Acquired disorders of the biliary tract in children

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Abstract

Acquired diseases of the biliary tract are less common in children than in adults. Gallstones, sclerosing cholangitis and biliary complications after liver transplantation are the most frequent problems but biliary obstruction can be secondary to pancreatitis, tumours and biliary sludge and bile leaks are a recognized risk following trauma to the liver. Biliary disease may be asymptomatic and suspected due to abnormal liver function tests or ultrasound scan. Right sided abdominal pain, features of biliary obstruction or sepsis occur in symptomatic children. Identification and relief of biliary obstruction requires a collaborative approach involving paediatric hepatologist, surgeon and radiologist. In those with long standing cholestasis, as can occur in sclerosing cholangitis, supportive management of itching and nutrition improves quality of life. The outcome following liver transplantation for those progressing to end stage liver disease is very good.

Keywords bile leak; biliary obstruction; biliary stenosis; gallstones; sclerosing cholangitis

Overview

Biliary disease in children can be congenital or acquired. Congenital disorders, including biliary atresia, choledochal cyst, Alagille syndrome, account for approximately 50% of the patients in paediatric liver units. Acquired disorders are less common but have a wide range of aetiologies which need to be identified to allow prompt and appropriate management. This review will discuss the latter group.

Aetiology and presentation

Table 1 lists the causes of acquired biliary disease presenting to our specialist paediatric liver centre over 12 years. Presentation ranges from asymptomatic children identified by abnormal liver function tests or ultrasound scan to those with evidence of biliary obstruction with jaundice, pale stools and dark urine. Symptoms also include fatigue, itching and right sided abdominal pain. Any child with features of biliary obstruction needs to be referred to hospital for further investigation. Children with cholangitis or perforation of the bile ducts can be acutely ill and need immediate hospitalization.

Pathophysiology

Obstruction of the biliary tract results in dilatation of the biliary tree proximal to the obstruction and poor bile flow into the duodenum. Inability to adequately excrete conjugated bilirubin causes high serum levels, bilirubinuria and acholic stools. High circulating levels of bile salts are associated with itching and chronically low levels of bile salts in the duodenum result in malabsorption of fat and fat soluble vitamins. Stasis of bile in the biliary tree can lead to infection or occasionally even perforation of the bile ducts and infective or chemical peritonitis. Chronic retention of bile salts is toxic to the hepatocytes and if this persists over months to years it eventually causes biliary cirrhosis and the attendant complications of portal hypertension, liver failure or hepatocellular carcinoma.

Investigation

In biliary obstruction liver function tests are abnormal with raised conjugated bilirubin, alkaline phosphatase and gamma glucuronyl transferase (GGT). Transaminases are also usually raised but not typically to the levels seen in hepatitis. A high amylase could suggest pancreatitis as the cause of the obstruction and evidence of haemolysis would be in keeping with pigmented gallstones. Ultrasound scan can demonstrate the level of obstruction, the presence of biliary sludge or gallstones, pancreatitis, pancreatic mass or other causes of external compression of the bile ducts. In sclerosing cholangitis the biliary dilatation is often more subtle and requires more sensitive imaging modalities such as Magnetic Resonance Cholangiopancreatography (MRCP) or Endoscopic Retrograde Cholangiopancreatography (ERCP).

Management

Specific management is mainly dependent on the cause of the biliary disease and is discussed in more detail below. Ursodeoxycholic acid (10–20 mg/kg/day) is used to improve bile flow through narrowed biliary tracts. In all children with chronic cholestasis of any aetiology supportive management includes antipruritic medication such as rifampicin, ondansetron or cholestyramine, aggressive nutritional support and supplementation with fat soluble vitamins.

Gallstones

Epidemiology

Gall bladder pathology is increasingly responsible for a consultation in a paediatric hepatobiliary clinic. Gallstones are being diagnosed more frequently, partly due to improved and readily available diagnostic tools but also due to increasing obesity amongst children and adolescents. They have been identified in all age groups, including the fetus. The prevalence of gallstones in children ranges from 0.13% to 0.22% and rises to 1.9% in children who undergo an ultrasound for abdominal pain. The incidence has two peaks, one in infancy with equal incidence between the sexes and the second in adolescents where females predominate as in adult gall bladder disease.

According to Hospital Episode Statistics there were 2808 paediatric cholecystectomies in England and Wales between

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Spectrum of acquired biliary problems presenting to a supra regional paediatric liver service over a 12 year period

Cause of biliary problem	No of cases	Additional information
Gallstones	117	15 Spherocytosis Eight sickle-cell anaemia Five parenteral nutrition Five neonatal cholestasis Four Gilberts/Crigler-Najjar 19 Others inc CF, Downs syndrome
Sclerosing cholangitis	66	20 Overlap with AIH 49 Associated IBD Three due to LCH One CD 40 ligand deficiency
197 Liver transplant recipients	32	14 Bile leaks 13 Anastomotic strictures Five non-anastomotic strictures
Pancreatitis causing biliary obstruction	19	Seven acute pancreatitis Nine chronic/fibrosing pancreatitis Three with gallstones
Tumours causing biliary obstruction	11	Four pancreatic tumours Three inflammatory pseudotumours Two lymphoma One neuroblastoma One leukaemia
Inspissated bile syndrome	11	
Biliary problems in 34 cases of liver trauma	7	All bile leaks
Spontaneous perforation of Bile ducts	1	

CF = cystic fibrosis, IBD = inflammatory bowel disease, LCH = Langerhan's cell histiocytosis.

Table 1

1997 and 2012. The incidence of cholecystectomy increased more than threefold, from 0.78/100,000 in 1997–8 to 2.7/100,000 in 2011–12. The increase was greatest among girls (1.1–4.36), but was also highly significant among boys (0.48–1.13). Such a drastic increase is more likely due to the proportionate increase in the prevalence of obesity rather than the availability of ultrasound. Furthermore, there is no evidence that this trend is slowing down.

Pathogenesis

In almost 50% of children the cause of cholelithiasis is unknown. Currently, haemolytic disorders including hereditary spherocytosis, sickle-cell anaemia, thalassaemia, probably account for 25% of gallstones in children. Other risk factors are obesity, genetic, obstruction to bile flow, medications (cyclosporine, ceftriaxone, furosemide, contraceptive pill), pregnancy, ileal resection/disease, total parenteral nutrition, cystic fibrosis and Downs syndrome.

Gallstones can be classified as pigment, cholesterol or mixed stones. Mixed and cholesterol stones are more common in adults and female adolescents and are typically associated with obesity. Pigment stones are more frequent in younger children. Black pigment stones are associated with haemolytic disorders and parenteral nutrition whereas brown pigment stones are seen in children with sepsis or biliary stasis.

Clinical features

Fetal and neonatal gallstones are often asymptomatic. However at any age gallstones can cause abdominal pain and biliary colic. Abdominal pain is poorly localized in young children but older children and adolescents will localize it to the right hypochondrium. Unfortunately 20% of children undergo an appendectomy before the correct diagnosis is established. Some patients will present with complications; cholecystitis, cholangitis, obstructive jaundice due to obstruction of the common bile duct, pancreatitis, empyema of the gall bladder (when a gallstone blocks the outflow of the gall bladder) or perforation of the gall bladder. In young children fatty food intolerance is not as common as in adults.

Diagnosis

An ultrasound scan will detect stones as small as 1.5 mm in diameter in the gall bladder. Acoustic shadowing occurs with slightly larger stones but not with biliary sludge. Often there are multiple stones and sometimes the wall of the gall bladder is thickened. Stones in the bile ducts can be more difficult to see with ultrasound. If the child has obstructive jaundice and dilatation of the bile ducts the offending stone can be demonstrated and removed endoscopically via ERCP.

Management

Management of gallstones is determined by the age of the child and the presence of symptoms. In a recent review of gallstones in 382 children the stones were no longer visible with ultrasound in 34% of children under 1 year of age and 13% of those older than 1 year. Thus it is common practice to observe asymptomatic gallstones with follow up ultrasound scans, particularly in infants. To date dissolution therapy for gallstones in children has been disappointing except in neonates.

In children with symptoms or complications cholecystectomy is advised. In those with haemolytic disease due to hereditary spherocytosis or thalassaemia major, cholecystectomy even for asymptomatic stones is recommended if the child is undergoing splenectomy. Most centres also have a low threshold for cholecystectomy in patients with sickle-cell anaemia even when their stones are asymptomatic, as it is difficult to distinguish between complications of gallstones and sickle-cell abdominal crisis.

Most surgeons favour laparoscopic cholecystectomy as it is less invasive and recovery is quicker. In children with a stone obstructing the common bile duct laparoscopic cholecystectomy with intraoperative cholangiogram preceded or followed by ERCP for stone removal is necessary.