64-Year-Old Woman With Diarrhea and Increased Abdominal Girth

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A 64-year-old woman presented to our institution for evaluation of diarrhea and increasing abdominal girth. She had a 1-month history of postprandial diarrhea unrelated to the type of foods she consumed. Her stool was watery, with no evidence of gastrointestinal bleeding. Concurrently, she also noted increasing abdominal girth requiring new pants with a larger waist size. She had no abdominal pain, nausea/vomiting, flushing, light-headedness, or constitutional symptoms.

Her medical history was notable for a previous stroke with a mild residual right hand tremor. She was a lifetime nonsmoker, had no history of illicit drug use, and drank alcohol rarely. She had no history of recent travel, infectious exposures, new medications, or herbal supplement intake.

Her blood pressure was 136/83 mm Hg, and her heart rate was 98 beats/min. Her oxygen saturation was 95% while she breathed room air, and her respiratory rate was 18 breaths/min. Her temperature was 36.9°C. Her mental status was normal. Her abdomen was soft, nontender, and mildly distended with hyperactive bowel sounds. Shifting dullness with a fluid wave was present.

1. **Which *one* of the following is the *most appropriate* diagnostic approach to evaluate the patient's abdominal symptoms?**
   a. Paracentesis
   b. Colonoscopy
   c. *Clostridium difficile* toxicology screen or polymerase chain reaction
   d. Serology testing for transglutaminase antibody
   e. Abdominal radiography

The patient's history and physical examination findings are indicative of ascites. For patients with new-onset ascites, spontaneous bacterial peritonitis (SBP) must be urgently ruled out. Diagnostic paracentesis is the most appropriate diagnostic step because it is a safe procedure that would reveal the presence of SBP and the etiology of ascites. Fluid neutrophil count greater than 250/μL or positive findings on fluid culture is diagnostic for SBP, which warrants prompt antibiotic administration. The presence of a serum ascites albumin gradient greater than 1.1 g/dL predicts portal hypertension. Furthermore, fluid cytology may indicate an underlying malignant disorder. Colonoscopy, *C difficile* toxicology/polymerase chain reaction, and transglutaminase antibody testing can be considered for a chronic diarrhea work-up. However, ascites fluid analysis to rule out SBP takes priority in this case. Abdominal radiography is useful for evaluating other causes of abdominal distention, such as bowel obstruction or bowel perforation. The patient's history and physical examination findings do not suggest these problems.

Our patient underwent ultrasound (US)-guided paracentesis, which yielded 2.5 L of straw-colored fluid. Her ascites neutrophil count was 68/μL, and the microbacterial culture showed no growth; therefore, the criteria for SBP were not met. The ascitic total protein was 2.6 g/dL. Her serum ascites albumin gradient was greater than 1.1 g/dL, which was diagnostic for portal hypertension.

Other pertinent laboratory findings (reference ranges provided parenthetically) included the following: macrocytic anemia (hemoglobin, 9.8 g/dL [12.0-15.5 g/dL]; mean corpuscular volume, 100.3 fL [81.6-98.3 fL]), leukocytosis (white blood cell count, 18.6×10^9/L [3.5-10.5×10^9/L]), thrombocytopenia (platelet count, 118×10^9/L [150-450×10^9/L]), and mild coagulopathy (international normalized ratio, 1.4 [0.8-1.2]). She had an elevated alkaline phosphatase (ALP) level (589 U/L [50-130 U/L]), but total bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and albumin levels were normal. Computed tomography (CT) of the abdomen with contrast medium revealed ascites, prominence of the left hepatic lobe, a patent umbilical vein, and splenomegaly. The biliary tree

See end of article for correct answers to questions.

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appeared normal. Incidentally, diffuse sclerosis was noted in the visualized bones but was most obvious in the vertebral bodies.

The patient was referred for a hepatology consultation.

2. The liver biochemical findings in this patient are *most* suggestive of which *one* of the following causes of liver injury?

a. Viral hepatitis
b. Autoimmune hepatitis
c. Nonalcoholic steatohepatitis (NASH)
d. Cholestatic liver disease (ie, hepatobiliary obstruction or infiltrative liver disease)
e. Alcoholic liver disease

Biochemical patterns of liver injury often provide clues about the etiology.[1] Hepatocellular damage such as viral and autoimmune hepatitis is characterized by a disproportionate increase in AST and ALT when compared with ALP and total bilirubin. Viral hepatitis is rarely accompanied by marked elevations in ALP, but it can be observed in the rapidly progressive entity known as fibrosing cholestatic viral hepatitis (B or C) arising after liver transplant. Autoimmune hepatitis does not manifest with substantial elevations in ALP unless there is an overlapping cholestatic disorder such as primary sclerosing cholangitis (PSC) or primary biliary cirrhosis. Patients with NASH may have normal liver test results or elevation of both AST and ALT that is typically no more than 2 to 5 times the upper limit of normal (ULN). Infrequently, mildly elevated ALP may be seen in patients with NASH (up to 2 to 3 times the ULN).

Our patient's markedly elevated ALP, which was more than 4 times the ULN, is suggestive of cholestatic liver disease. Of note, ALP is found in the biliary epithelium as well as in bones, intestines, and placentas. Alkaline phosphatase fractionation was performed in our patient because, as evident on CT, she had bony lesions that could contribute to an increase in ALP. Fractionation confirmed that her ALP elevation is related to hepatobiliary disease.

Cholestasis can arise from intrahepatic or extrahepatic causes. This patient did not have CT or US findings of extrahepatic biliary disease or ductal abnormalities suggestive of choledocholithiasis, stricture (ie, PSC), or tumor. It is important to note that normal findings on CT or US do not rule out PSC, especially small-duct PSC. Intrahepatic causes of cholestasis are myriad but include PSC, primary biliary cirrhosis, infiltrative liver diseases, and drug-induced liver injury.

Patients with alcoholic hepatitis classically have AST concentrations 2 to 3 times higher than the ALT concentration, and aminotransferase levels do not typically exceed 4 times the ULN.

Antimitochondrial antibody testing was performed to detect primary biliary cirrhosis, and serum protein electrophoresis with serum free light chain testing was undertaken to evaluate the possibility of a paraproteinemia; the results were unremarkable. Additionally, transthoracic echocardiography was performed to rule out congestive hepatopathy given that the ascitic fluid total protein level was more than 2.5 g/dL. Echocardiography revealed no abnormalities.

3. Which *one* of the following is the *most appropriate* next step to establish a definitive diagnosis?

a. Hepatic US with Doppler studies
b. Magnetic resonance cholangiopancreatography
c. Liver biopsy
d. α-Fetoprotein level measurement
e. Endoscopic retrograde cholangiopancreatography

Hepatic US is a noninvasive imaging modality to evaluate the anatomy of the biliary tree and hepatic parenchyma. It can detect biliary obstruction, cysts, and mass lesions within the liver and changes in the hepatic parenchyma. Doppler can detect abnormalities in hepatic vasculature such as clots or tumor. However, the findings on US rarely provide a definite diagnosis. Magnetic resonance cholangiopancreatography would be most helpful in situations in which biliary obstruction from tumor, stricture (ie, PSC), or a common bile duct stone is the suspected cause, but again, a definitive diagnosis requires more than an imaging evaluation.

Obtaining a tissue sample for histologic examination is the best way to reach a definitive diagnosis. A liver biopsy can measure the hepatic vein pressure gradient to confirm the presence of portal hypertension and identify

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