Changes in liver stiffness during the course of acute hepatitis A

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Backgrounds/Aims: In some patients with chronic hepatitis, liver stiffness (LS) findings do not reflect fibrosis stage. This study was performed to evaluate whether acute liver inflammation could influence LS findings. Methods: Patients with acute hepatitis A admitted to our hospital were included. Hepatitis was classified on admission using serum ALT and bilirubin levels as inflammation phase, jaundice phase, or recovery phase. Patients who admitted during the recovery phase (whose ALT and bilirubin levels fell continuously during hospitalization) and therefore, their peak-ALT and peak bilirubin levels could not be determined were excluded. Enrolled patients underwent FibroScan during hospitalization and after discharge. Results: Seventy-six patients with acute hepatitis A were enrolled (median age, 29 years; 46 men and 30 women). Among them, 33 (43.4%) and 43 (56.6%) patients were admitted during the inflammation phase and jaundice phase, respectively. For patients admitted during the inflammation phase, mean (±SD) time from symptom-onset day to maximum ALT level was 7 (±3) days. For all patients, mean time from symptom-onset to maximum bilirubin level was 11 (±4) days. Mean LS during admission was 8.9 (±3.3) kPa (median, 8.4 kPa). LS was significantly correlated with serum bilirubin level, which was the only factor found to be significantly associated with the increased LS (>7.08 kPa). In all patients, LS increased gradually from the symptom-onset and peaked at 8-9 days later. Conclusions: Severe hepatic inflammation can affect the LS findings and thus, care is required when assessing fibrosis stage using LS measurement in patients with severe inflammation. (Korean J Hepatol 2008;14:465-473)

Key words: Liver stiffness; Fibrosis; Inflammation; Acute hepatitis

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Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; GGT, gamma-glutamyl transpeptidase; ULN: upper limit of normal; kPa, kilopascal; LS, liver stiffness.
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Introduction

The accurate assessment of the liver fibrosis extent is essential for predicting prognosis and determining appropriate management in patients with chronic liver diseases. Liver biopsy is still considered the gold standard, but it is invasive and can lead to life-threatening complications. Furthermore, its accuracy for assessing fibrosis is suspected due to sampling errors and intra- and interobserver discrepancies.

In contrast, liver stiffness (LS) determined using Fibroscan is entirely non-invasive, and reduces the potential for sampling errors, because the liver volume measured is 100 times greater than that of liver biopsy specimens. In addition, LS measurements are reproducible with low intra- and interobserver variabilities. Furthermore, the correlation between LS and fibrosis stage seems to be unaffected by steatosis or degree of necroinflammation and several studies have suggested that LS is highly accurate for assessing liver fibrosis.

Unfortunately, in some patients with chronic hepatitis, LS and liver biopsy findings disagree and it has been suggested that this is usually caused by biopsy limitations and the design of the METAVIR grading system, rather than influence of liver inflammation on LS findings. However, the majority of patients enrolled in these studies had chronic hepatitis C with only marginal transaminases and bilirubin level deviations, and thus, the effects of such deviations on LS would have been difficult to determine. Furthermore, it was recently suggested that LS is dependent on liver inflammation in chronic hepatitis B and acute hepatitis.

Although the relation between liver inflammation and LS has been documented, relations between LS and transaminases and bilirubin levels remain unclear, because in previous studies cohort sizes were small and a focus was placed only on the relation between LS and alanine aminotransferase (ALT) levels. Therefore, we undertook this study to evaluate the changes in LS during the course of acute hepatitis A (AHA) and to identify those factors that influence LS.

Patients and Methods

1. Patients

This study is a retrospective observational study. We performed chart review of all consecutive patients with AHA hospitalized at our institution between September 2006 and March 2008. AHA was diagnosed when IgM antibody to hepatitis A virus was positive and serum ALT level was ≥10 times the upper limit of normal (ULN, 40 IU/L). Patients with previous or family history of liver disease were excluded, as were patients suspected of having another type of hepatitis based on the following findings: hepatitis B surface antigen, IgM antibody to hepatitis B core antigen, antibody to hepatitis C virus (HCV), HCV RNA quantification test, anti-nuclear antibody, anti-smooth muscle antibody, anti-LKM antibody, anti-mitochondrial antibody, copper, and ceruloplasmin. In addition, patients were excluded if peak bilirubin level could not be determined because it fell continuously during hospitalization.

At the time LS measurements were made, the following biochemical tests were also performed: serum aspartate aminotransferase (AST), ALT, alkaline phosphatase (ALP), gamma-glutamyl transpeptidase (GGT), and bilirubin level.