Liver Ca More Aggressive in Hepatitis B Patients

BY BETSY BATES
Los Angeles Bureau

SAN FRANCISCO — Patients with underlying viral hepatitis B are likely to present with hepatocellular carcinoma at a younger age and in better overall health than are patients with hepatitis C, but their tumors tend to be larger and more aggressive.

Important distinctions in the characteristics of liver cancer patients emerged when Dr. Spiros P. Hiotis of the department of surgery at New York University and associates examined the records of 127 patients diagnosed at the university medical center during a 12-year period.

Dr. Hiotis presented the results at a symposium sponsored by the American Society of Clinical Oncology.

Of 89 patients with underlying hepatitis B, 22 presented with hepatocellular cancer before age 40. None of the 38 patients with hepatitis C presented with cancer at such an early age. Among the 119 patients whose cirrhosis status was known, all 35 hepatitis C patients (100%) had cirrhosis at the time of diagnosis, compared with 50 of 84 hepatitis B patients (60%). Serum α-fetoprotein was more than 2,000 ng/mL in nearly half of the hepatitis B patients and in 5 of 35 hepatitis C patients.

Two-thirds of hepatitis B patients had tumors larger than 5 cm at their greatest diameter, compared with 14 of 37 hepatitis C patients (38%). Tumor size determines if a patient meets the Milan criteria, which are used to decide if a patient is a good candidate for a liver transplant. These criteria include having no solitary tumor more than 5 cm in diameter, or, in patients with multiple tumors, having no more than three tumors, none of which is larger than 3 cm.

On one hand, fewer hepatitis B patients met the Milan criteria than did hepatitis C patients (14% vs. 34%). On the other hand, nearly all hepatitis C patients had at least one comorbidity, compared with less than one-fourth of hepatitis B patients.

The typical presentation of advanced disease in hepatitis B patients heightens the need for more aggressive screening, Dr. Hiotis said at the meeting, which was also sponsored by the American Gastroenterological Association, the American Society for Therapeutic Radiology and Oncology, and the Society of Surgical Oncology.

He referred to new screening guidelines from the American Association for the Study of Liver Diseases, which were published by Dr. Jordi Bruix of the University of Barcelona and Dr. Morris Sherman of the University of Toronto. (See box.) ■

Screening for Hepatocellular Carcinoma

Patients at high risk for developing hepatocellular carcinoma (HCC) should be entered into surveillance programs.

The following groups of patients should be screened:

► **Certain hepatitis B carriers.** These carriers will also have either cirrhosis or a family history of HCC, or are Asian males 40 years and older or Asian females 50 years and older.

► **Other noncirrhotic hepatitis B carriers.** The risk of HCC depends on the severity of the underlying liver disease and the current and past hepatic inflammatory activity. Patients with high DNA concentrations of hepatitis B and those with hepatitic inflammatory activity remain at risk for HCC.

► **Certain patients with nonhepatitis B cirrhosis.** Those who should be screened will also have hepatitis C, alcoholic cirrhosis, genetic hemochromatosis, or primary biliary cirrhosis.

► **Patients with α1-antitrypsin deficiency, nonalcoholic steatohepatitis, and autoimmune hepatitis.** These patients are at elevated risk for HCC, but not enough data exist to justify a recommendation for surveillance.

► **Patients on the transplant waiting list.** The development of HCC advances patients on the waiting list. In addition, failure to screen for HCC could mean that the disease progresses beyond listing criteria.

Recommended screening methods and schedules are as follows:

► **Surveillance for HCC should be performed using ultrasound**. AFP levels alone should not be used for screening unless ultrasound is unavailable, because AFP as a screening tool has a high false-positive rate and is much less sensitive than is well-performed ultrasound.

► **Patients should be screened at 6- to 12-month intervals.** Dr. Sherman recommends 6-month intervals. The surveillance interval does not need to be shortened for patients at higher risk of HCC.

Source: American Association for the Study of Liver Diseases Practice Guidelines: Management of Hepatocellular Carcinoma (Hepatology 2005;42:1208-36).

Serum Peptide Profiles Accurately Detect Hepatocellular Carcinoma

BY JEFF EVANS
Senior Writer

BETHESDA, MD. — A test that measures six serum peptides appears to have high sensitivity and specificity in detecting hepatocellular carcinoma, Radoslav Goldman, Ph.D., reported at the annual meeting of the American Society of Preventive Oncology.

Dr. Goldman's research group at Georgetown University, Washington, analyzed serum samples from 78 patients with hepatocellular carcinoma (HCC) and 72 control patients. These patients were part of a larger case-control study of HCC that included 1,000 age- and gender-matched patients from Egypt.

The sensitivity and specificity of the tests climbed to 100% and 91%, respectively, when the results for all six peptides were combined.

The researchers compared the mass spectrometry profiles of serum from HCC and control patients. Six peptides were selected for further analysis from a set of nearly 300, said Dr. Goldman of the department of oncology at the university.

Three of the peptides occurred at significantly higher concentrations in serum from HCC patients, whereas the other three occurred at significantly higher levels in controls.

Each peptide on its own independently predicted HCC with a sensitivity and specificity comparable to the serum level of α-fetoprotein, which has been reported to detect HCC with 39%-64% sensitivity and 76%-91% specificity; α-fetoprotein testing is routinely used to detect the presence of HCC. The sensitivity and specificity of the peptides climbed to 100% and 91%, respectively, when the results for all six peptides were combined, Dr. Goldman said.

Of 45 HCC patients for whom the cancer stage was known, 11 had stage I or II and 34 had stage III or IV. "There is a nice trend for increase in the biomarkers with increasing stage of disease," Dr. Goldman said. He is currently analyzing whether the six-peptide test can detect early-stage HCC.

The peptide test might be used in combination with a liver biopsy or imaging methods that are currently used to diagnose HCC, he suggested.

Chronic hepatitis C virus (HCV) infection accounts for about 90% of the attributable risk for HCC in Egypt. In the United States, about 50% of HCC cases have a chronic HCV etiology, according to Dr. Goldman.

Significantly more patients with HCC were positive for HCV RNA (80%) or antibodies against HCV (88%) than were control patients (22% and 33%, respectively).

Many patients in both groups had detectable antibodies against hepatitis B virus (HBV), but only a small percentage of these patients had chronic HBV infections.

The difference in the prevalence of chronic infections "is the major difference between HCV and HBV viral hepatitis," he said. "Another important point is that for HCV, there isn't a vaccine, and there isn't one on the horizon." ■

Test Predicts Steatohepatitis In Nonalcoholic Fatty Liver

BY MELINDA TANZOLA
Contributing Writer

ATLANTA — A blood test can predict nonalcoholic steatohepatitis in patients with nonalcoholic fatty liver disease, according to results of a study presented at a meeting sponsored by the American Association for the Study of Liver Diseases.

Hepatocyte apoptosis is known to mediate liver injury in nonalcoholic fatty liver disease (NAFLD). The activation of caspases that mediate apoptosis can be measured in the plasma, thus allowing an indirect evaluation of liver damage.

Plasma caspase activation was detected using an enzyme-linked immunosorbent assay for cytokeratin-18 fragments, which are a byproduct of caspase activation. In the study, caspase activation was strongly linked to disease severity; a cutoff value of 395 U/L was 99.9% sensitive and 85.7% specific in predicting nonalcoholic steatohepatitis (NASH).

"A liver biopsy is the only reliable method to differentiate simple steatosis from NASH and stage disease severity," noted study author Dr. Anna Wieckowska of the Cleveland Clinic. However, biopsy has inherent risks and is not practical to perform multiple times.

Dr. Wieckowska and her associates evaluated a caspase activity blood test in 44 consecutive patients with suspected NAFLD. They measured caspase activity in plasma samples obtained at the time of liver biopsy, and then correlated the blood test results with histopathologic features.

Five patients were excluded because of a hemolyzed blood sample, two were excluded because they had borderline NASH, and two had alternative diagnoses, which left 39 evaluable patients.

Caspase activation was significantly elevated in patients with definitive NASH, with median cytokeratin-18 levels of 767 U/L, compared with 202 U/L in patients with simple steatosis. After adjustment for confounding variables, including aspartate aminotransferase/alanine aminotransferase ratio and body mass index, cytokeratin-18 levels were independently predictive of NASH, with a positive predictive value of 99.9% and a negative predictive value of 85.7%.

"This is potentially a very exciting breakthrough if confirmed in a larger series," commented Dr. Keith D. Lindor of the Mayo Clinic Foundation in Rochester, Minn. He added that "a noninvasive way to accurately predict mild degrees of fibrosis would allow us to select patients for treatment trials and also perhaps serve as a reliable and clinically relevant end point for these studies." ■