EDITORIALS

Liver Biopsy Remains the Gold Standard for Evaluation of Chronic Hepatitis and Fibrosis

Husain A. Saleh[1], Ahmad H Abu-Rashed[2]

1) Department of Pathology. 2) Section of Gastroenterology, Sinai Grace Hospital, Detroit, Michigan, USA

The diagnosis, grading and staging, and management of chronic hepatitis and fibrosis are dependent on many investigative studies and tests including imaging techniques, molecular biological methods and serologic or biochemical tests. However, in spite of recent advances in non-invasive techniques, liver biopsy continues to be the "gold standard" method in evaluating chronic hepatitis and fibrosis. This is true because the basic concepts and widely used fundamental classification of liver disease is based on the morphology and histological alterations in normal hepatic structures. This is also logical because examining a liver biopsy under the microscope is a direct way of visualizing a patient's liver abnormality and identifying the exact changes in hepatic tissue. In addition, the emphasis before was primarily on diagnosing the liver disease, but now pathologists are required and repeatedly asked, to evaluate patients for possible treatment. In addition they must monitor those already receiving medical therapy of various kinds including liver transplant.

Liver biopsy is considered an invasive procedure and is usually performed on inpatients, although it is also done as an outpatient procedure on carefully selected cases. General guidelines are established and should be followed to minimize the risk of complications such as bleeding and hematomas. Operator skills and professional training are also essential to safeguard against complications. The low mortality and morbidity rates reflected in practice and review studies during the last two decades have facilitated the widespread use of liver biopsy procedure (1). The excellent paper by Sporea et al in the last issue of the *Journal of Gastrointestinal and Liver Diseases* (2), very nicely demonstrated that, in experienced hands, percutaneous liver biopsy can obtain "good" histological material in the vast majority of cases. In their study, they retrospectively analyzed 250 echoassisted percutaneous liver biopsies obtained for staging of chronic hepatitis concerning the length and number of portal areas of the biopsy. In 87% of cases, the biopsy had 8-10 portal areas (good biopsy) and in 69% the biopsy had at least 11 portal areas (very good biopsy). In 13% of cases the biopsy was suboptimal containing less than 8 portal areas, and only 1.6% was inadequate with less than 4 portal areas. As for the length, 88% of cases had a biopsy longer than 2 cm, and only in 12% the biopsy was less than 2 cm.

A review study by Gebo et al in *Hepatology* (3) supported by Healthcare Research and Quality recently compared liver biopsies with biochemical and serologic tests in predicting treatment outcomes for chronic hepatitis C. They found that a liver biopsy may have some usefulness in predicting efficacy of treatment of these patients, while biochemical and serologic tests have only a modest value in predicting fibrosis on a liver biopsy.

Due to the advances in imaging techniques and development of reliable serological and virological tests, the indications for liver biopsy have changed and the techniques for the biopsy have been refined (4). Although blind percutaneous transcapsular biopsies are still used, ultrasound or CT- guided biopsies have become increasingly popular and more favored especially when targeting localized lesions within the liver and for direct visualization of the surrounding structures. Additionally, it is the quickest and safest technique with the lowest rate of reported complications (5-7). Sometimes, transvenous, particularly transjugular, biopsy samples are obtained. The choice of technique is largely dictated by the clinical setting (e.g. associated coagulation disorders, presence or absence of ascites, results of US examination), the operator's experience and the nature of the disease under investigation. In spite of these advanced imaging studies and advocating their use to evaluate chronic hepatitis and cirrhosis, the liver biopsy tissue is still regarded as the best method for assessing this liver disease. In a recent study by Guido and Rugge on liver biopsy sampling of 212 cases, histologic examination revealed cirrhosis in 10 cases found negative after US studies, whereas US suggested cirrhosis in 32 histologically negative cases (1).

The biopsy needle can be of a suction type (Menghini) or a cutting type (Tru-Cut). The Tru-Cut needle produces a larger sample but has been associated with more compli-

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Address for correspondence: Husain Saleh, MD, FIAC, MBA
Department of Pathology
Sinai-Grace Hospital
6071 W. Outer Dr.
48235, Detroit, MI, USA
E-mail: hsaleh@med.wayne.edu

cations. The Menghini needle produces a more fragmented sample but, because it remains in the parenchyma "one second" only, it has a lower risk of bleeding. The size of the biopsy can be large (obtained by 14-21 gauge needles) or thin (less than 21 gauge needle) which is highly recommended for the diagnosis of focal lesions. However, its use for grading and staging chronic hepatitis is under debate. In a recent study by Petz et al, in which large (17 gauge Menghini needle) and thin (20 gauge modified cutting Menghini needle) biopsies from 88 patients with chronic viral hepatitis were retrospectively re-evaluated, it was found that when clinical cirrhosis was taken as the "gold standard", cirrhosis was histologically diagnosed by thin samples in 44% of cases and by large samples in 60%. This means that the biopsy size was relevant (8). Another study by Colloredo et al provided evidence that both the length and width of the biopsy core impact grading and staging and that examining shorter and thinner biopsy samples leads to an underestimation of the severity of disease (9). Moreover, disease activity and fibrosis were underestimated in thin samples regardless of the length, suggesting that the main problem lies in the number of complete portal areas (must contain 11 or more), which are the site of damage in chronic hepatitis. The conclusion was that a liver biopsy 2.0 cm long and 1.4 cm thick guaranteed an adequate number of portal areas in 94% of cases. In general, the complications following percutaneous liver biopsy are related to the patient's clinical condition, the operator's expertise, the type of needle and the number of passes (1).

Because the biopsy is a very small piece of the whole liver organ (1/50000), there is a possibility of a sampling error if the disease is localized or focal such as a tumor or granuloma. If a focal disease or unevenly distributed disease is suspected, multiple biopsies should be obtained. However, available data confirm that in diffuse processes such as chronic hepatitis, a liver biopsy is representative of the liver disease and ensures accurate diagnosis (1). The general consensus is that, in most cases, an adequate size and properly processed biopsy is an essential tool for the assessment and accurate diagnosis of liver disease. Of course, the clinical, biochemical, serological and imaging information complement the biopsy findings and produce a more meaningful pathology report.

Most authors agree that a biopsy size of 2.0 cm containing a minimum 11 portal triads is required for correct interpretation, grading and staging of chronic viral hepatitis and fibrosis. Other authoritative literature, however, suggest that a 1.5 cm long biopsy with 4 to 5 portal areas is sufficient for the histological evaluation of chronic hepatitis and cirrhosis (10). An important study by Abdi et al (11) showed that the yield of diagnosis of cirrhosis was 80% with one biopsy sample, which reached 100% when three biopsy samples were obtained and examined. Superiority of multiple samples was also supported in a study by Maharaj et al (12). It is very important that the pathologist recognizes the limitations of a given liver biopsy. If it is of an inadequate small size, having only a few portal areas or improperly processed, this should be clearly stated and communicated to the clinician. Pathologists and hepatologists alike nowadays understand the recommendations of the important study by Colloredo et al, which introduced the concept of a "minimum number of complete portal tracts" required for accurate diagnosis.

Conclusion

In conclusion, liver biopsy is an essential method for assessing chronic hepatitis and fibrosis and the main goal of the biopsy is to grade and stage liver damage for prognosis and treatment. An adequate sample should be 2.0 cm or longer containing 11 or more complete portal areas. This conclusion was further reiterated by two recent studies by Bedossa et al and Brunetti et al (13, 14). The recent advances in imaging, molecular and biochemical tests complement but do not replace liver biopsy in this regard.

References

1. Guido M, Rugge M. Liver biopsy sampling in chronic viral hepatitis.
Semin Liver Dis 2004; 24: 89-97.
2. Sporea I, Sirli R, Popescu A, Cornianu M, Manciu C, Focsa M. The quality of the fragment obtained by liver biopsy for staging chronic hepatitis. J Gastrointestin Liver Dis 2007;16: 263-266.
3. Gebo KA, Herlong HF, Torbenson MS, et al. Role of liver biopsy in management of chronic hepatitis C: a systematic review. Hepatology 2002; 36(5 Suppl 1): S161-172.
4. Van Leeuwen DJ, Wilson L, Crowe DR. Liver biopsy in the mid-1990s: questions and answers. Semin Liver Dis 1995;15: 340-359.
5. Grant A, Neuberger J. Guidelines on the use of liver biopsy in clinical practice. British Society of Gastroenterology. Gut 1999; 45 Suppl 4: IV1-IV11.
6. Farrell RJ, Smiddy PF, Pilkington RM, et al. Guided versus blind liver biopsy for chronic hepatitis C: clinical benefits and costs. J Hepatol 1999; 30: 580-587.
7. Piccinino F, Sagnelli E, Pasquale G, Giusti G. Complications following percutaneous liver biopsy. A multicentre retrospective study on 68,276 biopsies. J Hepatol 1986; 2: 165-173.
8. Petz D, Klauck S, Rohl FW, Malfertheiner P, Roessner A, Röcken C. Feasibility of histological grading and staging of chronic viral hepatitis using specimens obtained by thin-needle biopsy. Virchows Arch 2003; 442: 238-244.
9. Colloredo G, Guido M, Sonzogni A, Leandro G. Impact of liver biopsy size on histological evaluation of chronic viral hepatitis: the smaller the sample, the milder the disease. J Hepatol 2003; 39: 239-244.
10. Bravo AA, Sheth SG, Chopra S. Liver biopsy. N Engl J Med 2001; 344: 495-500.
11. Abdi W, Milln JC, Mezey E. Sampling variability on percutaneous liver biopsy. Arch Intern Med 1979; 139: 667-669.
12. Maharaj B, Maharaj RJ, Leary WP, et al. Sampling variability and its influence on the diagnostic yield of percutaneous needle biopsy of the liver. Lancet 1986; 1: 523-525.
13. Bedossa P, Dargčre D, Paradis V. Sampling variability of liver fibrosis in chronic hepatitis C. Hepatology 2003;38:1449-1457.
14. Brunetti E, Silini E, Pistorio A, et al. Coarse vs. fine needle aspiration biopsy for the assessment of diffuse liver disease from hepatitis C virus-related chronic hepatitis. J Hepatol 2004; 40: 501-506.