Regular Review

Liver biopsy: techniques, clinical applications, and complications

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"It is often only by puncture biopsy of the liver that a precise diagnosis can be made and when diagnosis is doubtful, treatment, advice and prognosis are apt to be hesitant, and perhaps as a consequence, the handling of the patient ineffective."

H P Himsworth, 1950¹

Thirty years on, this statement remains true: and with its widespread application and the development of specialised staining techniques liver biopsy continues to be one of the most important diagnostic procedures in clinical hepatology. The maximum benefit from the procedure can be obtained, however, only when it is performed by properly trained and experienced personnel and when the histological examination is done by a histopathologist familiar with the morphological appearances of the liver in health and disease. Successful liver biopsy without complications demands good technique, and this applies particularly in patients with cirrhosis, in whom inadequate specimens and serious complications are the hallmarks of the inexperienced operator.

Techniques and types

The choice of technique used to biopsy the liver is dictated by the coagulation state of the patient, the presence of ascites, and whether the liver is cirrhotic or contains an obvious space occupying lesion. The ability of the patient to cooperate during the procedure is a further consideration, and general anaesthesia should be used in children from 2 to 10 years of age and in stuporous or psychotic patients. Otherwise the procedure is carried out under local anaesthesia.

Patients with a vitamin K resistant rise in the prothrombin time of four to six seconds above control values or a platelet count of less than $40 \times 10^9/l$ have an increased risk of bleeding and should be given two units of fresh frozen plasma or platelet concentrate as a continuous infusion starting half an hour before and continuing for one hour after the procedure. Alternatively, and in patients with more severe coagulation defects, the transjugular approach can be used (see below). This method is also best in patients with appreciable ascites, who otherwise risk lacerations of the liver substance from repeated attempts at conventional percutaneous biopsy.

In patients with suspected cirrhosis we consider it essential to use the Tru-Cut biopsy needle since the specimen rarely fragments (unlike that obtained with the Menghini needle), and an accurate diagnosis of cirrhosis is possible in most instances. Tissue may be obtained from discrete space occupying lesions within the liver by direct percutaneous biopsy of a

palpable mass, by an ultrasound guided approach for smaller intrahepatic lesions, or by biopsy under direct vision at laparoscopy.

Regardless of the type of needle used percutaneous biopsy is best performed with the patient in the supine position close to and parallel to the edge of the bed, with his right hand positioned behind the head. The site for the biopsy is selected by caudal percussion over the hemithorax between the anterior and midaxillary lines until an intercostal space is reached where dullness is maximal at the end of expiration. The intercostal space below this point is used, and to ensure a painless procedure 5-10 ml of lignocaine 2% (without adrenaline) is infiltrated, firstly subcutaneously, then into the intercostal area, and finally down to the diaphragm and capsule of the liver, care being taken to infiltrate each layer adequately.

The simplest and thereby safest technique is with the Menghini needle, a suction device which reduces the time spent within the liver substance to less than a second. The needle is 6 cm long with an oblique tip slightly convex towards the outside, and a retaining device is incorporated in its proximal end to prevent liver tissue being aspirated into the syringe. The diameter of the needle should not exceed 1.4 mm and a penetration limiter should be used for children and thin adult patients. Steady suction is applied to the syringe connected to the needle and the patient asked to exhale fully. The needle is then advanced into the liver and rapidly withdrawn. The specimen is discharged from the needle into a 10% formaldehyde solution.

The Tru-Cut biopsy needle is a disposable modification of the Vim-Silverman obturator and cannula; an obturator with a pointed end and a cannula are integrated into an all in one design. The device is advanced 2 to 3 cm into the liver substance in the closed position, the obturator is advanced holding the outer cutting sheath steady, and finally the sheath is advanced to cut the liver and the whole assembly is withdrawn. The entire manoeuvre should take less than three seconds, and specimens 1 mm in diameter and 1-2 cm in length are usually obtained.

After biopsy the patient should be monitored carefully for haemorrhage and other complications, with half hourly recordings of pulse rate and blood pressure for two hours and then hourly recordings for four hours. In Britain until relatively recently liver biopsy was considered an inpatient procedure requiring rest and observation in bed for 24 hours. Studies from North America on a total of 829 patients have shown, however, that the procedure may be carried out safely without serious complications on a day case basis with observation after the biopsy for three hours.² Our own experience with 200 consecutive day case biopsies was similar, with

only six patients developing complications requiring overnight observation, none of which were life threatening.³ At that time we considered patients suitable for biopsy on a day case basis if the prothrombin time was prolonged less than four seconds and the platelet count exceeded $80 \times 10^9/l$; it was contraindicated in the presence of ascites or suspected tumour or abscess. We have had no reason to change this policy in recent years. The patients are admitted to the day ward at 8 am, having had an ultrasound examination and a check prothrombin time and platelet count performed as an out-patient. After the procedure patients are monitored as described above for four hours, examined at six hours just before discharge, advised to remain within easy reach of the hospital overnight, and provided with the hospital telephone number and the name of a member of staff to contact should severe pain, syncope, or other features develop.

Transjugular liver biopsy

Liver biopsy through the internal jugular vein was first described in 1973 and has been advocated in patients with abnormal blood coagulation, in whom the risk of percutaneous biopsy may be unacceptable.⁴ A recent study detailed the use of a Tru-Cut needle mounted on a flexible coaxial cable, showing that adequate specimens could be obtained in over 95% of patients with few complications.⁵ The method has advantages with uncooperative patients and those with small livers or ascites, and when multiple specimens are required; it also permits simultaneous hepatic phlebography and measurements of free and wedged hepatic venous pressure.

Until recently the decision to perform liver biopsy was based largely on clinical impressions and the pattern of abnormal liver function values, both of which may be unreliable in distinguishing parenchymal liver disease from mechanical obstruction of the biliary tree. A mistaken diagnosis of extrahepatic biliary obstruction in patients with chronic parenchymal liver disease or intrahepatic cholestasis may lead to an unnecessary laparotomy—with its potentially serious consequences.⁶ Such disasters should be very much less likely now that ultrasonography is becoming widely available for the initial assessment. This non-invasive procedure is very reliable in differentiating between extrahepatic biliary obstruction and other causes of jaundice, detecting ductal dilatation in 95% of cases.⁷ In combination with cholangiography ultrasound will also define the likely nature of the obstruction, and so remove the need for liver biopsy—which in any event would have established only the presence of obstruction and not its cause.

Gall stones and space occupying lesions are readily detected by ultrasound, which can usually differentiate tumours, cysts, and abscesses. Ultrasound is of immediate diagnostic value in identifying those patients with hydatid liver disease (with the characteristic appearance of single or multiple thick walled, often calcified, cysts containing multiple daughter cysts)—in whom liver biopsy must be avoided because of the risk of peritoneal seeding and anaphylactic shock. In addition to detecting discrete space occupying lesions, ultrasound is also being used increasingly to guide the biopsy needle to these lesions when a histological diagnosis is considered necessary. The ultrasonic echo pattern may also indicate the presence of chronic liver disease such as cirrhosis, in which a bright highly packed heterogeneous pattern is seen. Thus any rational scheme of investigation of patients with liver disease should include an ultrasound examination as the first

investigation (figure). The procedure may be performed in outpatients, the results are immediately available, and the appropriate diagnostic process can be rapidly initiated with substantial savings in costs.

Rational scheme of investigation of liver disease. PTC=Percutaneous transhepatic cholangiography. ERCP=Endoscopic retrograde cholangiopancreatography.

Diffuse parenchymal liver

Patients are commonly referred after detection on medical screening of abnormalities of liver function values. Most often the abnormalities are related to alcohol intake. Histological confirmation of the diagnosis is important in establishing the severity of damage since the management of such patients will depend on whether the lesion is reversible (fatty infiltration), precirrhotic (alcoholic hepatitis), or irreversible (cirrhosis). In the last two stages of the disease maintained abstinence is imperative if the patient is to avoid the development of cirrhosis and the complications of established portal hypertension such as variceal haemorrhage. Abnormal liver function values may also be found on biopsy to be due to other forms of chronic liver disease such as primary biliary cirrhosis or chronic active hepatitis. Another important diagnostic category with implications for treatment is diffuse malignant infiltration with, for example, lymphoma; in such patients liver biopsy will establish the diagnosis and stage the disease. The presence of granulomatous hepatitis can be confirmed only with liver biopsy, which in a few instances will also establish its aetiology. In Britain most such patients have sarcoidosis or tuberculosis, though there are many other causes, and detailed investigations may be needed.⁸ Intrahepatic cholestasis, presenting clinically as an "obstructive" type jaundice, may usually be distinguished from mechanical obstruction of the biliary tree by the absence of ductal dilatation on ultrasound examination. Several other liver diseases, however, may present with cholestatic features, most notably primary biliary cirrhosis and alcoholic liver disease. Primary sclerosing cholangitis may be diagnosed on the liver biopsy appearances—though in this condition and in most of the other types of intrahepatic cholestasis endoscopic retrograde cholangiography is required as well as liver biopsy.

The likely aetiology and stage of different varieties of chronic hepatitis need to be established so that treatment may be planned. Patients with the histological features of chronic persistent hepatitis—minimal parenchymal necrosis and a mild to moderate lymphocytic infiltration confined to the portal tracts—have an excellent long term prognosis; indeed, though resolution may be delayed for many years, most such patients eventually recover, and treatment is unnecessary.⁹ Since, however, a few patients (particularly those with HBsAg positive and non-A, non-B chronic persistent hepatitis) may progress to chronic active hepatitis biopsy should be repeated at two year intervals—or earlier if

deterioration in liver function occurs. The prognosis of chronic active hepatitis is poor, particularly when severe parenchymal (piecemeal) necrosis is associated with bridging or multilobular collapse.¹⁰ The importance of diagnosing this form of chronic active hepatitis lies in its response to corticosteroids. Treatment gives a definite improvement in survival, particularly in those patients with the HBsAg negative "autoimmune" variant of chronic active hepatitis.¹¹ The goal of treatment is resolution of inflammatory activity, and though improvement in the results of liver function tests gives a general guide to the effects of treatment, only histological examination allows an accurate assessment of disease activity. Liver biopsy in such patients at roughly one to two year intervals permits reduction in the dosage of corticosteroids to the lowest possible levels necessary for control of disease. Since most such patients require corticosteroids long term¹² (they develop reactivation of disease when these are withdrawn) the minimum dosage must be used if serious side effects are to be avoided.

The histological appearances of chronic active hepatitis may be seen in several other conditions, including α_1 antitrypsin deficiency and Wilson's disease. The latter is an important and remediable cause of liver disease in young patients, and the copper content of the biopsy specimen, taken in a copper free container, should be determined if the diagnosis is suspected.

Complications

Reviews of large series of patients show a mortality of between 0.015% and 17%¹³⁻¹⁵ and an incidence of major complications of 0.32%.¹⁴

Transient pain in the tip of the shoulder lasting a few hours and epigastric discomfort during and after the biopsy are common; they require treatment with paracetamol only. More severe and persistent pain, particularly in the right hypochondrium, is likely to indicate a subcapsular accumulation of blood or bile, and the sudden onset of very severe pain suggests biliary peritonitis.

Intraperitoneal haemorrhage is the most frequently encountered serious complication; it usually results from puncture of the arterial tree within the liver or porta hepatis, though it may also be due to perforation of distended external portal vein radicles in patients with cirrhosis. Terry observed clinically significant haemorrhage in 0.2% of 7532 biopsies; four patients required laparotomy, but no deaths were recorded.¹⁴ Lindner reported 67 incidents of bleeding after 80 000 biopsies with the Menghini needle with 22 deaths,¹³ and our own experience is similar using the Tru-Cut needle—one death and eight laparotomies in 4000 biopsies. Haemorrhage after biopsy should initially be managed with blood transfusion, but when there is persistent hypotension and increasing abdominal distension laparotomy is indicated.

Haematobilia, a rare complication of liver biopsy, may be manifested at anything between one and 21 days after the procedure. It results from simultaneous perforation of closely approximated intrahepatic vascular and biliary tree radicles with the development of a persistent communication between these structures. The characteristic clinical syndrome consists of recurrent episodes of biliary colic and jaundice in association with melaena. Retrograde cholangiography or hepatic arteriography or both will establish the diagnosis and localise the bleeding point, which may be treated either by arterial embolisation or, if this fails, by direct surgical ligation

of the affected vessel. Prospective screening with liver scintiscans before and after biopsy have shown that localised intrahepatic haematomas are common after what appears to have been an uncomplicated biopsy.¹⁶ Occasionally these may become clinically apparent when they are of sufficient size to produce persistent pain or obstruction of the biliary tree. Haemorrhage into the pleural cavity has been reported as a result of pleural trauma or perforation of an intercostal artery. Such arterial damage can be avoided by inserting the needle close to the lower border of the intercostal space.

Bile peritonitis is almost entirely preventable by prebiopsy ultrasound screening, since it is seen most commonly in the presence of biliary obstruction. It may still occur, however, in the occasional patient in whom biliary obstruction is present in the absence of ductal dilatation and in patients with unusually positioned gall bladders—a problem seen particularly in patients with small cirrhotic livers. The patient develops severe localised or generalised abdominal pain and hypotension within minutes of the procedure. Biliary peritonitis is usually self limiting and should be managed conservatively with analgesia and antibiotics to prevent secondary infection; only very occasionally is surgical intervention required. Transient bacteraemia has been observed in up to 13% of patients undergoing liver biopsy and patients with valvular heart disease should receive prophylactic antibiotic cover.¹⁷

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