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Gallbladder disease in children

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ABSTRACT

Biliary disease in children has changed over the past few decades, with a marked rise in incidence—perhaps most related to the parallel rise in pediatric obesity—as well as a rise in cholecystectomy rates. In addition to stone disease (cholelithiasis), acalculous causes of gallbladder pain such as biliary dyskinesia, also appear to be on the rise and present diagnostic and treatment conundrums to surgeons.

Introduction

The spectrum of pediatric biliary tract disease continues to change. Although congenital and neonatal conditions such as biliary atresia and choledochal cysts remain relatively constant, the incidence of cholelithiasis and biliary dyskinesia have dramatically increased over the past several decades.[1] This has resulted in a significant increase in the number of cholecystectomies performed by pediatric surgeons.[2]

Gallstones

Etiology and incidence

Until recently, pediatric gallstones were frequently pigmented stones from hemolytic diseases such as hemolytic anemia, sickle cell disease, hereditary spherocytosis, thalassemia major, pyruvate kinase deficiency, and other processes with red blood cell breakdown. Hemolysis causes release of hemoglobin, and its degradation results in increased bilirubin; further conjugation of bilirubin with calcium leads to pigmented gallstones. As many as half of children under 10 years of age with sickle cell disease have gallstones, many asymptomatic. The incidence is lower in hereditary spherocytosis.[3] The incidence of pigmented hemolytic gallstones in children has remained stable at 15%.[4]

In recent decades the incidence of gallstone disease in children has risen, principally related to the epidemic of pediatric obesity.[4] In these patients, the etiology of the gallstones is supersaturation of bile due to excess cholesterol, and this variety is the most common type of stone encountered in children today. The proximate cause of cholesterol stones is bile that is saturated with cholesterol beyond the point at which it is completely soluble.

Other than obesity, another factor which has led to an increased incidence of cholelithiasis in the pediatric population over time is improved survival of critically ill neonates who have received long-term total parenteral nutrition and/or have underlying abnormalities resulting in short-gut syndrome.

In a report by Walker et al.,[4] the number of cholecystectomies (for non-pigmented gallstones) performed in children increased by 213% over a 9-year period ending in 2012. The incidence of cholecystectomy in England has been reported to have tripled since 1997, the increase being primarily in white females.[5]

Diagnosis

The majority of children and adults with cholelithiasis are asymptomatic (> 75%). Right upper quadrant abdominal pain is the most common complaint in the remainder, with the classic description of biliary colic being sharp, intermittent, cramping pain radiating to the right shoulder, nausea, and vomiting. The pain occurs most commonly after a fatty meal and may last for several hours. Other symptoms include nausea, vomiting, and occasionally fever. Ultrasound is the most appropriate imaging study to evaluate the biliary tree. Sonographically, gallstones appear as hyperechoic, mobile structures with acoustic shadowing. Ultrasound has a sensitivity and specificity greater than 95% in the detection of gallstones. Endoscopic ultrasound is being used more often in children in the setting of complicated biliary stone disease. Computed tomography has little utility in the diagnosis of

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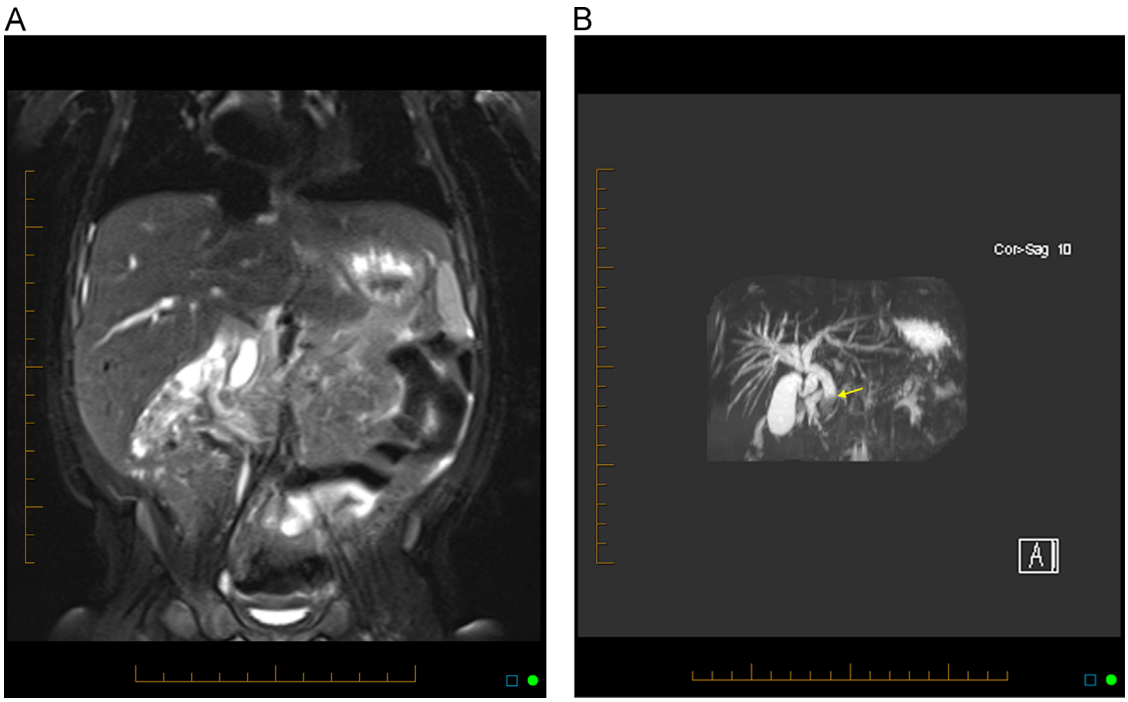

Fig. 1. (A) MRCP with coronal T2 sequence through the dilated common bile duct demonstrates obstructing stone in the distal duct. (B) 3D MIP of the biliary system demonstrates intra- and extra-hepatic ductal dilatation as a result of the obstructing stone in the distal duct (arrow). (*Courtesy*: Kristin Fickenscher, Kansas City, MO.)

gallstones, since greater than 60% of gallstones are radio-lucent and the imaging modality exposes patients to radiation unnecessarily. Though not helpful in the diagnosis of cholelithiasis, magnetic resonance imaging (MRI) and magnetic resonance cholangiopancreatography (MRCP) are useful in identifying common bile duct (CBD) stones and delineating pancreatic and biliary tract anatomy (Figure 1A and B). There are no lab tests specific in diagnosing cholelithiasis; however, liver function tests and amylase and lipase are helpful in screening for CBD stones and pancreatitis.

Complications of gallstones

Acute calculous cholecystitis

Inflammation of the gallbladder is most often due to obstruction of the cystic duct by stones. The obstruction results in gallbladder swelling followed by bile acid concentration, wall ischemia and occasionally, bacterial infection. Symptoms of biliary colic usually precede acute calculus cholecystitis with the addition of increased vomiting and fever. Most patients have significant right upper quadrant tenderness on exam and occasionally a palpable mass. Ultrasound can identify stones, gallbladder wall thickening ($>$ 4–5 mm) and edema (double-wall sign), gallbladder sludge, pericholecystic fluid, and a sonographic Murphy's sign. MRCP may be helpful in selected cases. White blood cell counts and C-reactive protein levels are frequently elevated.

Common bile duct obstruction

Common bile duct stones (choledocholithiasis) are identified in approximately 10% of adults with cholelithiasis and 5–18% of adults undergoing elective cholecystectomy. The exact incidence of choledocholithiasis in children is unknown, but presumably is increasing as cholelithiasis increases. A recent report noted that 11% of children undergoing cholecystectomy were found to have CBD stones.[6] Associated signs include jaundice, acholic stools, and dark urine. Patients with common bile duct stones can present with acute cholangitis, manifested by fever, jaundice, and right upper quadrant pain. Acute cholangitis is a surgical emergency and prompt biliary decompression is necessary.

Pancreatitis

Gallstones are one of the leading causes of acute pancreatitis in adults. Though biliary tract disease is reported to be a cause of pediatric pancreatitis in up to 30% of adult cases, the exact incidence of gallstone pancreatitis in children is not clear but appears to be increasing. A recent report found that 25% of pediatric pancreatitis had a biliary (gallstone) origin.[7] Patients with gallstone pancreatitis present with epigastric abdominal pain, nausea, and vomiting, and may or may not have a history of previous gallbladder-related symptoms. Amylase and lipase are elevated, and jaundice/elevated conjugated serum bilirubin is often present. Ultrasound is again the first-line imaging study.

Acute acalculous cholecystitis

Acute acalculous cholecystitis (AAC) is an inflammation of the gallbladder, which is not associated with the presence of gallstones and may account for greater than 50% of pediatric cholecystitis cases. Although this pathology was initially described in critically ill patients, currently most pediatric cases have been observed during several infectious diseases. Symptoms are abdominal pain (mild to severe), often more pronounced at the right upper quadrant, and fever. The diagnosis of AAC is usually obtained through abdominal ultrasonography that can reveal increased gallbladder wall thickness ($>$ 4–5 mm), pericholecystic fluid, and presence of mucosal membrane sludge (Figure 2A and B). The presence of at least two of these US criteria, in addition to the absence of gallstones, defines the diagnosis of AAC in the pediatric population. AAC was originally described in complex and often critically ill children. Tsakayannis et al.[8] described a cohort of 25 patients (observed between 1970 and 1994): most children developing AAC presented with an underlying clinical condition, such as