Cholecystitis and Gallstone Disease

90

Nathan Maassel and David H. Stitelman

Gallstone disease, while rare in the pediatric population, is increasing in prevalence. Despite similarities in the overarching pathway for diagnosis and management of gallstone pathology in both children and adults, the etiology and risk factors unique to children and adolescents require nuanced care. Gallstones form due to an imbalance in the bile milieu (bile salts, bilirubin, lecithin, cholesterol, calcium) leading to a variety of types of stones and distinct differences in the proportions of these stone types in children and adults. In neonates and infants, hyperalimentation, short bowel syndrome, infection, dehydration, and cystic fibrosis predispose children to development of gallbladder pathology. In young children, a smaller proportion of stones are cholesterol-based (25%), with the majority being pigmented stones (>50%) due to an excess of bilirubin, predominantly in patients with hematologic disorders. The majority (80%) of cholelithiasis in adolescence is due to cholesterol-based stones resulting from an excess of cholesterol in bile, which parallels the most common risk factors in this population (female sex, obesity, hyperlipidemia, sedentary lifestyle).

Diagnosis

Upper abdominal pain can be due to a variety of causes, some pertinent to the biliary tree (Table 90.1). Cholelithiasis, cholecystitis, and biliary dyskinesia all present with abdominal pain, but with varying time courses and imaging findings. These diagnoses should be considered along with other causes such as gastroesophageal reflux disease, appendicitis, obstruction, pneumonia, and intussusception. Bowel obstruction from a gallstone eroding through the gallbladder into the bowel (gallstone ileus) occurs in adults but has not been described in children.

Table 90.1 Clinical and radiographic characteristics of gallbladder and gallstone-related pathologies

Diagnosis	Stone location	Acute inflammation	Jaundice
Cholelithiasis	Gallbladder	N	N
Cholecystitis	Cystic duct	Y	N
Choledocholithiasis	Common bile duct	N	Y
Cholangitis	Common bile duct	Y	Y
Gallstone pancreatitis	Ampulla	Y	N
Biliary dyskinesia	n/a	N	N
Acalculous cholecystitis	n/a	Y	N

In a patient with pain and no jaundice, cholecystitis or gallstone pancreatitis should be considered; in a jaundiced patient, cholangitis and choledocholithiasis should be considered. Older children with cholelithiasis causing symptoms of biliary colic commonly complain of episodic right upper quadrant or epigastric pain and associated nausea. Occasionally, pain can also radiate to the back. These episodes classically come on after a fatty meal and last less than 4 h. Pain persisting beyond 6 h, especially when accompanied by fever, points more towards cholecystitis. In younger patients, the story may be less clear with only vague generalized abdominal discomfort or irritability.

On physical examination, right upper quadrant (RUQ) tenderness is suggestive of cholecystitis rather than biliary colic. The classic physical examination sign for cholecystitis is Murphy's sign, which involves abrupt cessation of inspiration with deep palpation in the RUQ. Again, in younger children the abdominal tenderness may be non-specific or generalized. Labs should include a complete blood count, total and direct bilirubin, alkaline phosphatase (ALK-PHOS), transaminases, gamma-glutamyl transferase (GGT), and amylase. In patients with cholecystitis, a leukocytosis is commonly present and there can be mild elevations in transaminases and ALK-PHOS. Elevated direct bilirubin (>2.5), GGT, and ALK-PHOS are indicative of choledocholithiasis,

N. Maassel · D. H. Stitelman (✉)
Yale-New Haven Children's Hospital, New Haven, CT, USA
e-mail: Nathan.maassel@yale.edu; David.stitelman@yale.edu

P. Mattei (ed.), *Fundamentals of Pediatric Surgery*, https://doi.org/10.1007/978-3-031-07524-7_90

while elevated serum amylase would suggest the possibility of pancreatitis.

Patients with acute acalculous cholecystitis are usually critically ill with concomitant issues including sepsis, massive burns, Kawasaki's disease, or prior surgery. Depending on the age and mental status of the patient, the diagnosis might depend more on objective data such as fever, jaundice, leukocytosis, imaging findings, and elevated bilirubin or serum amylase.

A RUQ US is the initial diagnostic tool of choice to help discern gallbladder pathology. Gallbladder wall thickening, pericholecystic fluid, stones or sludge, and dimensions of the common bile duct (CBD) are important diagnostic clues. A sensitive test for cholecystitis on ultrasound is the sonographic Murphy's sign, in which the patient is most tender when the radiographer compresses the gallbladder with the US probe.

In patients without a clear diagnosis of but persistent suspicion for cholecystitis, the hepatobiliary iminodiacetic acid (HIDA) scan is a very sensitive test for cholecystitis. The absence of gallbladder back-filling with radiotracer and visualization of the duodenum provides evidence of cystic duct obstruction. HIDA scans can also be useful adjuncts in the diagnosis of biliary dyskinesia in the patient with a normal US but persistent complaints of episodic RUQ or epigastric pain that otherwise suggests biliary colic. In the absence of other upper gastrointestinal pathology, cholecystokinin can be administered and HIDA scan obtained to generate a gallbladder ejection fraction. An ejection fraction of <35% is a commonly used cutoff to suggest biliary dyskinesia.

Jaundice, elevated direct bilirubin, or a dilated common bile duct on US suggests the possibility of choledocholithiasis and often warrants further imaging with magnetic resonance cholangiopancreatography (MRCP). We find this to be most useful in the borderline patient that has a modest elevation in bilirubin, but a normal-appearing CBD to guide whether endoscopic intervention is necessary. Patients with choledocholithiasis and signs of inflammation or ascending cholangitis present with Charcot's triad (RUQ pain, jaundice, fever) and can become quite sick and unstable. Historically, Reynold's pentad is Charcot's triad with the addition of hypotension and confusion due to sepsis. Patients with cholangitis need resuscitation, antibiotics and decompression, usually in the form an endoscopic retrograde cholangiopancreatography (ERCP) and percutaneous transhepatic cholangiography (PTC).

The diagnosis of biliary colic or cholecystitis can be more difficult in patients with hematologic disorders such as hereditary spherocytosis, thalassemia major, or sickle-cell disease (SCD) as these patients may have hemolysis masquerading as gallbladder pathology. Particularly in the patient with SCD and fever, abdominal pain, and jaundice, these symptoms can be due to a hemolytic crisis rather than gallstones. Using a direct bilirubin level and total bilirubin to calculate an indirect bilirubin can help differentiate hemolysis from biliary obstruction.

Treatment

Elective cholecystectomy should be offered to all patients with symptomatic gallstones. Patients with SCD and symptomatic gallstones require preoperative intravenous (IV) hydration or blood transfusion to a hemoglobin of 10 (mg/dL), which reduce the likelihood of painful crises by decreasing the proportion of circulating hemoglobin S prior to the stress of surgery. Children with hereditary spherocytosis who are recommended for splenectomy should also be screened with an US and if stones are present a cholecystectomy should be considered and can usually be performed in conjunction with splenectomy. Biliary dyskinesia is another relatively common indication for elective cholecystectomy; however, because up to 30% will have pain despite removal of the gallbladder, patients should be counseled appropriately.

Patients presenting with cholecystitis probably benefit from undergoing cholecystectomy during their index admission, usually within the first 24 h. Standard management starts with adequate IV fluid resuscitation and broad-spectrum antibiotics, despite the lack of strong evidence, especially in mild cases.

In cases of gallstone pancreatitis, patients should probably have their cholecystectomy during their index admission as well, though patients are typically given IV fluids and observed until the abdominal pain—and presumably the acute inflammation—have resolved. Most stones that cause pancreatitis seem to pass on their own without intervention (so ERCP for gallstone pancreatitis is not always warranted); however, jaundiced patients or those with impressive or persistent elevations in bilirubin or liver function tests should have choledocholithiasis ruled out.

Though rare, a small percentage of children can present with stones in their common bile duct. In general, patients with clinical concern for choledocholithiasis at our institution will undergo ERCP prior to cholecystectomy. The effectiveness of ERCP has increased significantly over the past decade and while minor complications are not uncommon (up to 10%), major complications are rare. If ERCP fails, another option is PTC by interventional radiology to decompress the biliary tree. If non-operative decompression is unsuccessful or common bile duct stones are identified on intraoperative cholangiogram, the biliary tree can be irrigated at the time of cholecystectomy. Choledocoscopy and the use of wire baskets are another option at centers with experience in the technique, which allows direct visualization of the biliary mucosa and removal of intraductal stones via endoscopy.

The rare critically ill child with acalculous cholecystitis and a prohibitive surgical risk may benefit from percutaneous cholecystostomy rather than cholecystectomy. Less severe cases may be treated expectantly with fluid resuscitation and antibiotics. The sub-population of neonates and infants with gallstones related to total parenteral nutrition (TPN) might also benefit from non-operative management and observation, but care is tailored for each patient. About 6 months to a year from cessation of TPN, infants without complicated disease can be re-evaluated and potentially avoid cholecystectomy as stones have been reported to dissolve after resumption of oral feeds. Although limited high-quality evidence exists for its effectiveness, ursodeoxycholic acid can be used in an attempt to hasten stone dissolution.

Mirizzi syndrome, extrinsic obstruction of the hepatic bile duct by a stone impacted in the infundibulum of the gallbladder or the cystic duct, is very rare in adults and reportable in children, but important to keep in mind as its spectrum of severity can warrant a much more complex operation. Pre-operative diagnosis can be difficult, but this process should be considered in children with obstructive symptoms of cholangitis. The syndrome can be associated with a cholecystobiliary fistula (type I has no fistula, types II-IV have fistulas of varying size and involvement of surrounding structures). Patients, due to their obstructive presentation, may undergo ERCP first where the diagnosis of Mirizzi syndrome can be made and a sphincterotomy performed prior to definitive repair. When the diagnosis is made in the operating room, an intraoperative cholangiogram should be performed to determine the presence and size of a fistula. For patients with no fistula, laparoscopic cholecystectomy is preferred if achievable; however, subtotal cholecystectomy or open cholecystectomy may be necessary. Patients with a fistula usually need a more complex, open reconstruction. If the entire wall of the bile duct is involved, a Roux en-y choledochojejunostomy is required. If only a small portion of the bile duct wall is involved, cholecystectomy with placement of a T-tube has been described (in adults).

Laparoscopic Cholecystectomy

For those requiring cholecystectomy, laparoscopy is the standard of care as it is associated with less pain, shorter length of hospital stay, and less scarring than the open approach. We usually obtain access to the abdomen via the periumbilical region through direct visualization. This can be infra- or supra-umbilical depending on body habitus. A 12 mm port is placed and the abdomen is insufflated to an age and weight-appropriate pressure. Three 5 mm ports are then placed in the sub-xiphoid, right subcostal, and right lateral positions. From the subcostal port, toothed forceps are used to grasp the gallbladder fundus and retract over the dome of the liver towards the patient's right shoulder, exposing the infundibulum. This facilitates gallbladder neck dissection. The peritoneum is dissected off the medial and lateral edges of the gallbladder, which allows visualization of the cystic duct and artery. This can be accomplished with either hook cautery or blunt dissection. Staying as close to the gallbladder as possible will reduce the risk of injuring aberrant anatomy or straying too far from the operative field. Once the gallbladder neck is dissected circumferentially, the goal is to obtain the critical view, which requires adequate dissection such that only two structures are seen to be entering the gallbladder (cystic duct and artery) with only liver parenchyma seen in the background. Each structure is sequentially divided, after first placing clips with two placed on the patient side and one on the specimen side. The length and course of the cystic duct can be variable and the safest place to clip and cut the gallbladder is as close to the infundibulum as possible. Often the relationship of the cystic duct to the common bile is less direct than what is depicted in textbooks, but difficult to appreciate intra-operatively as it is best to avoid seeing the common bile duct. It is also important to recognize that the cystic duct can take a circuitous path (Fig. 90.1).

The gallbladder is separated from the liver bed between the planes of the visceral peritoneum with electrocautery. Once the gallbladder is free from the liver bed, it can be removed with a specimen bag through the umbilical port. Any spillage of stones or bile should be removed from the abdomen and the operative field inspected for hemostasis. The umbilical port fascia is closed.

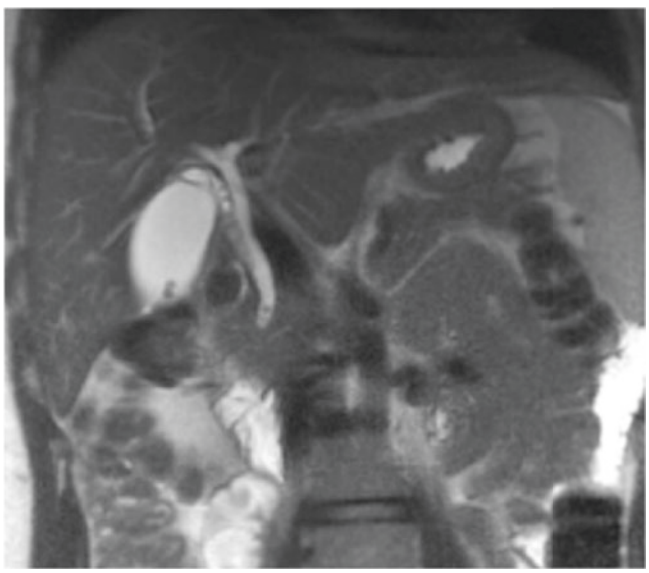

Fig. 90.1 MRCP of cholelithiasis and choledocholithiasis in a 16-year-old female patient. The position of the gallbladder and cystic duct in relation to the common bile duct can be appreciated here

Difficult Dissections

If there is extensive inflammation and the relationship and location of the cystic and common bile duct are poorly defined, one should consider performing an intraoperative cholangiogram: using an Olsen clamp, we place a 5-French catheter though a small opening in the gallbladder and inject water-soluble contrast (diluted 50:50 with saline with care to remove air bubbles) to generate a map of the biliary anatomy under fluoroscopy. To enter the biliary tree and to allow exchange of other catheters, a 0.035″ wire can be passed through the 5-French catheter. Cholangiogram is also indicated in patients with persistent suspicion for biliary obstruction. If retained common bile duct stones are noted, the cholangiogram catheter can be flushed to remove stones. If ERCP is not feasible or available, more advanced maneuvers such as wire baskets can be used to remove the stone either with fluoroscopy or under visualization with a choledocoscope.

If there is significant inflammation and poor visualization at the gallbladder neck due to severe inflammation or fibrosis, a critical view might be impossible to achieve, in which case a top-down approach can be used. The dissection starts at the fundus, where the gallbladder is separated from the liver parenchyma as in the final steps of the traditional approach. This dissection moves towards the infundibulum of the gallbladder where the cystic duct can then be transected at a safe location. In some cases, with a particularly short or non-existent cystic duct, a subtotal cholecystectomy can be performed, preferably using a stapling device, to avoid narrowing of the common bile duct with clips. Alternatively, the anterior wall of the gallbladder can be opened to identify the cystic duct internally which can then be closed after the gallbladder is removed. Open cholecystectomy is an option when the gallbladder cannot be visualized well laparoscopically or the disease process is severe enough to distort anatomy. Typically, a right subcostal (Kocher) incision is used for access. The operation may then proceed in a top-down manner.

Postoperative Care

Following an uncomplicated elective cholecystectomy in an otherwise health patient, same-day discharge or an overnight admission is usually the extent of hospitalization. Patients are commonly started on clear liquids and advanced to a regular diet as tolerated. Patients with SCD need to maintain good hydration and analgesia in the post-operative period to avoid the precipitation of painful crises.

While retrospective reviews of laparoscopic cholecystectomy in the pediatric population demonstrate minimal morbidity and essentially no mortality, complications do occur. In the short term, these include cystic stump leak, retained common bile duct stones, and common bile duct injury. The first step in assessing patients who return with pain is an US and laboratory studies including liver function tests. While fluid in the gallbladder bed is a normal postoperative finding, children returning with pain and elevated Liver Function Tests (LFTs) may require percutaneous drainage. If bile is aspirated from a fluid collection, ERCP and sphincterotomy should be performed with possible stenting to decompress the biliary tree. For patients with retained stones, ERCP is also the treatment of choice to retrieve the stone and perform sphincterotomy. Although rare, delayed common bile duct injuries are preferentially treated with a Roux-en-Y choledochojejunostomy. Patients are sometimes temporized preoperatively with a percutaneous transhepatic biliary catheter. In the long term, patients frequently describe looser stools, which typically recovers over the course of a few months.

Editor's Comments

Cholecystectomy is also not entirely without risk and can also result in the unpleasant and sometimes intractable problem of fecal urgency and loose stools. The most common indications for cholecystectomy in children include gallstones and biliary dyskinesia, each accounting for about half depending on local preferences. Gallstones probably rarely, if ever, disappear, so children with asymptomatic gallstones are usually recommended for cholecystectomy, though some are observed for indefinitely or prescribed ursodiol in the hope that the stones might resolve. Acalculous acute cholecystitis is rare in children and usually seen in the immunocompromised or critically ill. It is usually best treated with percutaneous cholecystostomy rather than cholecystectomy.

An increasingly common but controversial indication for cholecystectomy, biliary dyskinesia is characterized by intermittent RUQ or epigastric pain precipitated by meals, usually accompanied by nausea, and a positive CCK-HIDA scan (gallbladder ejection fraction <35%). If all three of these are present for at least several weeks or months, relief of pain can be expected in 90% of the cases. If the pain is atypical or not associated with nausea, or if the pain is typical but the gallbladder ejection fraction (GBEF) is within normal limits, the likelihood of success is diminished and cholecystectomy should be offered only if the patient is truly debilitated, all other likely causes have been thoroughly excluded, and the patient understands the likelihood of success might be closer to 50%. Some patients with an extremely high GBEF also seem to benefit from cholecystectomy.

Intra-operative cholangiogram is rarely necessary and really only indicated in the case of anatomic confusion. Children with a traditional indication for cholangiogram (jaundice, pancreatitis, dilated CBD) but whose symptoms

have resolved can usually safely undergo simple cholecystectomy. If they are thought to have a stone in the CBD, they should undergo ERCP prior to cholecystectomy. If an IOC shows CBD stones, the surgeon must decide between immediate common duct exploration and postoperative ERCP.

Three-trocar cholecystectomy is feasible but affords no significant advantage and the risks are higher. The single-port operation is used by some but whether it can be done with consistent safety remains to be seen. Robotic-assisted single-site cholecystectomy was promising as a useful and safe technique but has not caught on is now rarely performed. Ideally, the operating surgeon controls both the dissector and a grasper and, in order to achieve the critical view, must fight the natural tendency to retract the infundibulum cephalad and instead retract it laterally, such that the cystic duct and CBD form a Y. The cystic duct should be seen exiting the gallbladder so there is absolute certainty before it is ligated and divided. The cautery hook may be used more like a spatula, dividing tissue that has been placed under tension by gentle traction, rather than using it to hook every bit of tissue. If the cystic duct is too wide for a hemoclip, an endoscopic linear stapling device is a safe alternative.

Avoiding a rare but potentially devastating CBD injury starts with a self-questioning humility bordering on paranoia but includes a low threshold to obtain intraoperative imaging (cholangiogram), take the GB from the top down, or convert to open. Repair is usually best accomplished with Roux-en-Y hepatico- or choledochojejunostomy, though it is somewhat prone to stricturing due to the small caliber of the normal duct in a child. Simple repair of a seemingly minor bile duct injury is tempting but usually ill-advised. Bile leak is also quite rare but treated in the standard fashion (percutaneous drainage, ERCP with sphincterotomy, stent). Workup should include US and HIDA scan. Every attempt should be made to retrieve spilled stones, though intraperitoneal stones discovered incidentally months or years later are rarely cause for concern.

Further Reading

Al Talhi Y, et al. Laparoscopic cholecystectomy for cholelithiasis in children with sickle cell disease. Clin J Gastroenterol. 2017;10(4):320–6.

Frybova B, et al. Cholelithiasis and choledocholithiasis in children; risk factors for development. PLoS One. 2018;13(5):e0196475.

Lai SW, et al. Outcomes of laparoscopic cholecystectomy for biliary dyskinesia in children. J Laparoendosc Adv Surg Tech A. 2017;27(8):845–50.

Lau BJ, Sydorak RM, Shaul DB. Laparoscopic techniques for safe and successful removal of common bile duct stones in pediatric patients. J Laparoendosc Adv Surg Tech A. 2014;24(5):362–5.

Murphy PB, et al. The increasing incidence of gallbladder disease in children: a 20 year perspective. J Pediatr Surg. 2016;51(5):748–52.

Walker SK, et al. Etiology and incidence of pediatric gallbladder disease. Surgery. 2013;154(4):927–31; discussion 931-3