MAYO CLINIC

23-Year-Old Man With Jaundice and Elevated Liver Enzymes

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A 23-year-old man presented to an outside hospital with a 3-day history of dark-colored urine, yellow discoloration of the eyes, and pain in the chest and lumbar area. He denied having confusion, fever, chills, or light-colored stools. He reported consuming small amounts of alcohol once a month and never using tobacco or illicit drugs. His medical history was positive only for anxiety, which was not treated pharmacologically. The patient stated that he had not taken nonprescription medications, herbal supplements, or prescribed medication in the preceding year. Physical examination revealed his vital signs to be within normal limits. Auscultation of the heart was negative for murmurs, the lung fields were clear bilaterally, and the abdomen did not reveal fluid wave, organomegaly, or tenderness. Laboratory test results on admission revealed (normal ranges provided parenthetically): aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels of 2683 U/L (8-48 U/L) and 3496 U/L (7-55 U/L), respectively; an alkaline phosphatase level of 185 U/L (45-115 U/L); and total and direct bilirubin levels of 6.24 mg/dL (0.0-1.2 mg/dL) and 5.1 mg/dL (0.0-0.3 mg/dL), respectively. Urinalysis showed bilirubin but was otherwise unremarkable.

Viral hepatitis serology test results (hepatitis A antibody total, hepatitis C antibody diagnostic, hepatitis B surface antigen and antibody, envelope antigen and antibody) were negative; an acetaminophen test ruled out toxicity; and iron study results revealed a transferrin saturation of 85% (14%-50%) and a ferritin level of 2000 mcg/L (24-336 mcg/L). Duplex ultrasound displayed normal appearance of the liver parenchyma and a contracted gallbladder, with no signs of an acute process.

1. Which *one* of the following tests is *most appropriate* to order next to narrow the differential diagnosis of liver disease in this patient?

a. Liver biopsy
b. Computed tomography (CT) of the abdomen with contrast
c. Copper levels in 24-hour urine
d. Serum ammonia level
e. Percutaneous transhepatic cholangiography

A liver biopsy is not essential in the evaluation of all patients with acute liver disease; therefore, less-invasive options should be considered first. A CT scan with contrast may reveal cirrhotic changes, such as a nodular contour, as well as an enlarged left lobe, an atrophied right lobe and splenomegaly, portosystemic shunts, and a re-canalized umbilical vein, if portal hypertension is present. However, a CT scan is not the reference standard for the diagnosis of cirrhosis. A hepatobiliary ultrasound, which is less expensive than a CT scan and does not expose the patient to ionizing radiation, may reveal parenchymal abnormalities and differentiate between cystic and solid lesions. Additionally, the Doppler analysis may yield important information about the hemodynamics of hepatic and portal vessels. However, neither a CT scan nor an ultrasound would help narrow the differential diagnosis.

Typical laboratory abnormalities in Wilson's disease include a high serum copper level, elevated copper levels in 24-hour urine, and a low ratio (<4) of alkaline phosphatase to bilirubin.[1] Elevated AST and ALT levels usually remain below 2000 U/L. Given that the ratio of alkaline phosphatase to bilirubin was not decreased in our patient, a 24-hour urine copper level was the most appropriate test to rule out Wilson's disease. Elevated

See end of article for correct answers to questions.

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serum ammonia levels may be seen in advanced liver disease,[2] but the finding is not specific to any particular entity. Our patient had a serum ammonia level of 64 mcmol/L (0-30 mcmol/L). Percutaneous transhepatic cholangiography may be helpful in patients who have biliary obstruction that cannot be addressed with placement of internal stents via endoscopic retrograde cholangio-pancreatography.

Serum and urine copper levels were normal, and a CT scan of the abdomen revealed no focal lesions but was suspicious for fatty liver changes. The initial international normalized ratio was 1.3, and slightly higher (1.6) the next day. All serum immunoglobulin levels were normal. Test results for serum antinuclear antibodies and smooth muscle antibodies were negative. A liver biopsy revealed moderate-to-severe hepatitis with mild cholestasis and no viral inclusions. HFE gene test results for C282Y and H63D mutations were negative, and the elevated ferritin level was interpreted as a nonspecific acute phase reactant. The patient remained stable, and no signs of encephalopathy were observed.

2. Which *one* of the following is the *most likely* cause of hepatitis in this patient?

a. Idiopathy
b. Budd-Chiari syndrome
c. Nonalcoholic steatohepatitis
d. Drug-induced liver injury
e. Autoimmune hepatitis

Idiopathic acute liver failure describes non—A-E viral liver injury that does not have a known or describable cause.[2] Given that an extensive workup in our patient did not sufficiently explain a specific etiology, describing it as idiopathic was medically appropriate. Budd-Chiari syndrome is a disease of outflow obstruction of the hepatic venous system in which patients may present with acute liver failure.[2] However, duplex ultrasonography did not detect venous thrombus in our patient. A CT scan with contrast can readily identify the disease in most cases. Nonalcoholic steatohepatitis, a subtype of fatty liver disease, may present with abdominal discomfort and elevated liver enzymes and hepatomegaly.[3] A CT scan of the liver may show low attenuation, especially when compared with the spleen, whereas an ultrasound may reveal increased echogenicity, particularly when compared with the renal cortex. Transaminases are usually only moderately elevated in nonalcoholic steatohepatitis. Drug-induced liver injury may be idiosyncratic or predictable, and it can be classified as hepatocellular, cholestatic, or mixed.[4] Although signs and symptoms may not differ from those in other forms of hepatitis, the clinical history of present illness and medication reconciliation is very important. Our patient had not taken medications, ingested harmful substances, or used illicit drugs. Autoimmune hepatitis is typically diagnosed with serology tests. However, these tests are not always definitive and liver biopsy may be needed. Hypergammaglobulinemia is present in approximately 80% of cases.[3] Our patient had a negative autoimmune workup, and serum immunoglobulin levels were normal, although patients with severe cases may not have elevated IgG levels.

Serum transaminases reached a plateau within 5 days, and then began to fall, which correlated with clinical improvement and recovery. The patient was discharged in stable condition and underwent biweekly follow-up laboratory tests. Approximately 5 weeks later, his AST was 445 U/L, and his ALT was 511 U/L. Although he remained asymptomatic, a progressive decline in hemoglobin levels, white blood cell count, and platelet count was observed, and a hematologist was consulted regarding progressive pancytopenia.

3. Which *one* of the following tests is the *most appropriate* next step to evaluate the new laboratory findings?

a. Serum lactate dehydrogenase (LDH) level
b. Serum platelet antibody count
c. Serum haptoglobin level
d. Bone marrow biopsy
e. Serum vitamin B12 and folate levels

An elevated LDH level aids in the diagnosis of hemolytic anemia, which may be accompanied by jaundice and indirect hyperbilirubinemia.[5] The patient experienced improvement in liver function and showed no signs of hemolysis, as his bilirubin returned to a normal range. Immune thrombocytopenia is often a diagnosis of exclusion and does not explain the drop in the red and white blood cell counts.