CLINICAL @LERT

To perform or not to perform liver biopsy—that is the question

R W Chapman

Should liver biopsy be performed to determine the cause of abnormal liver biochemical tests in the absence of diagnostic serology?

COMMENT

One of the most difficult management decisions in clinical hepatology, especially for the general gastroenterologist, is whether to perform a liver biopsy in a patient with abnormal liver function tests, particularly in the absence of diagnostic serology, or a history of drug or alcohol use. At first sight the benefits of performing an invasive procedure in such asymptomatic patients are not obvious when balanced against the potential hazards of bile leak or haemorrhage.[1]

Histological causes of abnormal liver biochemistry have been studied previously in patients with excess alcohol ingestion or advanced liver disease.[2 3] However, to date, there have been few published histological data on asymptomatic patients with persistently abnormal liver enzyme abnormalities on which to base management decisions such as liver biopsy. In a recent Scandinavian study, 150 asymptomatic patients with elevated serum transaminases underwent liver biopsy.[4] While fibrosis was observed in half of the biopsies, only 2% were cirrhotic, and in the majority a mild pericellular fibrosis was seen, the clinical significance of which was unclear. Despite the lack of evidence, a recent review concluded that liver histology should be obtained in such asymptomatic patients.[5] Is this conclusion correct? The study from Skelly and colleagues[6] would suggest that it is. In this important prospective study, 354 patients with persistently abnormal liver enzymes (more than twice the upper limit of normal for greater than six months) underwent liver biopsy. Although not definitely stated, it is implied that patients were asymptomatic. Perhaps not surprisingly, in view of similar results obtained by Daniel and colleagues,[7] by far the most prevalent histological findings in the study were non-alcoholic steatohepatitis (NASH) and the associated lesion non-alcoholic fatty liver disease (NAFLD), which was found in two thirds of the patients studied. Does this matter? Recent evidence would suggest that approximately one third of NAFLD patients will progress to fibrosis and 20% will develop cirrhosis.[8 9] Accurate diagnosis of fibrotic liver disease, found in 20% of the patients in this study, may expedite earlier therapeutic intervention which may prevent progression to end stage liver disease.

The most important finding of the study was that in 18% of patients their management was directly altered by the histological findings. Six per cent were found to have cirrhosis, and a wide variety of chronic liver diseases (some familial) were diagnosed. Previously unsuspected alcohol was discovered in 10 patients, as Kingham has pointed out, "I suspect one man's NASH is another man's ASH".[10] Interestingly, very similar results were obtained in a smaller prospective study from the Mayo Clinic[11] but the authors reached an exactly opposite conclusion viz that "routine biopsies with chronically abnormal liver tests are of limited clinical value". They reached this conclusion on the grounds that little specific therapy is available for NAFLD. I believe however that the study by Skelly *et al* has made a strong case for liver biopsy in the majority of asymptomatic patients with persistently abnormal liver tests.

The unresolved question from this study is whether a liver biopsy is indicated in patients with an isolated rise in serum gammaglutamyl transpeptidase. In the present study, 11% of such patients had fibrosis although the degree is not described. However, in a report from our unit, none of our patients, all of whom were alcoholic, had any fibrosis or signs of progressive liver

Skelly MM, James PD, Ryder SD. Findings on liver biopsy to investigate abnormal liver function tests in the absence of diagnostic serology. *J Hepatol* 2001;**35**:195–9.

Background: The use of liver biopsy in determine the cause of abnormal liver biochemical tests in the absence of diagnostic serology is unclear.
Objective: To describe histological findings on liver biopsy of a large number of patients with abnormal liver biochemical tests in whom the aetiology was unclear from serological tests.
Design: A prospective case series.
Patients: Consecutive patients at the University Hospital, Queen's Medical Centre, Nottingham, UK, who underwent liver biopsy for investigation of unexplained abnormal liver function tests (n=354). Patients were excluded if they had positive serological testing for autoantibodies, viral markers, copper and iron storage, α_1 antitrypsin deficiency, or a known diagnosis of liver disease or a history of alcohol intake above the recommended limits.
Results: There were 21 normal liver biopsies (6%). Final diagnoses included non-alcoholic steatohepatitis in 120 (34%) cases and fatty liver in 115 (32%). Cryptogenic hepatitis was described in 32 (9%) patients and drug related damage in 27 (7. 6%). Other diagnoses included alcohol related disease in 10 (2.8%) patients, autoimmune hepatitis in seven (1. 9%), and a variety of other autoimmune and storage diseases in small numbers. Some degree of fibrosis was found on biopsy in 93 patients (26%), including cirrhosis in 21 cases (6%), but biochemical abnormality did not predict liver biopsy findings.
Conclusions: Liver biopsy was helpful in the diagnosis and management in patients with abnormal liver biochemistry with negative serological markers. The most common abnormalities were non-alcoholic steatohepatitis and fatty liver. Biochemical abnormality was a poor predictor of stage of liver disease.

disease.[12] Further larger studies are required to answer this important issue.

Gut 2002;**50**:9–10

Author's affiliation
R W Chapman, Department of Hepatology/Gastroenterology, John Radcliffe Hospital, Headington, Oxford OX3 9DU, UK; roger.chapman@ndm.ox.ac.uk

REFERENCES

1 **Grant A**, Neuberger J. Guidelines on the use of liver biopsy in clinical practice. British Society of Gastroenterology. *Gut* 1999;**45**(suppl 4):IVI.
2 **Van Ness NM**, Diehl AM. Is liver biopsy useful in the evaluation of patients with elevated liver enzymes? *Ann Intern Med* 1989;**11**:473–8.
3 **Hay JE**, Czaja AJ, Rakela J, *et al*. The nature of unexplained chronic aminotransferase elevation of a mild to moderate degree in asymptomatic patients. *Hepatology* 1989;**9**:193–7.
4 **Mathiesen UL**, Franzen LE, Fryden A, *et al*. The clinical significance of slightly to moderately increased liver transaminase values in asymptomatic patients. *Scand J Gastroenterol* 1999;**34**:85–91.
5 **Pratt DS**, Kaplan MM. Evaluation of abnormal liver-enzyme results in asymptomatic patients. *N Engl J Med* 2000;**342**:1266–71.
6 **Skelly MM**, James PD, Ryder SD. Findings on liver biosy to investigate abnormal liver function tests in the absence of diagnostic serology. *J Hepatol* 2001;**35**:195–9.
7 **Daniel S**, Ben-Menachem T, Vasudevan GCK, *et al*. Prospective evaluation of unexplained chronic liver transaminase abnormalities in asymptomatic and symptomatic patients. *Am J Gastroenterol* 1999;**94**:3010–14.
8 **Powell EE**, Cooksley WGE, Hanson R, *et al*. The natural history of non-alcoholic steatohepatitis; a follow up study of forty-two patients for up to 21 years. *Hepatology* 1990;**11**:74–80.
9 **Bacon BR**, Farahvash MJ, Janney CG, *et al*. Non-alcoholic steatohepatitis: an expanded clinical entity. *Gastroenterology* 1994;**107**:1103–9.
10 **Kingham JGC**. Dissecting out cryptogenic liver disease. *Gut* 2000;**47**:328–9.
11 **Sorbi D**, McGill DB, Thistle JL, *et al*. An assessment of the role of liver biopsies in asymptomatic patients with chronic liver test abnormalities. *Am J Gastroenterol* 2000;**95**:3206–10.
12 **Ireland A**, Hartley L, Ryley N, *et al*. Raised gamma-glutamyltransferases activity and the need for liver biopsy. *BMJ* 1991;**303**:388–9.