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Serum Levels of 7S Collagen in HCV-Ab Positive Chronic Liver Diseases

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ABSTRACT. Serum 7S collagen was measured in 100 patients with Hepatitis C virus (HCV)-Ab positive chronic liver disease using RIA kit (7S-RIA : Japan DPC Corporation). The serum levels of 7S collagen were significantly higher in all types of liver diseases than those in 20 healthy controls (3.9±0.4 ng/ml). The 7S collagen level was 8.4±3.6 ng/ml (n=30) in chronic hepatitis (CH), 14.4±8.1 ng/ml (n=30) in liver cirrhosis (LC), 14.5±8.6 ng/ml (n=40) in hepatocellular carcinoma (HCC). In chronic hepatitis, chronic active hepatitis had a mean 7S collagen value of 9.8±3.8 ng/ml (n=19), while that of chronic inactive hepatitis was 6.1±1.8 ng/ml (n=11). In decompensated liver cirrhosis, the 7S collagen value was 17.6±9.2 ng/ml (n=17), whereas that of compensated LC was 10.2±3.1 ng/ml (n=13). In HCC, 7S collagen was examined according to the size of the tumor. In HCC with a diameter of less than 3 cm, the value was 11.0±4.2 ng/ml (n=5). In 3 to 5 cm lesions, it was 12.5±5.8 ng/ml (n=16) and those more than 5 cm in diameter, it was 17.1±10.8 ng/ml (n=19). Although there were no significant differences according to size, there was a tendency for the level of 7S collagen to increase with the size of the tumor. The HCV-Ab titer and 7S collagen level showed no significant correlation. Measurement of serum 7S collagen may be useful for the evaluation of the degree of progression of LC and HCC.

Key words : serum 7S collagen — HCV-Ab positive chronic liver diseases

There are 13 known collagen phenotypes. Among these, types Ⅰ, Ⅲ, Ⅳ, Ⅴ, Ⅵ and Ⅻ exist in the liver. Type Ⅰ and type Ⅲ collagen are the main components of the collagen forming interstitial collagen, while type Ⅳ collagen is a membranous type collagen consisting of basement membrane with laminin. In experimental acute and chronic liver damage, type Ⅳ collagen plays an important role in the progress of fibrosis.[1] Recently the 7S collagen RIA kit in which the ^{125}I labeled 7S domain of type Ⅳ collagen isolated from human placenta is used as the tracer,[2] has been developed and has come into commercial use. Several reports have suggested that measurement of serum 7S collagen is a reliable test for the detection of fibrosis in chronic viral liver diseases and alcoholic liver damage.[3-5] In this report, we examined the serum 7S collagen of 100 cases of HCV-Ab positive chronic liver disease, including 30 of chronic hepatitis (CH), 30 of liver cirrhosis (LC), and 40 of hepatocellular

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carcinioma (HCC) using the RIA kit (7S-RIA ; Japan DPC Corporation). With this assay we demonstrated elevated 7S collagen in the sera of both HCC and LC.

MATERIALS AND METHODS

Samples ; Sera were obtained from 100 patients with HCV-Ab positive chronic liver disease and 20 normal volunteers in our laboratory.

Assay ; The serum Type Ⅳ collagen 7S domain (Ⅳ-7S) was assayed using 7S kit (DPC Corporation). 200 μl of serum was incubated for two hours at 37℃ with 100 μl of Ⅳ-7S antibody. 100 μl of ^{125}I Ⅳ-7S was added and the serum was incubated for a further two hours. Then 1 ml of B/F separation reagent was added to the serum and it was mixed and centrifuged at 2000 × g for 15 min. Radioactivity included in the supernatant was counted by a γ-counter. HCV-Ab was assyed by EIA kit (Ortho HCV-Ab ELISA kit).

RESULTS

1. Comparison of serum 7S collagen in healthy controls and patients with HCV-Ab positive chronic liver disease

As shown in Table 1, the mean serum 7S collagen activity of healthy controls was 3.9±0.4 ng/ml. The mean serum 7S collagen activity in patients with LC (14.4±8.1 ng/ml) was significantly higher ($p<0.001$) than that (8.4± 3.6 ng/ml) in patients with CH. In HCC it was 14.5±8.6 ng/ml, which was almost the same as in LC. The distributions of 7S collagen are shown in Fig. 1. In all of the CH cases, 7S collagen activity remained below 20 ng/ml, but in 4 out of 30 LC cases (13%) and 8 out of 40 HCC cases (20%), it exceeded 20 ng/ml.

Table 1. Serum 7S collagen levels in patients with HCV-Ab positive liver disease.

	n	Ⅳ 7S collagen (ng/ml)
Normal	20	3.9±0.4
CH	30	8.4±3.6**
LC	30	14.4±8.1**
HCC	40	14.5±8.6**

** $P<0.01$

CH : chronic hepatitis
LC : liver cirrhosis
HCC : hepatocellular carcinoma

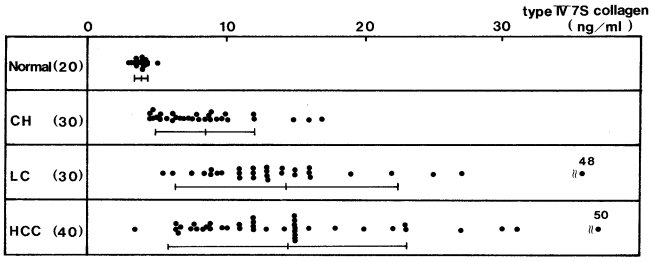

Fig. 1. Distribution of serum 7S collagen in various liver diseases. High levels of 7S collagen of more than 20 ng/ml was noted in LC and HCC but not in CH.

2. *Serum 7S collagen in chronic liver disease*

Of our 30 chronic hepatitis cases, 19 were classified as chronic active hepatitis (CAH) and 11 as chronic inactive hepatitis (CIH) by liver biopsy findings. Liver cirrhosis cases were divided into compensated cases (c-LC) (n=13) and decompensated cases (d-LC) (n=17) depending upon the presence or absence of ascites, jaundice, and hepatic encephalopathy. Fig. 2 shows that significant difference were noted between CAH (mean 9.8) and CIH (mean 6.1), as well as between c-LC (mean 10.2) and d-LC (mean 17.6).

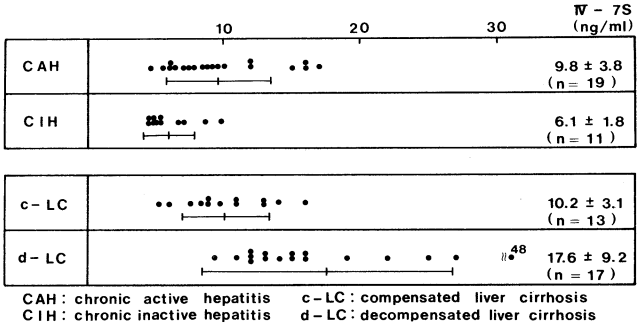

Fig. 2. Serum levels of 7S collagen in CH and LC.

3. *7S collagen in HCC*

HCC cases were divided by the size of the tumor. Fig. 3 shows the distribution of 7S collagen level according to the differences in tumor size. There was a tendency for 7S collagen to increase as the tumor became bigger, but there was a considerable overlapping of serum levels and no significant differences was noted among these cases.

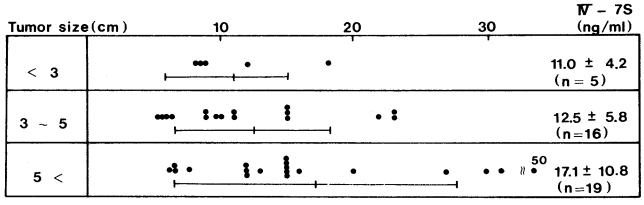

Fig. 3. Serum levels of 7S collagen in HCC according to the size of the tumor.

4. HCV-Ab titer and 7S collagen level

Fig. 4 shows the HCV-Ab titer in our chronic liver disease cases. More than 70% were strongly positive for HCV-Ab with the lowest proportion being in LC. Fig. 5 shows the correlation between the HCV-Ab titer and 7S collagen and indicates that there was no correlation between the two parameters.

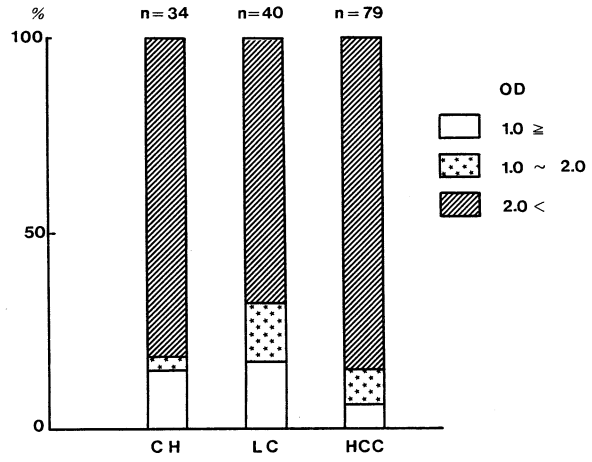

Fig. 4. HCV-Ab titer in various liver diseases.

DISSCUSSION

It is well known that serum 7S collagen increases in chronic liver diseases and especially in LC. Several reports[6–10] have indicated that serum 7S collagen is higher in CAH than in CIH, and the highest level is seen in LC (Table 2). It has also been reported that 7S collagen is higher in alcoholic LC

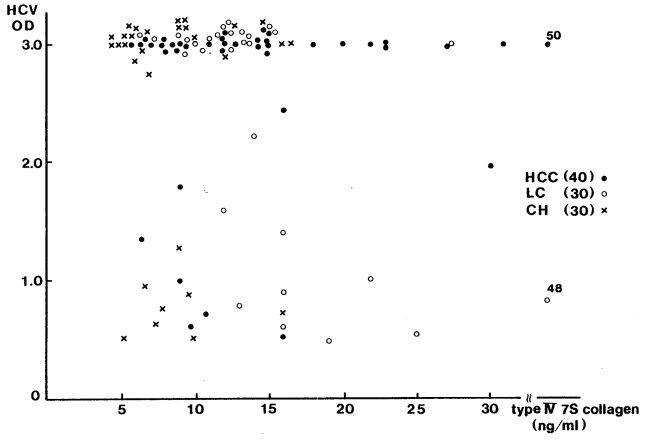

Fig. 5. Correlation between HCV-Ab titer and serum 7S collagen.

than in nonalcoholic LC.[8,9] In the present report, with non-alcoholic HCV-Ab positive chronic liver diseases, the level of serum 7S collagen was highest in LC (14.4±8.1 ng/ml), followed by those for CAH (9.8±3.8 ng/ml), and CIH (6.1±1.8 ng/ml). These data coincide well with report by Yamada *et al.*[9] As for discrepancies in the level of 7S collagen in HCC in our cases and those of other reports,[6-9] these may be explained by accompanying renal disturbance,[6] coexisting LC,[7] and destruction of the basement membrane due to the growth of the tumor.[11] From the above data it may be germane to say that serum 7S collagen increases with the progression of chronic liver diseases and thus it can be a good marker of liver fibrosis.

Table 2. Reports of serum 7S collagen found in the literature.

	Normal	CIH	CAH	LC	HCC
Nakayama (1990)	3.7±0.1 (n=42)	5.1±0.5 (n= 7)	7.1±0.3 (n=21)	9.2±0.6 (n=16)	17.4±1.7 (n=33)
Igarashi (1990)	3.7±1.1 (n=20)	3.1±1.6 (n=36)	4.5±2.1 (n=30)	6.7±2.9 (n=65)	7.8±2.7 (n=36)
Saga (1990)	4.1±0.9 (n=44)	5.4±1.8 (n=10)	5.8±1.7 (n=55)	7.8±2.9 (n=45)	11.6±7.6 (n=27)
Yamada (1990)	4.2±0.9 (n=30)	6.5±2.5 (n=16)	9.5±3.8 (n=25)	14.4±7.5 (n=29)	14.7±6.9 (n=30)
Misaki (1990)	3.7±0.6 (n=34)	4.1±1.1 (n= 9)	5.3±1.7 (n=13)	8.6±2.8 (n= 9)	
Present cases (1990)	3.9±0.4 (n=20)	6.1±1.8 (n=11)	9.8±3.8 (n=19)	14.4±8.1 (n=30)	14.5±8.6 (n=40)

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