Elevated Serum Transaminase as a Presenting Clue for Precirrhotic Hemochromatosis

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Clinical Studies

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For patients in whom unexplained elevations in SGOT and SGPT concentrations are found, determination of the serum iron level is recommended to screen for asymptomatic precirrhotic hemochromatosis. Care must be taken to differentiate between hereditary hemochromatosis and secondary iron accumulation due to liver disease.

Multiphasic blood chemistry testing is commonly used to evaluate ill patients as well as in the screening of asymptomatic patients, and it is not uncommon to find incidental, unexpected abnormalities. One such abnormality is mild to moderate elevation in the serum transaminases — glutamic-oxaloacetic transaminase (SGOT) and glutamic-pyruvic transaminase (SGPT), even in the presence of normal alkaline phosphatase concentration. Such abnormalities should not be ignored or dismissed as “nonspecific.” Elevated transaminase may be a clue to significant disease, as the following cases demonstrate.

Case Reports

Case 1
A 38-year-old white man presented for a routine physical examination. He complained of mild fatigue and recurrent chest pains, which were interpreted as musculoskeletal in origin. He had a remote history of duodenal ulcer, and a 45-pack-year history of cigarette smoking but none of alcohol abuse, jaundice, blood transfusions, or use of medications containing iron. No family member was ever known to have hemochromatosis.

Positive physical findings included an S-4 gallop cardiac rhythm, a left inguinal hernia, and a liver edge palpable at the right costal margin. The size of the liver was normal as determined by percussion. Complete blood count, all values of multiphasic screening, urinalysis, VDRL, and chest x-ray were normal except for the SGPT of 240 units and SGOT of 79 units. Serum iron was 278 mcg/dl initially and 256 mcg/dl on repeat assay. Iron binding capacity was 256, and the ferritin level was 479. Liver biopsy disclosed a marked increase in hepatocyte iron, but cirrhosis was not present. The patient undergoes weekly phlebotomy.

Case 2
A 39-year-old white man came to us for a physical examination after living in England for six years. He had no symptoms and no abnormal physical findings. He had no history of alcohol abuse, jaundice, blood transfusions, or use of medications containing iron, and no family history of hemochromatosis. Complete blood count, multiphasic screening tests, urinalysis, VDRL, and chest x-ray were normal except for SGPT of 240 units and SGOT of 79 units. Serum iron was 278 mcg/dl initially and 256 mcg/dl on repeat assay. Iron binding capacity was 256, and the ferritin level was 479. Liver biopsy disclosed a marked increase in hepatocyte iron, but cirrhosis was not present. The patient undergoes weekly phlebotomy.

Discussion

In most cases, significantly elevated transaminase levels discovered incidentally by multiphasic screening proce-

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dures in non-acute ill patients are due to laboratory error, to chronic alcoholism, chronic hepatitis, or the use of hepatotoxic drugs. Determination of the SGOT and SGPT levels should be repeated before an investigation is made to determine the etiology. In cases in which none of the above causes seem to apply, less common etiologies must be considered. Wilson's disease, especially in teenage and young adult patients, and hemochromatosis must be excluded. The term "hemochromatosis" in the world medical literature has various meanings. Here, it is defined as the HLA-related genetic idiopathic iron overload state of parenchymal cells with or without tissue damage that apparently results from hyperabsorption of iron in normal diets.

That the serum iron level may not be a sufficiently sensitive screening test to detect early hemochromatosis has been demonstrated in studies of siblings or children of patients with hemochromatosis (1-3). It may be difficult to detect early hemochromatosis even when determinations of serum iron concentration, transferrin saturation, and ferritin levels are employed. However, determination of the serum iron level is suggested as a reasonable test to screen for hemochromatosis in patients who have unexplained abnormal liver enzymes.

This approach is justified for two reasons. First, because unexplained transaminase elevation is a relatively common finding, the determination of serum iron concentration, transferrin saturation, and ferritin levels in all such patients is economically unacceptable. Second, when the iron overload state is sufficiently severe to result in liver enzyme abnormalities, the serum iron level will be elevated in virtually all such patients. Although we recognize that not all patients with elevated serum iron levels have hemochromatosis and, conversely, that not all patients with hemochromatosis and abnormal liver function tests have consistently elevated serum iron, our experience demonstrates the utility of this simple procedure. If the presence of hemochromatosis is strongly suspected or if persistent liver enzyme abnormalities remain unexplained, more extensive studies may be required, including transferrin saturation, ferritin assay, the desferoxamine test, and, ultimately, liver biopsy.

Serum ferritin assay may not be adequate as a health screening test because normal levels have been reported in patients with precirrhotic hemochromatosis (4). However, these studies were performed to screen family members of patients with hemochromatosis, not in subjects who had unexplained biochemical signs of liver disease.

Crosby et al (5) reported serum iron measurements from 500 presumably healthy people. Of these samples, 30 (6%) had levels of serum iron greater than 200 mcg%. On second sampling, three of these 30 subjects had normal serum levels. When the results of other serum chemistry tests on the 470 "controls" were compared with those of the 30 subjects who had abnormally high serum iron levels, this study found an increased frequency of elevated total protein concentration, bilirubin levels greater than 1 mg/dl, and abnormally elevated liver enzymes in the group with increased serum iron values. Nevertheless, it is highly improbable that 6% of apparently healthy people have an iron overload state. Consequently, elevated serum iron concentration alone is not confirmation of iron overload.

Thus, there are risks in using the serum iron level to screen for hemochromatosis in patients who have unexplained elevated liver enzymes. There are many other causes of elevated serum iron (5). Both nonhemochromatotic liver disease and chronic alcoholism can be associated with elevated serum iron levels and transferrin saturation greater than 70% (6,7). Approximately 35% of patients with either alcoholic or nonalcoholic liver disease have increased iron absorption when their iron stores are not deficient (7). The newly described noninvasive magnetic measurement of hepatic iron stores may help to clarify this difficult differential diagnosis (8).

References


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