FATTY LIVER

By Pierre Gholam, MD

A 46 YEAR OLD Caucasian female presents to the Liver Clinic with the finding of asymptomatic elevation of her liver enzymes. Blood tests had been checked routinely as part of an annual check up with her primary care physician. The patient has a history of hypertension for which she has been on Diovan for many years. She has been overweight for most of her adult life and currently weighs 186 pounds (Body Mass Index of 32). She does not report any abdominal pain, swelling in the lower extremities, excessive itching and has never been jaundiced. She had a cholecystectomy at age 27 but has never had a blood transfusion. She got a tattoo at a local parlor 5 years ago. She has never used illicit drugs. She is lifetime non smoker. She consumes 3 glasses of wine per week.

Her vital signs are notable for a blood pressure of 150/90 but are otherwise unremarkable.

On physical exam, she has an obese abdomen but no organomegaly. The rest of the exam is unremarkable. She states that she has had a mostly sedentary lifestyle over the past decade with steady weight gain during that period.

Repeat testing in liver clinic reveals the following: ALT 89, AS7 67, Alkaline Phosphatase 82, Total Bilirubin 0.4, Albumin 4.0. Additional work up in liver clinic includes serological testing for viral hepatitis B and C which is negative. Testing for the autoimmune makers Anti-Nuclear Antibody (ANA) and Anti Smooth Muscle Antibody (ASMA) shows no detectable titers. Her ferritin is mildly elevated at 321. Transferrin saturation is normal at 33%. Ceruloplasmin and Alpha One Anti-trypsin levels are normal.

Ultrasound of the liver reveals diffuse increase in echogenicity consistent with fatty infiltration.

She returns to the office following the completion of her work up to discuss the results. She is told that, in the presence of sonographic findings consistent with fatty infiltration and in the absence of heavy alcohol consumption and any other causes of chronic liver disease, the most likely diagnosis is Non Alcoholic Fatty Liver Disease (NAFLD). NAFLD is a common condition affecting about 1 in 5 Americans. Risk factors for NAFLD include obesity as well as metabolic risk factors namely hypertension, hypertriglyceridemia and hyperglycemia. Mild elevations in ferritin are not uncommon in NAFLD and do not usually reflect iron overload. NAFLD encompasses a spectrum of disease severity ranging from simple triglyceride deposition in the liver with no evidence of inflammation or scarring to a more progressive condition associated with inflammation of liver cells and progressive fibrosis which can lead to cirrhosis. The latter is known as Non Alcoholic Steatohepatitis (NASH). An exact estimate of the prevalence of NASH is not known but it is thought to occur in about 3-7% of the general population. Risk factors for NASH appear to include diabetes and older age. Currently, the only test that can distinguish between NASH and simple fatty liver is a liver biopsy which also provides prognostic information.

Unfortunately, there are no current proven therapies for NASH. Vitamin E appears to confer some benefit in a randomized controlled trial but the risks and benefits of long term vitamin E therapy need to be considered before such intervention is implemented. PPAR-gamma agonists such as pioglitazone and rosiglitazone may provide some improvement in histology while on therapy but also result in net weight gain and may have additional adverse events with prolonged therapy. Diet and exercise is advised as it appears to be a promising intervention and would also improve her cardiovascular risk.

She decides to pursue a liver biopsy which shows some lobular inflammation and pericellular fibrosis consistent with mild NASH. She is also placed on a statin for an elevated LDL which is safe in the setting of chronic liver disease as long as liver enzymes are appropriately monitored and therapy stopped if ALT increases 3 fold or more from its baseline. Her liver enzymes remain stable while being monitored during statin therapy. A year later, she has lost 25 pounds through diet and exercise and her ALT is 61. The plan is to follow her in clinic every 6 months and enroll her in clinical trials for NASH as they become available.

Dr. Pierre Gholam is Medical Director, Liver Disease Center of Excellence, Digestive Health Institute, University Hospitals in Cleveland. He is also an assistant professor at Case Western Reserve University. ■