

# Medical Writers' Circle

a series of articles

written by medical  
professionals about  
the management  
and treatment of  
Hepatitis C

## Role of Liver Biopsy in Evaluation and Management of Viral Hepatitis

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**L**iver biopsies have been done for many years. Prior to about 1950, they were performed rather rarely and usually surgically at the time of open surgical operations of the abdomen. The technique of needle biopsy of the liver has become commonplace during the past 50 years, and the great majority of biopsies are now done by this method. In it, patients are generally given a local anesthetic at the right side. Often times, patients now-a-days request and receive a small amount of conscious sedation just prior to the procedure. After suitable preparation, a small needle is quickly put into the liver, and a very small amount of liver is either sucked into the needle through the use of a syringe or a very small amount of liver is cut away and captured in the needle. The amount of liver that is actually removed in such a biopsy ranges between about 20 to 80 mg wet weight of liver. Since the normal adult liver weighs approximately 150,000 mg

(1,500 gm), it is obvious that the amount of liver removed at the time of a needle biopsy is inconsequential and will have no effect on overall liver functioning.

Biopsies performed in this way are quite safe, particularly if suitable precautions are taken prior to the biopsy being done. There should always be a medically sound indication for performance of liver biopsy, the procedure should be explained fully to the patient or the patient's guardian, possible history of a tendency for excessive bleeding should be obtained, patients should not be taking anticoagulants, aspirin, other non-steroidal anti-inflammatory agents, or other agents that may adversely effect the ability of the blood to clot, and coagulation studies and platelet counts should be obtained prior to biopsies being performed. When these precautions are observed, the risk of serious adverse effects is extremely low.

The other major factor that makes liver biopsy safe is for operators to use speed

during the technique. The less time that the needle is actually within the liver, the less chance there is that there will be movement of the patient or the patient's liver and this will minimize the possibility of a tear of the liver capsule or other adverse event, which could increase the risk of leakage of blood or bile as a result of the biopsy. Such leakage is the most common unwanted or adverse event after liver biopsy.

### Major indications for liver biopsy

Liver biopsy is done mainly to make a firm diagnosis (or to exclude a diagnosis of any serious or significant liver disease) and to help provide information about the severity of liver disease. In the case of patients with known viral hepatitis, biopsies are typically not performed during the acute phase of disease. This is because most patients with **acute hepatitis** recover from the disease and because routine liver biopsy of such patients will not alter their management or their outcome.

An exception to this rule is when patients develop very severe or **fulminant hepatitis**. In such instances, emergency liver transplant may be indicated. Biopsy may be performed in order to assess the extent of death of liver cells and help to indicate that transplant is urgently needed.

The situation is quite different for patients with **chronic viral hepatitis**, defined as the known presence

disease, protoporphyria, and disorders of glycogen or other sugar metabolism.

The interpretation of liver biopsies in patients with chronic viral hepatitis include particularly assessment of the “stage” and “grade” of disease. The stage of liver disease refers to the extent of scar tissue or “fibrosis” that is present in the liver. This is generally graded on scales between 0 and 4 (the Metavir

cure only about 50% of patients. Furthermore, the treatments are lengthy and unpleasant. In particular, there are numerous adverse effects and unpleasant side effects of interferon and ribavirin. Many patients have strong relative, if not absolute, contraindications to receive treatment. The major ones of these are a history of depression, or other significant emotional disturbances and

In patients who are not sure if they want to be treated, a liver biopsy showing only mild severity of disease is reassuring and can provide the patient with comfort that it is “safe” to wait and not be treated right away. On the other hand, if the biopsy shows extensive fibrosis or cirrhosis, there would be a much stronger sense of urgency about being treated immediately.

Performance of pretreatment liver biopsies is nearly always required if patients are enrolled in clinical trials. The reason is that most clinical trials include improvement in the histopathology of the liver as an end point. This is not universally true, but it continues to be true for most clinical studies. It is certainly true for studies that are designed not to try to cure the viral infection, but rather to improve or slow down the progression of liver fibrosis and cirrhosis. This is because, at this time, liver biopsy is the only adequate means that we have of telling whether there is or is not progression of such liver disease. Although numerous attempts have been made to develop and define blood tests that would provide good, less invasive methods for estimating the degree of hepatic fibrosis, none of them has proven sufficiently sensitive or specific to obviate the need for liver biopsies.

## **Other considerations**

Because chronic viral hepatitis is a disease that affects the liver uniformly throughout all parts of the

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of viral infection and hepatitis for at least 6 months.

Biopsies are often indicated in such patients to exclude other causes of liver disease and to help provide information about the severity of the viral hepatitis. The major other causes of liver disease, which may be present instead of or in addition to chronic viral hepatitis, include alcoholic liver disease, drug- or toxin-induced liver disease, fatty liver disease, autoimmune liver disease, other inflammatory or infectious liver disease including granulomatous hepatitis, and a variety of metabolic diseases. Among the metabolic diseases, the major ones that are capable of causing hepatitis or liver injury are iron overload disease, especially hereditary hemochromatosis, alpha-1 antitrypsin deficiency, Wilson’s

scoring system) or 0-6 (the Ishak scoring system). The grade of hepatitis refers to the severity of inflammation in the liver and evidence of liver cell death (so called “necroinflammation”). The severity of these changes is also scored generally on scales between 0 and 4+ for different parts of the liver including the portal tracts, the interfaces between portal tracts and the surrounding liver cells, and the liver lobules.

An additional important role of liver biopsies is to help gauge the effectiveness of antiviral, anti-inflammatory, and/or anti-fibrotic therapy. For example, although our ability to treat chronic viral hepatitis with pegylated interferon plus ribavirin has improved considerably, in the case of chronic hepatitis C, we are currently still able to

difficulties. Unfortunately, depression and other such disturbances are often made much worse or caused by interferon. Then, too, interferon may precipitate or trigger a number of autoimmune abnormalities, the most common of which is the development of autoimmune thyroiditis.

Because of all these potential adverse and unpleasant effects, many patients are hesitant or reluctant to begin therapy. In such patients, who are not sure that they want to be treated with the currently available “best” treatment, performance of pretreatment liver biopsy is useful to help patients decide whether to undergo treatment right away or whether to wait a few years, hoping that more effective and less toxic treatment will be developed.

liver, the routine performance of imaging studies prior to performance of liver biopsies is not generally indicated or needed. Doing biopsies with guidance of ultrasound, CT or MRI is generally only needed if a specific localized abnormality in the liver is to be targeted for biopsy. This is hardly ever the case with chronic viral hepatitis. In my experience with over 30 years and thousands of biopsies, routine performance of such imaging procedures prior to routine liver biopsy does nothing except add to the complexity, the cost, and the time required for biopsy. This may not be true in all settings (for example, if the physician doing the biopsy has his own ultrasound machine that he can bring right to the bedside), but, at least, in the U.S.A., there are few gastroenterologists and hepatologists who have such machines.

Imaging studies prior to biopsy are indicated if patients have evidence of advanced cirrhosis, in which there is often a loss of mass and volume of the right lobe of the liver with enlargement of the left lobe of the liver. These patients may also develop ascites or free fluid within the abdomen, which is a relative contraindication to liver biopsy. When large amounts of such fluid are present, the fluid may need to be removed prior to liver biopsy being performed. Another indication for pre-liver biopsy ultrasound or other imaging of the liver is prior surgery in the right

upper abdomen other than cholecystectomy (removal of the gall bladder). Other major surgeries may have led to the bowel being between the skin or the chest wall and the liver. In general, it is not desirable for the needle to penetrate the bowel during liver biopsy.

Under special circumstances, especially when there is severe liver disease with inability of the blood to clot and/or inability to correct clotting disorders, liver biopsy can be obtained by going through a vein and into the liver with a special needle. This is generally done by getting into the veins from the large internal jugular vein in the neck, and the entire technique is called "transjugular liver biopsy." Such biopsies are generally done by specialists called "interventional radiologists" who have a lot of experience in getting into blood vessels and manipulating catheters or other devices within the blood vessels. These procedures need to be done where there is fluoroscopy so that the exact location of the catheters and the needles can be confirmed prior to biopsy being performed.

In other special circumstances, liver biopsies can be performed at the time of laparoscopy or minimally invasive abdominal surgery. With this technique, a specialist, generally a surgeon, examines the abdominal contents, including the liver with devices that televise the appearance and images obtained with special optical

devices called laparoscopes. This can be useful when focal liver disease is known or suspected, based upon prior imaging studies. The laparoscopist, if all goes well, is able specifically to do biopsies of affected areas of the liver. However, for routine purposes, especially with diffuse liver diseases such as chronic viral hepatitis, there is no reason for laparoscopy to be performed. ■



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