Rule Out Eight Conditions Before Fatty Liver Disease Dx

BY SHERRY BOSCHERT
San Francisco Bureau

SOUTH LAKE TAHOE, CALIF. — Attribute a mild chronic elevation in alanine aminotransferase to fatty liver disease only after considering eight other diagnoses, Dr. Christopher L. Bowlus advised at an update in gastroenterology and hepatology sponsored by the University of California, Davis.

He offered an algorithm for work-up of a patient whose serum alanine aminotransferase (ALT) is 1.5 times higher than the upper limit of normal, as defined by your clinical laboratory. If a physician doesn't do the work-up he described, a treatable condition will be missed in these patients 10% of the time, studies suggest.

The algorithm is based on consensus among physicians, because data on the subject are sparse, he added. "These are very common problems, but no one has really taken the time to look at what is the most effective or cost-effective way of evaluating patients," said Dr. Bowlus of the university.

After ruling out four common causes of mild, chronic ALT elevation (alcoholic hepatitis, hepatitis B or C infection, and exposure to drugs or toxins that alter ALT), consider four less common diagnoses before fatty liver disease: hemochromatosis, autoimmune hepatitis, alpha-1 antitrypsin deficiency, and Wilson's disease.

When taking the patient's history, ask about alcohol use and parenteral exposures to viral infection through sexual activity, intravenous drug use, or blood transfusion prior to 1990. Inquire about illicit or prescribed drugs or herbal therapies, supplements, and over-the-counter medications that may affect ALT levels. The presence of diabetes is a risk factor for fatty liver disease.

Determine not only if the patient is an immigrant from a region with endemic hepatitis B but also if the patient's parents fit this description. "I've seen lots of positive hepatitis B students born in the United States" whose parents are immigrants, he said.

The physical exam will lead to a specific diagnosis in a minority of patients with ALT elevations. Look for signs of chronic liver disease, such as "spider" lesions on the skin (which can be subtle and usually are on the upper torso), palmar erythema, temporal wasting, hepatomegaly (common in alcoholic liver disease), and splenomegaly (often an early sign of portal hypertension). If the ALT elevation has been present for at least 6 months or the patient is symptomatic or has risk factors for hepatitis B or C infection, it's reasonable to order some lab tests. Get a hepatitis B surface antigen test and a hepatitis C antibody test; negative results rule out these viral infections. An ultrasound of the liver would be appropriate.

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DR. BOWLUS

A transferrin saturation test is a good screening tool for hemochromatosis. If you need further testing for this condition, a genetic test is the way to go, but be prepared to explain potentially confusing results, Dr. Bowlus suggested.

If none of these leads to a diagnosis, order an antinuclear antibody test to screen for autoimmune hepatitis. A more specific screening tool is the anti–smooth muscle antibody level; a serum protein electrophoresis also can test for this disease.

Get a serum alpha-1 antitrypsin level to screen for alpha-1 antitrypsin deficiency. "We think of this as causing lung disease, but it can cause liver disease alone without lung disease," he said.

A ceruloplasmin test is helpful to screen for Wilson's disease, an uncommon disease of copper metabolism that usually presents in childhood or early adulthood, although there have been case reports of diagnosis in people in their 50s and 60s.

If none of these potential diagnoses hits the mark, ask the patient to refrain from alcohol and any potentially offending medications or herbs and retest the ALT level in 3-6 months, he said. If ALT remains elevated, repeat all tests.

"If all this is negative, then you should consider that they might have fatty liver disease, particularly if the ultrasound is consistent with fatty liver disease and they have risk factors for fatty liver disease," he said.

For many patients with elevated ALT who are diabetic or have high cholesterol, all these tests will be negative except that the ultrasound will show a fatty liver.

The appropriateness of a liver biopsy at this point is controversial. ■

Lamivudine Is Still Useful Against Some Hepatitis B

BY SHERRY BOSCHERT
San Francisco Bureau

SOUTH LAKE TAHOE, CALIF. — Lamivudine and interferon alfa still have independent roles to play in treating some patients with chronic hepatitis B, Dr. Eddie C. Cheung said at an update in gastroenterology and hepatology sponsored by the University of California, Davis.

Lamivudine has shown consistent, rapid antiviral effects, but its role has diminished over time, primarily because of the high rate of drug resistance.

Interferon alfa is another drug that has fallen out of favor for treating hepatitis B, but it may be the treatment of choice for a young, highly motivated patient.

However, even without resistance being present, the drug's antiviral effects have been surpassed by those of entecavir, although lamivudine remains less expensive.

"Resistance is what killed this as a monotherapy," said Dr. Cheung, chief of hepatology at the Veterans Affairs Northern California Health Care System, Martinez, Calif.

He is a speaker or adviser for GlaxoSmithKline, which makes lamivudine, and for Schering-Plough, which makes interferon alfa.

Lamivudine still is useful in at least three settings, he suggested. First, it can be a good and safe monotherapy if used for less than 6 months. "The resistance is really not an issue" with short-term treatment, he said.

Second, emerging data suggest that lamivudine is useful for treating pregnant women with chronic hepatitis B and a high viral load, to prevent vertical transmission. Treating with lamivudine 6 weeks before delivery can significantly reduce the chance of neonatal infection, Dr. Cheung said.

And third, all chronic hepatitis B carriers who are scheduled to undergo chemotherapy or immunotherapy should be started on prophylactic lamivudine to prevent a flare of their hepatitis B disease. "Please, if [the] oncologist forgets, make sure those patients are on prophylactic lamivudine, which is a good drug for that purpose," he said.

Another drug that has fallen out of favor for treating hepatitis B—interferon alfa—similarly can be the right treatment for a specific patient. Interferon alfa generally has been replaced by peginterferon alfa.

Interferon alfa may be the treatment of choice for a young, highly motivated patient willing to withstand its significant side effects in order to undergo a relatively short course of therapy with a more durable response and a higher rate of hepatitis B surface antigen loss compared with oral adefovir or entecavir therapy. This treatment strategy carries a higher cost, but its duration is finite.

A young woman who wants to get rid of the virus and start a family, for example, may be a good candidate for interferon alfa monotherapy after counseling about efficacy and side effects.

"This is not an easy therapy to take, so it has to be a really motivated, well-informed patient," Dr. Cheung said.

The drug is dangerous in patients with cirrhosis and is contraindicated in decompensated patients. For noncirrhotic patients, or those with cirrhosis who are clinically and biochemically compensated, a 16- to 24-week course of interferon alfa may produce hepatitis B e antigen (HBeAg) loss in 33% and HBeAg conversion in 18%. After 5 years, 11%-25% will have HBeAg loss.

No drug-resistant mutants have emerged from this treatment, a unique feature of interferon alfa among hepatitis B therapies. ■

Acetaminophen Linked to Deaths in Acute Viral Hepatitis

BY MARY ELLEN SCHNEIDER
New York Bureau

LOS ANGELES — Even small amounts of acetaminophen can cause acute liver failure and death in some patients with acute viral hepatitis, according to research presented at the annual Digestive Diseases Week.

Acetaminophen adducts—the toxic byproducts of acetaminophen liver damage—were found in serum samples of 9 out of 72 patients (12.5%) with confirmed hepatitis A or B that had progressed to liver failure. The patients were part of a registry of acute liver failure cases, said senior study author Dr. William M. Lee, professor of medicine at the University of Texas Southwestern Medical School, Dallas.

The investigators compared the findings with serum results from 10 patients whose acute liver failure was known to have been induced by an overdose of acetaminophen. The acetaminophen adducts found in the 10 patients who had overdosed were significantly higher than the levels in the 72 patients, which was consistent with patient reports that they had used acetaminophen in the days before the study but not in doses greater than 4 g per day. The study also showed that about two-thirds of the acute viral hepatitis patients with acetaminophen adducts died within 3 weeks of admission to the study, compared with 27% of hepatitis patients without adducts.

Acetaminophen is a dose-related toxin and for patients with hepatitis A or B, there is a serious risk of liver failure with even therapeutic doses of the drug, Dr. Lee said. Patients may inadvertently take excessive doses of the over-the-counter pain reliever either by taking it in combination with an acetaminophen-containing narcotic or in combination with an over-the-counter flu medication that also contains acetaminophen. Since many patients with early viral hepatitis experience flu-like symptoms, it's key that they are educated about the risks of taking acetaminophen, according to Dr. Lee.

The study was supported by a grant from the National Institutes of Health. ■