.

Conflicts of Interest

The authors have no conflicts to disclose.

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