This syndrome is caused by extrinsic compression from an impacted stone in the cystic duct that impinges on and obstructs the common bile duct (see Table 40-1). Portal hypertensive biliopathy (or vascular biliopathy) is characterized by anatomic and functional abnormalities of the intrahepatic, extrahepatic, and pancreatic ducts in patients with portal hypertension associated with extrahepatic portal vein obstruction or, less frequently, cirrhosis. These morphologic changes, consisting of dilatation and stenosis of the biliary tree, are caused by extensive venous collaterals that develop in an attempt to decompress the portal venous blockage. The condition is usually asymptomatic until it has progressed to a more advanced stage such as biliary cirrhosis.

Immunoglobulin G4 (IgG4)–related sclerosing disease has recently been recognized as a distinct disease entity that can affect the bile ducts, gallbladder, pancreas, and other sites. Most cases of IgG4-related pancreatobiliary disease are associated with elevated serum IgG4 levels, extensive IgG4-positive plasma cells, and infiltration of lymphocytes into various organs, which leads to fibrosis. Several established systems are used to diagnose IgG4 disease; they rely on a combination of imaging findings of the pancreas, bile duct, and other organs; serologic findings; pancreatic histologic findings; and response to corticosteroid therapy.

CLINICAL APPROACH TO THE EVALUATION OF JAUNDICE

Because the differential diagnosis of jaundice is broad, a thorough history and physical examination and judicious use of laboratory and imaging studies are needed to define its cause. Jaundice appears as yellowing of the skin and sclera. Other conditions may mimic this presentation (e.g., carotinemia, Addison's disease, quinacrine ingestion), but scleral and mucosal discolorations are absent in these conditions. In hypercarotinemia, for example, the yellowish-orange coloration typically involves only the palms of the hands and soles of the feet.

An elevated serum bilirubin level, usually higher than 3 mg/dL, confirms the clinical impression of jaundice. The most important initial step is to define whether the jaundice is predominately caused by an elevation of unconjugated or of conjugated bilirubin. If jaundice is primarily the result of unconjugated bilirubin, evaluation for hemolysis and other conditions with shortened red blood cell survival is required. In patients with elevated conjugated bilirubin, the clinical challenge lies in determining whether biliary obstruction or impaired hepatic excretion is responsible (see Chapter 39).

In cholestatic jaundice caused by biliary obstruction the alkaline phosphatase level is typically increased to more than three times normal, whereas serum transaminases are usually elevated less than 5-fold to 10-fold (E-Fig. 40-3; see Chapter 39). Patients with cholestasis also may develop pruritus and malabsorption of fat and fat-soluble vitamins (vitamins A, D, E, and K). More specific causes of biliary obstruction are suggested by recurrent abdominal pain and nausea (gallstones) or epigastric pain radiating to the back with weight loss and gallbladder distention (carcinoma of the pancreatic head). In complete biliary obstruction, conjugated hyperbilirubinemia is prominent and usually peaks at about 30 mg/dL in the absence of renal failure. Eosinophilia may accompany drug-induced jaundice. Inquiry about the use of drugs known to cause cholestasis, serologic testing for antimitochondrial antibody in suspected PBC, and endoscopic retrograde cholangiopancreatography (ERCP) or magnetic resonance cholangiopancreatography (MRCP) to evaluate PSC may be helpful.

In jaundice produced by hepatocellular disease (see Chapters 41 and 43), serum transaminases are characteristically elevated more than 10-fold and alkaline phosphatase levels are less than three times normal. Evidence of hepatocellular damage is commonly associated and includes a prolonged prothrombin time, hypoalbuminemia, and clinical features of hepatic dysfunction (palmar erythema, spider angiomas, gynecomastia, and ascites). A careful evaluation includes inquiry about the use of drugs known to cause hepatocellular injury, alcohol, risk factors for viral hepatitis, and preexisting liver disease. More selected laboratory studies, such as serologic testing for hepatitis, are usually required (see Chapter 41).

A diagnostic approach to jaundice is outlined in E-Figure 40-2. If extrahepatic obstruction is suspected, noninvasive studies such as ultrasound or computed tomography should be used to determine whether bile ducts are dilated. If dilated ducts are found on noninvasive imaging, then direct cholangiography (either endoscopic or radiologic) provides the most reliable approach to management and potential treatment of cholestatic jaundice. If intrahepatic cholestasis is suggested clinically and extrahepatic obstruction is excluded by noninvasive means or by direct cholangiography, then the emphasis is placed on further laboratory testing to define the specific cause. Liver biopsy is sometimes required to define a specific histologic diagnosis, rule out other causes of disease, and assess the degree of injury and fibrosis.

For a deeper discussion on this topic, please see Chapter 147, "Approach to the Patient with Jaundice or Abnormal Liver Tests," in Goldman-Cecil Medicine, *25th Edition.*

SUGGESTED READINGS

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