Acidic glycosaminoglycans in human liver cirrhosis at various stages

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Liver cirrhosis becomes evident on the accumulation of acidic glycosaminoglycan (AGAG) content in the human liver increases with the fibrotic process in proportion to the collagen content. Not much study of the AGAG components, however, was undertaken at various stages of liver cirrhosis. The present study is a report on AGAG components at various fibrotic stages in the human liver; for this purpose, enzymatic assay methods and electrophoretic characterization were mainly used. This approach is feasible to analyze the AGAG components in liver tissue, in which various microheterogeneity of the AGAG components has been indicated with advancing age (Fig. 1).

Liver specimens were obtained from normal human liver and at various stages of liver cirrhosis within 7 h following death at which time the stages of liver cirrhosis were classified as early, typical and advanced, according to the histopathological examination. All liver specimens (10 g wet tissue weight) were obtained at the convex of the right lobe and cut into small pieces. The procedure of preparation and purification for the AGAG in organs was principally made by the method reported previously. After digestion with pronase, treatment with DNAase followed by RNAase was carried out in 0.1 M Tris buffer at pH 7.4 for 18 h and 5 % cetylpyridinium chloride (CPC) was added to form the CPC-AGAG complex. The result showed that the total AGAG content in duplicates was very close, exceeding 92%.

The AGAG content in human cirrhotic liver was 5—6 times that in the normal state (0.1 mg/g DFTW). The most predominant AGAG components in normal human liver tissue were heparan sulfates (HS) which accounting for 63% of the total AGAG, followed, by a moderate amount of dermatan sulfate (DS) and small amounts of chondroitin sulfate isomers and hyaluronic acid (HA). In addition, the oversulfated DS could be detected in human liver. The increase in both HS and DS content reflects an increase in total AGAG with advancing liver cirrhosis. The ratio of non-sulfated AGAG, HA plus chondroitin, to DS plus its oversulfated isomer was 0.24 in the normal state but it increased to 0.80 at the early stage of liver cirrhosis. However, the ratio decreased to 0.36 and 0.21 at the typical and advanced stages of liver cirrhosis, respectively, with progress in the fibrotic process.

In the present study, a specific change in the AGAG components in human liver was found to occur at the early stage of liver cirrhosis, at which time HA and chondroitin content increased. Also, this paper first reported that over-sulfated DS is present in human liver and suggesting to be the same components as reported in animal liver.

References
Fig. 1. Elution profiles of AGAG depend on molecular weights at various stages of human liver cirrhosis by Sephadex G-200 column chromatography. Note the shift of AGAG to larger molecular weight with the severity of fibrosis. ▼—▼, normal; □—□, early stage; •—•, advanced stage.

Fig. 2. Molecular weight-dependent distribution of AGAG at the typical stage of liver cirrhosis. The △ Di-S were prepared from the corresponding AGAG fraction of Fig. 1 after digestion with chondroitinase ABC. Note that △ Di-4S (derived from DS) was predominant at the moderate size fractions accompanying with △ Di-diS. HA and chondroitin were prominent at larger molecular weight fractions.