Care of the Cholestatic Patient

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KEYWORDS

• Cholestasis • Biliary tract disease • Bile duct obstruction • Primary biliary cirrhosis • Primary sclerosing cholangitis • Cholestatic liver disease

KEY POINTS

- Cholestasis may be identified through blood work or may be clinically evident.
- Causes of cholestasis require a thorough review of the patient's medical and surgical history, medication list, and symptomatology.
- Initial evaluation of the patient with cholestasis should include imaging of the liver and biliary tree.
- Management of reversible conditions may require endoscopic or surgical intervention.
- Chronic cholestatic liver disease may contribute to fatigue, pruritus, fat-soluble vitamin deficiencies, and bone loss.

INTRODUCTION

Cholestasis is defined as impairment of bile formation or bile flow. Care of the patient with cholestatic features is dependent on identifying the cause of the cholestasis, initiating appropriate treatment of reversible conditions, and the recognition and management of cholestasis-specific complications. Cholestasis may include extrahepatic ducts and intrahepatic bile ducts, or may be limited to one or the other. Jaundice and pruritus are the hallmarks of cholestasis clinically but biochemical evidence may, and often does, precede the clinical manifestations.

DIAGNOSIS

Clinical Presentation

Patients with cholestasis may present with pruritus, fatigue, or jaundice. Dark urine and acholic stools are also symptoms of cholestasis. Many patients, however, are entirely asymptomatic and are diagnosed only after the discovery of liver test abnormalities on routine blood work.

Clinically, a cholestatic disorder can often be differentiated from a primarily hepatocellular disorder by the enzyme pattern. If there is a greater elevation proportionally in

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the alkaline phosphatase when compared with the aminotransferases, the profile is more consistent with cholestasis. The increased serum levels of alkaline phosphatase are thought to be caused by the damaging effect of high concentrations of bile acids on intracellular and biliary membranes.[1] If an alkaline phosphatase is elevated in isolation, isoenzyme fractionation may be warranted. The gamma glutamyltranspeptidase is also often elevated in cholestasis.

Patients who are cholestatic may present with conjugated hyperbilirubinemia. Extrahepatic biliary obstruction causes conjugated hyperbilirubinemia in 80% of patients. Serum bile acids are the most sensitive test for cholestasis but testing is usually not readily available in the clinical setting.

Cholestasis is considered chronic when present for greater than 6 months. It may be further defined as primarily intrahepatic or extrahepatic, and many cases are acute on chronic. Most chronic cases of cholestasis are intrahepatic and approximately 50% of these patients demonstrate conjugated hyperbilirubinemia.

Evaluation

Obtaining a thorough patient history is essential to the diagnostic process. First, a patient's medication list should be thoroughly reviewed for potentially offending agents. Any medicines taken within the previous 6 weeks should be considered. The list of possible medicines to consider is extensive but may include estrogens, oral contraceptives, anabolic steroids, phenytoin, cyclosporin, dapsone, and erythromycin (**Box 1**). Use of herbal medicines or teas, vitamins, and other supplements should be reviewed and discontinued when possible. Total parenteral nutrition may also cause cholestasis. A history of fever, especially when accompanied by rigors or right upper quadrant abdominal pain, is more suggestive of cholangitis caused by obstructive processes, such as choledocholithiasis. These symptoms may be seen in alcoholic disease, however, and rarely in the setting of viral hepatitis.[1] Recent surgery in the region of the biliary system may have resulted in an inadvertent injury to a bile duct and should also be considered as a possible cause.

Abdominal ultrasound (US) is often the initial imaging performed when evaluating cholestasis. Advantages of US include relatively low cost, noninvasiveness, and the absence of radiation. US can effectively evaluate for intrahepatic and extrahepatic bile duct dilation and the presence of mass lesions; however, operator variability can be an issue. US is highly dependent on the skill of the sonographer and the experience of the interpreter. In addition, technical limitations include the inability to penetrate bone, and bowel gas obstructing the view. Ultrasound can differentiate between intrahepatic and extrahepatic causes of biliary tract disease, however, and can readily identify gallbladder pathology.[2]

Computed tomography is less operator dependent than US, is more effective when imaging obese patients, and is less susceptible to bowel gas when evaluating the distal bile ducts. Computed tomography is more accurate than US at identifying the level (88%–97% vs 23%–95%) and the cause (70%–94% vs 38%–94%) of biliary obstruction if present.[3] It is not as able to identify choledocholithiasis, however, and exposes the patient to radiation.[4] Computed tomography is reserved for equivocal US findings rather than for first-line imaging.

Magnetic resonance imaging is useful in the diagnosis of chronic versus acute causes of cholestasis. Use of magnetic resonance cholangiopancreatogram (MRCP) is considered a safe, noninvasive tool for evaluating the biliary tree. Advantages include the lack of radiation and sharp contrast resolution between normal and abnormal tissues. The accuracy of MRCP is comparable with endoscopic cholangiography. A review of 67 studies found that MRCP sensitivity and specificity to