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Reminder of important clinical lesson

Gallbladder agenesis with midgut malrotation

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Summary

A 28-year-old female presented with a 4 year history of intermittent right upper quadrant pain. Clinical examination and ultrasound suggested a diagnosis of cholelithiasis and the patient was eventually booked for a laparoscopic cholecystectomy. Intraoperatively the patient was found to have gallbladder agenesis and small bowel malrotation with the duodenojejunal flexure to right of midline. The gallbladder fossa was filled with fibrous tissue. Both gallbladder agenesis and midgut malrotation are rare congenital abnormalities. Gallbladder agenesis has a similar presentation to more common gallbladder pathologies, such as cholecystitis. This case illustrates the limitations of and our over reliance on radiological imaging. Moreover, it highlights the need to have a high index suspicion of gallbladder agenesis when ultrasound is inconclusive. Further investigations and imaging with modalities such as MRI should be used to reduce the risks associated with unnecessary surgical intervention.

BACKGROUND

Gallbladder agenesis is a rare congenital biliary abnormality, which was first reported in 1701.[1] The prevalence of isolated gallbladder agenesis is estimated between 13 and 65 per 100 000 population.[2 3] Midgut malrotation occurs in 1/6000 live births and reported in 0.5% to 1% of autopsies.[4] While both these events are independently rare phenomenon, their occurrence together is documented in the literature.[5 6] About a quarter of these patients will become symptomatic in their lifetime with symptoms mimicking biliary tract pathology and patients often require medical intervention.[2 3]

Despite good history taking, clinical examination, laboratory investigations and recent advances in radiological imaging, a firm diagnosis is usually elusive. This leads to unnecessary investigations and interventions, which may increase the overall risk to the patient. We describe a case of gallbladder agenesis and midgut malrotation, the former diagnosed at laparoscopy, and discuss the presentation and management of these two conditions.

CASE PRESENTATION

A 28-year-old female was admitted from outpatients' clinic with right upper quadrant abdominal pain, which was continuous and low-grade in nature with intermittent spasms. Each episode was gradual in onset and lasted anywhere from 30 min to 3 h. The pain had no relation to the intake of food and was occasionally associated with vomiting, steatorrhoea and diarrhoea. The patient's abdominal pain occurred about once every 2 months for a total of 4 years.

The patient's medical history included anticitrullinated protein antibody positive rheumatoid arthritis, which had been treated with leflunomide, sulfasalazine, hydroxychloroquine, prednisolone, methotrexate and entarercept. Her surgical history included an appendicectomy as a child.

On admission, the patient's vital signs were all within the normal ranges. On physical examination, there was a well healed appendicectomy scar in the right iliac fossa. The patient had tenderness in the right upper quadrant with guarding, rebound and percussion tenderness, and was Murphy's sign positive. There was no jaundice. The rest of her physical examination was unremarkable.

INVESTIGATIONS

Laboratory tests results: haemoglobin 12.3 g/dl, white blood cells 8.3×10^9/l, platelets 280×10^9/l, C reactive protein 30.4, alanine aminotransferase 39 U/l, alkaline phosphatise 61 U/l, total bilirubin 14 µmol/l, albumin 31 g/l, amylase 63 U/l. Urea, creatinine and electrolytes were all within the normal ranges.

An ultrasound scan of the abdomen showed an impacted gallbladder with sludge and small stones. There was no intrahepatic biliary dilatation however the pancreas appeared bulky with mildly dilated pancreatic duct of 1–2 mm.

Interestingly, our patient first presented 4 years earlier with abdominal pain and deranged liver function tests, initially thought to be secondary to methotrexate treatment for her rheumatoid arthritis. Over the 4 year period leading up to her current admission, the patient had seven ultrasound scans; three reported the presence of a gallbladder, three reported that it was not possible to see the gallbladder and one failed to comment on the gallbladder. In addition, the patient had three CT scans performed. The gallbladder was not seen in two CT scans and was reported as likely being collapsed and one report did not contain a comment on the gallbladder. There was also an incidental finding of malrotation of the bowel with the whole of the small bowel to the right of the midline and the large bowel on the left (figure 1). In addition, the orientation of the superior mesenteric vein (SMV) and superior mesenteric artery (SMA) were reversed with the SMV to the left of the SMA. Three magnetic resonance cholangiopancreatography (MRCP) scans were performed; one reportedly showing a 'gallbladder', one did not show a gallbladder and one did not comment on the presence or absence of

the gallbladddder. MRCP initially demonstrated right and left intrahepatic duct dilatation, but later suggested mild sclerosing cholangitis. The patient also underwent a liver biopsy showing mild steatosis, and an oesophageogastroduodenoscopy and colonoscopy where nothing abnormal was detected.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for right upper quadrant abdominal pain is vast. However, given the history, physical examination findings and the results of investigations we will concentrate only on pertinent differential diagnoses.

Differential diagnoses for gallbladder disease includes cholelithiasis, cholecystitis and ascending cholangitis. Hepatomegaly can also cause right upper quadrant pain when the liver capsule is stretched. Causes of hepatomegaly include hepatic congestion secondary to congestive heart failure, lymphoma, chronic myeloid leukaemia or with autoimmune diseases including primary biliary sclerosis. Gastritis and pancreatitis may also present with right upper quadrant pain. Right lower lobe pneumonia, pleurisy and pulmonary embolism can also present with apparent right upper quadrant abdominal pain. A rare cause of right upper quadrant pain is Fitz–Hugh–Curtis syndrome where there is inflammation of the liver capsule associated with a genital tract infection.

TREATMENT

Taking into account the patient's presentation, physical examination, and the results of her laboratory and radiological investigations a diagnosis of cholelithiasis was made and the patient was booked for a laparoscopic cholecystectomy. Intraoperatively, the gallbladder fossa was filled with fibrous tissue only and no gallbladder was identified. Histology of the excised tissue showed no gallbladder tissue was present. At the time of surgery small bowel malrotation was confirmed with the duodenojejunal flexure to right of midline. An artery supplying the gallbladder remnant, likely a hypoplastic cystic artery, was clipped before the excision of the gallbladder remnant.

OUTCOME AND FOLLOW-UP

The patient made a good recovery postoperatively and remains symptom-free for over a year now following her operation.

DISCUSSION

Gallbladder agenesis occurs due to the failure of the cystic bud to develop as a ventral outgrowth from the caudal aspect of the foregut in utero in the fourth week of life. The development of the midgut occurs in weeks 5 to 12 in three stages. Initially the bowel elongates exceeding the abdominal cavity size and herniates from the abdomen. It rotates 270° anticlockwise around the SMA with the duodenum now lying across the midline in the left upper quadrant attached by the ligament of Treitz at the duodenojejunal flexure to the posterior abdominal wall. Disruption in the rotational stage can cause malrotation. Combined midgut and choledochal abnormalities, as in this case, are caused by the synchronous occurrence of separate gastrointestinal developmental abnormalities.[6]

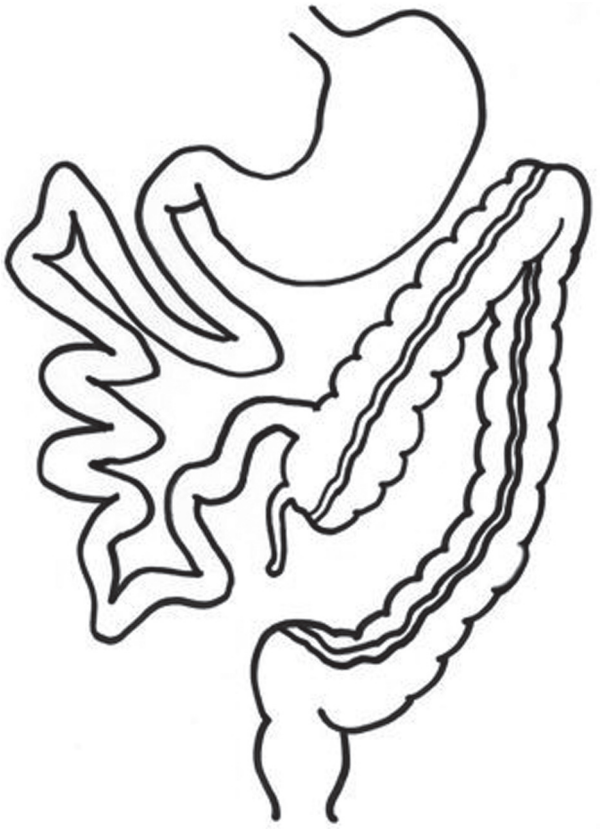

Figure 1 Schematic drawings of midgut malrotation malrotation of the bowel with the whole of the small bowel to the right of the midline and the large bowel on the left.

Patients with gallbladder agensis can be grouped into three categories of patients: (1) those with multiple fetal abnormalities detected peri-natally (15%); (2) asymptomatic cases found at autopsy or found incidental intraoperatively; and (3) symptomatic cases that usually present in the third to fourth decade of life (50%).[7] Patients with symptoms present with numerous symptoms notably right upper quadrant pain (90%), nausea and vomiting (66%), fatty food intolerance (37.5%) and diarrhoea (12%). Interestingly, the mean duration of the existence abdominal pain is 5.6 years illustrating the long duration before diagnosis.[7]

Malrotation is rarely diagnosed in adulthood with 85% of cases being diagnosed in the first year of life.[8] It usually presents with chronically with vague abdominal symptoms including generalised abdominal postprandial pain, which are commonly misconstrued to be secondary to biliary pathology, or acutely as volvulus or bowel obstruction.[8 9] The vague nature of such symptoms and the rarity of the condition make both conditions a challenging diagnosis.

In both the published literature on gallbladder agenesis and our patient, multiple radiological investigations are carried out before diagnosis. Ultrasound scans often suggest a diagnosis of chronic cholecystitis with a shrunken gallbladder. Factors such as intestinal gas artefact, peri-portal tissue or subhepatic peritoneal folds can lead to false positive findings indicating the presence of a gallbladder.[10] Clearly ultrasound scans can be misleading in gallbladder agenesis. Apparently, when the gallbladder is not visualised or inconsistently visualised clinicians usually do not often consider

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the potential absence of the gallbladder. The absence of the Wall–Echo–Stone triad, which includes gallbladder wall visualisation, echo of a stone and an acoustic shadow, and a double-arc shadow should raise the possibility of gallbladder agenesis.[11] A decision tree for the investigation of symptoms suggestive of biliary disease has been proposed.[12] If the gallbladder is reported as not identified or shrunken then the patient should proceed to MRCP, CT scanning, endoscopic retrograde cholagiopancreatography or endoscopic ultrasound scanning. If gallbladder agenesis is confirmed at this stage then the patient should be treated conservatively. If diagnostic uncertainty remains the patient should be re-investigated at a later stage after the acute phase. An ectopic gallbladder must also be excluded.

The symptoms of gallbladder agenesis are thought to be secondary to biliary dyskinesia with a higher resting sphincter of Oddi pressures and retrograde ampullary sphincteric musculature contractions, which promote dilatation of the common bile duct.[13 14] Biliary stasis is also though to contribute to symptoms. This may account for the duct dilatation witnessed in our patient. In midgut malrotation, chronic symptoms are thought to be caused by Ladd bands – fibrous bands which attach the caecum to the abdominal wall – which can intermittently compress the duodenum.[9]

The management of both gallbladder agenesis and midgut malrotation is conservative. Diagnosing gallbladder agenesis avoids unnecessary surgery, including laparotomy with its associated risks. Furthermore, if the patient ever requires surgery for any reason, surgeons aware of the anatomical variance can plan and perform procedures as safely as possible. For example, gallbladder agenesis affects the dissection of the porta hepatis and common bile duct due to lack of cranial gallbladder traction.[14] Correct diagnosis also allows the more prompt initiation of targeted treatment thus reducing number of investigation, interventions and patient suffering. Treatment includes smooth muscle relaxants and analgesia, with the option of sphincterotomy if symptoms fail to resolve.[7]

Learning points

- Doctors especially gastroenterologists, radiologists and surgeons must be aware of gallbladder agenesis and to consider it when faced with a patient with long-standing biliary symptoms and inconclusive investigations.
- Doctors should be aware of the limitations of the radiological investigations of the biliary tree and have a high index of suspicion of gallbladder agenesis if the gallbladder is not visualised.
- It is important to diagnose gallbladder agenesis in order to prevent unnecessary operations and other interventions with their associated risks.
- Co-existence of other congenital abnormalities can occur, which must be considered when interpreting symptoms, interpreting investigations and considering management, including when planning operations.
- Potential treatments of gallbladder agenesis are smooth muscle relaxants and analgesia. Surgical management can include sphincterotomy.

Competing interests None.

Patient consent Obtained.

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