

The Kinetics of Macrophages, Myofibroblasts and Mast cells in Carbon Tetrachloride - Induced Rat Liver Cirrhosis

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Hepatic fibrosis/cirrhosis is characterized by increased production and deposition of collagen, noncollagenous glycoproteins, and proteoglycans, which mainly compose the extracellular matrix(ECM). Recently, activations of macrophages, myofibroblasts and mast cells are thought to be associated with the accumulation of ECM. In order to investigate the kinetics of macrophages, myofibroblasts and mast cells and the relationship between these cells and the accumulation of ECM in carbon tetrachloride (CCl₄)-injected rat liver, we induced liver cirrhosis of rat by an injection of CCl₄ for 14 weeks. The observation of the association between the presence of mast cells and the accumulation of ECM was initiated to characterize the role of these cells during liver fibrosis/cirrhosis. Macrophages and myofibroblasts were observed with immunohistochemistry in the three regions (perivenular, periportal and midlobular regions). In the rat liver injured by CCl₄, mast cell numbers increased in proportion to the development of liver fibrosis at maximum number on week 14. The number of ED1-positive macrophages increased during weeks 4 to 10 and peaked on week 8 in the perivenular regions and on week 10 in the periportal and midlobular regions. In the periportal and midlobular regions, the number of ED1-positive macrophages decreased from weeks 12 to 14 and from weeks 10 to 14 in the perivenular regions. From weeks 4 to 10, the number of α -SMA-positive myofibroblasts gradually increased and then, decreased on weeks 12 and 14 in the three regions. These findings suggest that the increased numbers of macrophages and myofibroblasts correlate with the development of rat liver fibrosis, but not with cirrhosis. Furthermore, increased mast cells are associated with both fibrosis and cirrhosis. However, there was no significant relationship between the former two cells and mast cells regarding their numbers in cirrhotic liver of rat.