An Enlarging Liver in a Young Diabetic Male

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**Question:** A 22-year-old man with history of type 1 diabetes mellitus, alpha-1-antitrypsin deficiency (ZZ phenotype), gastroesophageal reflux disease, hyperlipidemia, and depression presented to the hospital for increasing right upper quadrant pain and nausea for 2 weeks. The patient was a former heroin user and an active smoker, but denied significant alcohol use. The patient’s home medications included insulin, atorvastatin, dexlansoprazole, paroxetine, buprenorphine, and trazodone. The patient had poorly controlled diabetes, requiring 6 hospitalizations for diabetic ketoacidosis within the last year.

Physical examination revealed a soft, nondistended abdomen with diffuse tenderness and severe hepatomegaly without ascites, jaundice, spider angioma, or other stigmata of advanced liver disease. Laboratory studies showed an alanine aminotransferase of 223 U/L, aspartate aminotransferase of 331 U/L, alkaline phosphatase of 223 U/L, total bilirubin of 0.3, albumin of 3.4, platelet count of 302 U/L, International Normalized Ratio of 0.9, and hemoglobin A1C of 14.6%. Hepatitis B and C serologies were negative and the alpha-1-antitrypsin level was <60 mg/dL. MRI revealed a significantly enlarged liver with marked interval increase of 21.2 to 25.8 cm from 8 months prior. No focal hepatic lesions were identified. There was no intrahepatic or extrahepatic biliary ductal dilatation (Figure A, B). A core biopsy of the liver was performed showing hepatocytes are swollen with cleared cytoplasm (Figure C). Figure D, E, shows hepatocytes are strongly and diffusely positive for Periodic acid–Schiff stain and largely negative for Periodic acid–Schiff diastase stain suggesting that the hepatocytes were swollen with glycogen that was digested with diastase. Periodic acid–Schiff diastase also highlights alpha-1-antitrypsin globules.

Based on the clinical scenario, imaging, and pathologic findings, what is the diagnosis?

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Conflicts of interest
The authors disclose no conflicts.

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Answer to: Image 4: Glycogenic Hepatopathy

Liver biopsy demonstrated diffuse clearing of cytoplasm of the hepatocytes with strong periodic acid-Schiff positivity. There was no evidence of fibrosis, steatosis, inflammation, iron staining, or Mallory bodies. Combined with the clinical history of poorly controlled type 1 diabetes, these liver biopsy findings were consistent with glycogenic hepatopathy. Although the patient had alpha-1-antitrypsin deficiency, it was not believed to have contributed to his elevated liver enzymes because there were minimal scattered alpha-1-antitrypsin globules and no inflammation or fibrosis on biopsy. With better glycemic control, the patient's liver enzymes returned to normal levels. Unfortunately, the patient had a relapse because his diabetes again became uncontrolled.

Glycogenic hepatopathy is a disease process in which abnormal glycogen deposits in the liver, causing elevation of serum transaminases. It is usually seen in patients with poorly controlled type 1 diabetes, with clinical signs and symptoms including abdominal pain, nausea, vomiting, and hepatomegaly. The key histologic findings of glycogenic hepatopathy are swollen and pale-staining hepatocytes on hematoxylin and eosin stains and extensive glycogen accumulation seen on periodic acid-Schiff stains. Other histologic features include prominent glycogenated nuclei, giant mitochondria, and scattered acidophilic bodies. The marked accumulation of glycogen in hepatocytes is believed to cause hepatomegaly and leakage of transaminases. Rapid enlargement of the liver results in stretching of the liver capsule and abdominal pain.

References