

Assessment of Activity in Inflammatory Liver Diseases: A Critical Appraisal

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In the context of chronic liver disease, the term “activity” is used to describe ongoing damage (usually inflammation), which has the potential to lead to progressive liver injury in the form of fibrosis or cirrhosis. Other manifestations of activity that can be assessed histologically include fatty change, hepatocyte ballooning and bile duct injury.

Two main patterns of liver inflammation are recognised - portal/periportal and lobular. Portal inflammation is the main pattern occurring in most chronic liver diseases and may be associated with varying degrees of activity in the form of interface hepatitis. Lobular inflammation typically predominates in acute hepatitis, but is also frequently present in many chronic liver diseases. The severity of lobular inflammatory activity is assessed according to the extent of the associated liver cell apoptosis/ necrosis (spotty, confluent, bridging, panacinar or multiacinar). The degree to which histological inflammatory activity correlates with biochemical markers of activity (e.g. serum transaminase levels) is variable.

Assessing the severity of inflammatory activity has been shown to have prognostic value and thus also has therapeutic implications. For example in chronic inflammatory liver diseases related to hepatitis C virus (HCV) infection, primary biliary cirrhosis (PBC) or autoimmune hepatitis (AIH), the severity of interface hepatitis is predictive for the development of progressive periportal fibrosis. In AIH, interface hepatitis usually responds to treatment with immunosuppression, whereas severe lobular inflammatory activity (bridging or panacinar necrosis) is associated with disease progression and a poor response to immunosuppression. Histological assessment of inflammatory activity is also used to guide therapy in patients with suspected autoimmune overlap syndromes.

A number of semi-quantitative scoring schemes for grading necro-inflammatory activity have been described. These include the systems proposed by Knodell (1981), Scheuer (1991), the French METAVIR Group (1994), Ishak (1995) and Batts and Ludwig (1995). Although these approaches are useful, particularly for research studies and clinical trials, there are a number of problems which limit their utility in routine clinical practice. Observer agreement is generally less good for inflammatory grade than for fibrosis stage. Sampling variability is also a consideration, particularly in the more severe forms of lobular necro-inflammatory activity, which are typically patchy in distribution. Advances in the knowledge of the natural history of some chronic liver diseases have also changed the role of liver biopsy. For example, in chronic HCV infection therapeutic decisions are now based on viral genotype, which determines the likelihood of achieving a sustained virological response and liver biopsy is no longer routinely used to assess inflammatory activity.

Alternative grading systems have been proposed for the assessment of non-alcoholic fatty liver disease, where the severity of steatosis and hepatocyte ballooning are also thought to be important in predicting disease progression (e.g. Brunt 1999 and Kleiner 2005). A recent scheme has also been proposed for grading disease activity in PBC (Hiramatsu 2006).

There has been considerable recent interest in non-invasive methods for assessing the severity of liver disease. These have mostly focused on the assessment of liver fibrosis and are likely to change the role of liver biopsy in this regard. The extent to which non-invasive approaches may be used to assess aspects of disease activity requires further study.

References:

1. Burt AD, Portmann BC, Ferrell LD eds. *MacSween's Pathology of the Liver*, 5th edition. Edinburgh: Churchill Livingstone, 2007.
2. Scheuer PJ, Lefkowitz JH. *Liver Biopsy Interpretation*, 7th edition. Philadelphia : Elsevier Saunders, 2006.