Biopsy Not Always Needed to Diagnose Fatty Liver

BY ROBERT FINN
San Francisco Bureau

SAN FRANCISCO — The liver biopsy remains the preferred method for diagnosing nonalcoholic fatty liver disease, but biopsy candidates should be chosen with care. Not all patients with signs of the disease will require a biopsy, Dr. Nathan M. Bass said at the Third World Congress on Insulin Resistance Syndrome.

Patients who are eventually diagnosed with nonalcoholic fatty liver disease (NAFLD) present initially in a variety of ways, said Dr. Bass of the University of California, San Francisco.

For example, an insurance exam can turn up an incidental aminotransferase elevation or an enlarged liver. An abdominal imaging study may reveal a fatty liver. A patient may have a complication of cirrhosis. Or NAFLD patients may be identified by screening high-risk populations with liver enzyme tests or liver ultrasound. In addition, an increasing number of NAFLD patients are being identified by liver biopsy during weight-reduction surgery, Dr. Bass said.

But it's not practical or desirable to screen all at-risk patients with a biopsy, and there are some good reasons not to do so. (See box.) About 25% of patients will experience significant pain during the biopsy. In addition, 1%-3.5% of patients will have morbidities such as hypotension, pneumothorax, hemoperitoneum, hemobilia, and gall bladder penetration. About 0.1% of patients will die from the procedure.

There are five situations in which a liver biopsy is essential: when a patient's liver enzymes show an unusual pattern or are 3-5 times normal; when other liver disease can't be excluded; when the patient doesn't have metabolic syndrome; to confirm a clinical suspicion of cirrhosis; and for qualifying a patient for entry into a clinical trial.

Although a definitive diagnosis still requires a biopsy, there are several alternatives for assessing the liver, Dr. Bass said.

Elevated liver enzymes can be very suggestive of NAFLD, but in a phenomenon Dr. Bass called "The Silence of the Labs," some patients with NAFLD have normal liver enzymes. He pointed to one study of patients undergoing gastric bypass in which 68% had normal ALT and AST, but only 52% had a normal liver biopsy. Among the remaining 48% with abnormal biopsy results, about 27% were found to have nonalcoholic fatty liver, and the others had nonalcoholic steatohepatitis.

The diagnosis of NAFLD is often made by exclusion. After the physician excludes alcoholic liver disease, drug-induced liver injury, iron overload, hepatitis B and C, and autoimmune hepatitis, NAFLD is the diagnosis that remains.

It can be difficult, however, to exclude a significant contribution from alcohol, especially since patients are not always truthful. For the purposes of inclusion in clinical trials, NIH defines "nonalcoholic" as less than 14 units of alcohol per week for men or less than 7 units per week for women. A unit is one can of beer, one glass of wine, or one shot of hard liquor, but there's considerable variation in the alcoholic content of drinks within each class.

The combination of ultrasound evidence of fatty liver plus liver enzyme elevation without markers for hepatitis C or B yields a 96% positive predictive value for NAFLD, according to one study. The problem is that although ultrasound is sensitive, it's not very specific.

CT imaging is somewhat more specific. In CT, a normal liver has about the same density as the spleen, whereas in NAFLD, the spleen will be quite a bit brighter than the liver. Unfortunately, CT is too expensive for routine screening.

At least three serological tests for hepatic fibrosis are under development, Dr. Bass said. In addition, transient elastography—a combination of 5 MHz ultrasound and 50 Hz elastic waves—may make the diagnosis simpler in the near future. ■

Deciding Whether to Biopsy

Pros

- Grade and stage of NAFLD are determined.
- Confidence in the diagnosis is 100%.
- Patients are motivated to lose weight.
- Biopsy is essential for enrollment in clinical trials of treatments.

Cons

- Risk of morbidity is increased with biopsy.
- Noninvasive diagnosis is quite accurate.
- Natural history of NAFLD is benign in most patients.
- NAFLD is a common disorder.
- There is no proven, specific treatment for NAFLD.

Source: Dr. Bass

Early Resection in Patients With Cholangiocarcinoma Shows Promise

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

CAMBRIDGE, MD. — An early resection with negative tumor margins remains the only hope for long-term survival in patients with cholangiocarcinoma, Dr. Richard Schulick said at a hepatobiliary update sponsored by Johns Hopkins University.

Worldwide, long-term survival in this disease is only about 3.5%, said Dr. Schulick. But in the United States, carefully selected patients whose early tumors are resected with negative margins can potentially have long-term survival, he said.

Patients typically present with right upper quadrant pain, which may be misdiagnosed as cholecystitis, stones, or pancreatic or bile duct cancer. The common cancer symptoms of weight loss and nausea are often present. Neither carcinoembryonic antigen nor carbohydrate antigen 19-9 are sensitive enough to be used exclusively for diagnosis, "although they can be useful in tracking recurrence," said Dr. Schulick of Johns Hopkins University, Baltimore.

In the 20 patients whose tumors had negative margins, 5-year survival was 68%, compared with 33% for the 9 patients with positive margins.

When assessing resectability, Dr. Schulick considers the biliary, vascular, and parenchymal systems separately. "The questions are, 'Can I preserve a portion of the biliary tree, the vascular in- and outflow of that section of the liver, and will there be enough liver left for the patient to survive?' " he said.

He presented survival data from 564 cases of cholangiocarcinoma treated at Johns Hopkins from 1973 to 2004.

Intrahepatic tumors occurred in 44 patients and were treated with hepatic resection, with or without lymph node removal. These patients had the best long-term survival rates. In the 20 whose tumors had negative margins, 5-year survival was 68%. This dropped to 33% for the nine patients whose tumors had positive margins. Fifteen patients received palliative care; their median survival was only 7 months.

Perihilar tumors occurred in 281 patients. These tumors, located in the hepatic duct bifurcation, are treated by excising the extrahepatic biliary tree, with or without lymph nodes. A hepatic resection and/or caudate lobectomy might be required. Operative mortality is relatively high: 4%-10%, Dr. Schulick said. "This is a reflection of the aggressiveness of the operation."

Long-term survival was not as good in this group, Dr. Schulick said. Of the 52 patients with margin-negative tumors, only 27% were alive at 5 years. Only 8% of the 121 with margin-positive tumors were alive at 5 years. Most of the patients (108) were not candidates for surgery and received palliative care; their median survival time was 9 months.

Distal tumors, located in the distal common bile duct, occurred in 239 patients. These tumors were treated by pancreaticoduodenectomy or excision of the extrahepatic biliary tree.

Again, long-term survival was not good. Of the 187 patients with margin-negative tumors, 21% were alive at 5 years. Only 6% of the 42 with margin-positive tumors were alive at 5 years. Ten patients received palliative care; their median survival time was 13 months. ■

NAFLD Patients Should Lose Weight, Avoid Alcohol

SAN FRANCISCO — With no specific treatment available for nonalcoholic fatty liver disease, the best current strategy centers on monitoring the patient's condition and managing the patient's lifestyle and metabolic syndrome, Dr. Nathan M. Bass said at the Third World Congress on Insulin Resistance Syndrome.

The patient's liver enzymes, liver function (bilirubin levels, albumin levels, and prothrombin time), and platelet count should be monitored. Each patient also should undergo regular ultrasound exams.

Patients with nonalcoholic fatty liver disease (NAFLD) should be instructed to avoid hepatotoxins—especially alcohol—and should be advised to pursue gradual weight loss with diet and exercise.

"Weight loss remains the simplest advice you can give," said Dr. Bass of the University of California, San Francisco. He pointed to a study showing that even modest weight loss (less than 10% of the patient's initial body weight) can reduce intrahepatic fat while leaving intramuscular fat unchanged. This level of weight loss also improved basal and insulin-stimulated glucose metabolism (Diabetes 2005;54:603-8).

Bariatric surgery can be helpful for some patients with NAFLD, but it should be the newer restrictive surgery that involves gastric banding; this approach tends to decrease steatosis, fibrosis, and nonalcoholic steatohepatitis. The older malabsorptive surgical strategies can be dangerous; they can lead to increased steatosis, fibrosis, nonalcoholic steatohepatitis, and liver failure.

The insulin-sensitizing agent metformin appears to be helpful in patients with NAFLD; however, the published studies tend to be small and open label, and thus the available evidence base is not overwhelming.

The thiazolidinediones pioglitazone and troglitazone appear to improve liver enzymes and fibrosis measured histologically, but once again, the evidence comes from open-label trials.

Dr. Bass noted some caveats to be observed regarding thiazolidinediones: They can cause weight gain and relapse upon discontinuation, and some patients experience serious side effects, such as heart failure and hepatotoxicity.

—Robert Finn