CLINICAL VIGNETTE

Early Recognition of Autoimmune Hepatitis

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Case Presentation

A 58-year-old male with no significant past medical history who was referred by his primary care provider to evaluate elevated liver enzymes found incidentally. Symptoms included minor aches/pains, including diffuse joint pains for one-month, as well as malaise and fatigue. He did not have abdominal pain, abdominal swelling, or edema. He denied jaundice, fevers, chills, nausea, vomiting, or diarrhea. There was no chest pain or shortness of breath. He did report weight loss over the past year without night sweats. He also noted foul swelling, dark urine. He had taken large amounts of acetaminophen for pains but stopped for the past two weeks. He was taking turmeric and tart cherry tart to help with joint pains, but no new medications, changes in diet, or supplements/vitamins.

Review of his record noted mildly elevated liver enzymes AST/ALT 54/79 with alkaline phosphatase 166 two years ago. Ten days before admission labs included with AST/ALT 339/428 and alkaline phosphatase 295 and the day before admission AST/ALT 925/1362 and alkaline phosphatase 278. Bilirubin was not reported. His acute hepatitis panel was negative within the past month.

On exam in the Emergency Department, he was afebrile with normal vital signs. Abdominal exam unremarkable. Labs showed normal CBC and coagulation factors, but CMP showed AST/ALT 910/1434 with alkaline phosphatase 265, total bilirubin 7.5. Urine dipstick showed bilirubin. Acetaminophen level was negative. Ultrasound of the gallbladder was not consistent with cholecystitis nor choledocholithiasis. After admission GI consultants recommended CT imaging as well as MRCP to rule out gallstone pancreatitis. CT abdomen pelvis showed hepatomegaly with reactive changes at the hepatic hilum/pancreas or reactive changes to acute cholecystitis, HIDA scan was then done and normal. MRCP did not show any choledocholithiasis. Laboratory testing showed elevated Anti-Mitochondrial antibody, and increased GI suspicions for autoimmune hepatitis vs PBC. The patient was started on IV methylprednisolone 80 mg BID with improvement in daily liver function testing. Other negative labs included Hepatitis C, Hepatitis B, ANA, HIV, Alpha 1 Anti-trypsin, Anti-Smooth Muscle Antibody. After continued improvement in azathioprine and prednisone taper he was discharged and he remained stable on daily azathioprine 50 mg with normal transaminases. Follow up plans includes indefinite azathioprine 50 mg and avoiding alcohol and supplements and future fibroscan. His condition has 80% risk of reactivation without treatment.

Discussion

Patient presenting with elevated liver enzymes have a large differential. The type of elevation (AST vs ALT), degree of elevation (100s vs 1000s), and symptoms may suggest a different diagnosis. Differentials may include a variety of phenotypes, which complicate establishing diagnosis. Autoimmune hepatitis may be included in this differential. This inflammatory liver disease is caused by autoantibodies and has increased serum gamma globulin levels. There is a wide spectrum of presentations ranging from completely asymptomatic patients through those with debilitating cirrhosis. Symptoms include nausea, vomiting, ascites, weight loss, generalized fatigue, and severe protein/calorie malnutrition.[1-4] The age of presentation varies widely. Studies report large numbers of patients presenting in their 20s as well as other in their 50s-60s.[5] Asymptomatic patients may be discovered during routine physicals, blood donation laboratory testing, or insurance examinations. Alanine aminotransferase/Aspartate aminotransferase (ALT/AST) may be elevated without other lab abnormalities, physical examinations are usually normal. Other patients have severe liver failure, elevated bilirubin, and abnormal coagulation labs and thrombocytopenia. These labs are commonly found on initial presentation. Patients may have signs/symptoms of chronic liver disease or acute liver failure including gross jaundice, ascites, anasarca.[6] Some initially present with erythematous rashes or joint pains.[7]

Patients may present acutely with ALT/AST values in the thousands with the ratio of alkaline phosphatase to ALT/AST less than 1.5. In contrast, patients with chronic disease may present with cirrhosis or other chronic liver disease stigmata. Values of ALT/AST may be only 1.5 to 5 times the upper limit of normal with lower rates of alkaline phosphatase to ALT/AST of about 1.2.[8] Immunoglobulin G (IgG) is often elevated and may indicate circulating autoantibodies. Other autoantibodies that may be elevated in autoimmune hepatitis include anti-nuclear antibodies (ANA), anti-smooth muscle antibodies (ASMA), Anti-neutrophil cytoplasmic antibodies (ANCA), Anti-Mitochondrial antibodies (AMA), and Anti-Liver-Kidney microsomal antibodies. These autoantibodies do not need to be positive for diagnosis, but higher titers provide more evidence for autoimmune hepatitis. There are no specific imaging findings for autoimmune hepatitis, and images are obtained on a case by case basis.[9]

Other laboratory tests are obtained in a stepwise order. The first step includes: ANA, ASMA, Anti-LKM, AMA, and IgG

levels.[10] MRI abdomen can evaluate for primary sclerosing cholangitis in selected cases. These include patients with baseline inflammatory bowel disease or a ratio of alkaline phosphatase to aminotransferases suggesting a cholestatic/ obstructive pattern rather than hepatocellular injury. Liver biopsy is not necessary for diagnosis but can confirm diagnosis and help with treatment. Autoantibody positive patients with IgG elevation high enough to strongly suspect diagnosis.[11]

Diagnostic criteria include elevation of either AST or ALT > two times the upper limit of normal, as well as at least one positive additional laboratory test, such as increased total IgG or gamma-globulin levels, ANA, ASMA, Anti-LKM. Other diseases that also increase aminotransferases such as viral hepatitis, drug-induced liver injury, ischemic liver injury, alcoholic liver injury should be ruled out.[10]

Evaluation for possible adverse effects should be assessed prior to treatment. Testing may include thiopurine methyltransferase (TPMT) level, hepatitis B labs, and bone density testing. Drug therapy is the main treatment with a goal to improve debilitating symptoms, reduce inflammation, decrease elevated aminotransferase and IgG levels, and prevent progression to liver failure or cirrhosis. Close lab monitoring is needed after starting treatment.[10,12] Long term management is coordinated with hepatology, and includes alcohol abstinence, and vaccinations including Hepatitis A and Hepatitis C. Indications to start therapy include AST/ALT > 10 times upper limit of normal, Serum IgG > 2 times upper limit of normal, elevated aminotransferases with symptoms, cirrhosis with inflammation on biopsy, and pediatric patients.[13] Therapy initially is glucocorticoid with azathioprine as needed if TPMT activity is normal. These medications are started separately to assess for individual response. Most patients show lab improvement by four weeks.[13] Addition of thioprine allows lower glucocorticoid doses to reduce side effects. Patients will need remain on the thioprine indefinitely.

Autoimmune hepatitis may cause acute hepatitis with high transaminases enzyme elevations. Presentations vary from asymptomatic patients with abnormal labs found on routine testing to patients with floridly decompensated cirrhosis. Our patient had incidental findings of elevated liver enyzmes, complicated by recent use of acetaminophen as well as cherry tart/turmeric supplements. It is helpful to keep autoimmune hepatitis on the differential while ruling out other causes of acute liver disease. Early diagnosis allows for appropriate short term and long term, treatments.

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