

Activated hepatic stellate cells in liver cirrhosis. A morphologic and morphometrical study

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SUMMARY

Hepatic stellate cells have been considered the most important cell-type involved in hepatic fibrogenesis. Proliferation and differentiation of hepatic stellate cells into myofibroblast-like cells has been related to the development of liver fibrosis. The alpha-actin expressed by hepatic stellate cells was considered a marker of their activation to myofibroblast-like cell.

The aim of this study is to evaluate the changes in morphology, distribution, percentage and alpha-smooth muscle actin expression of hepatic stellate cells in normal and cirrhotic livers, and to correlate activated hepatic stellate cells with the progression of fibrosis.

Human liver biopsies (n=121) were divided in five groups: 1) normal livers (controls); 2) cirrhosis post-HCV hepatitis; 3) cirrhosis post-HBV hepatitis; 4) non viral related cirrhosis; 5) recurrent HCV hepatitis after orthotopic liver transplantation. Samples immunostained with anti alpha-smooth muscle actin antibody by immunoperoxidase method were semi-quantitatively evaluated. Liver fibrosis was quantified by computer image analysis on specimens stained with Masson's trichrome.

In normal adult livers stellate cells were very rarely stained for alpha-smooth muscle actin. In cirrhotic livers, a strongly enhanced percentage of stellate cells expressing alpha-smooth muscle actin was detected in cirrhotic fragments with respect to the control group, with a significant correlation between alpha-smooth muscle actin positive stellate cells and the volume fraction of fibrosis. Moreover, liver biopsies of recurrent hepatitis revealed an increased number of activated stellate cells compared to normal livers, and intermediate volume fraction of fibrosis.

These results confirmed that a direct correlation existed between activated stellate cells and the progression of fibrosis. Alpha-smooth muscle actin confirmed to be a reliable marker of hepatic stellate cells activation also in precocious stages of the disease.