

Gallbladder Agenesis: A Case Report

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Gallbladder agenesis (GA†) is an extremely rare congenital entity. The incidence is around 1 per 6500 live births. The majority of patients, estimated between 50 to 70 percent, remain asymptomatic while those who are symptomatic report symptoms mimicking biliary colic. Initial workup for suspected gallbladder pathology such as right upper quadrant ultrasound (US) can be misleading or inconclusive. Furthermore, advanced diagnostic studies such as hepatobiliary iminodiacetic acid (HIDA) scan and endoscopic retrograde cholangio-pancreatography (ERCP) may report non-visualization of the gallbladder and erroneously lead providers to a diagnosis of cystic duct obstruction rather than GA. Consequently, some GA patients are only finally diagnosed intraoperatively. Surgery can be risky in these patients because unnecessary dissection while looking for the non-existent gallbladder can result in injury of the biliary tree, hepatic vasculature, or small bowel. Therefore, clinicians should keep GA on their differential diagnosis list and imaging modalities such as magnetic resonance cholangiopancreatography (MRCP) should be obtained when other tests prove inconclusive. We report a 35-year-old female presenting with chronic symptoms consistent with biliary colic and an equivocal US reported as cholelithiasis. She underwent laparoscopy during which the absence of the gallbladder was noted. Postoperative MRCP confirmed the diagnosis of GA.

INTRODUCTION

The absence of the gallbladder, also known as gallbladder agenesis (GA), is an extremely rare anatomic anomaly. The incidence has been reported to be of less than 1 per 6500 live births [1]. Most patients suffering from GA remain asymptomatic throughout their lifespan. Hence, the majority of the cases are found either at autopsy or incidentally while undergoing diagnostic imaging or surgery. However, about 23 percent [2] to 50 percent

[3] of patients can present with symptoms of right upper quadrant pain that can be mistaken for cholecystitis or symptomatic cholelithiasis. Routine preoperative ultrasound (US) can be misleading and patients can be subject to unnecessary surgical procedures. We report a case of GA in a 35-year-old female who presented with symptoms consistent with symptomatic cholelithiasis and an equivocal US, whose gallbladder was absent on surgical laparoscopy. Postoperative MRCP confirmed the diagnosis of GA.

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†Abbreviations: GA, Gallbladder agenesis; US, ultrasound; HIDA, hepatobiliary iminodiacetic acid; ERCP, endoscopic retrograde cholangio-pancreatography; MRCP, magnetic resonance cholangiopancreatography; WES, Wall Echo Shadow.

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CASE PRESENTATION

The patient was a 35-year-old female who presented to clinic for evaluation of abdominal pain compatible with symptomatic cholelithiasis. She described intermittent, cramping, right upper quadrant pain starting six months prior to presentation. The pain usually lasted up to one hour and was exacerbated by eating. She denied fevers, chills, nausea, vomiting, jaundice, and changes in the color of her stool and urine. Her past medical history was relevant for morbid obesity (BMI of 42), diabetes mellitus, hypertension, and irritable bowel syndrome. She had undergone recent colonoscopy but had no prior abdominal surgeries. On social history she endorsed occasional alcohol use but denied tobacco and illicit substance consumption. Her physical examination was only remarkable for obesity. Her right upper quadrant was non-tender to palpation and she had no palpable organomegaly, hernia, or mass. The patient had undergone laboratory work up which included a complete blood count, comprehensive metabolic panel, and liver function tests all of which were within normal limits. An abdominal ultrasound did not demonstrate a well-delineated gallbladder. There was increased echogenicity on the proximal edge of the gallbladder fossa compatible with a Wall Echo Shadow (WES) sign suggestive of either large calcified or multiple small calcified gallstones in the gallbladder (Figure 1). No sonographic Murphy's sign was elicited and the common bile duct measured 4 mm.

Taking into consideration the patient's characteristics (obese female of childbearing age), along with the history of intermittent right upper quadrant pain, and the US findings, the decision was made to take the patient to the operating room for a laparoscopic cholecystectomy in the setting of presumed symptomatic cholelithiasis. Upon entry into the abdominal cavity using standard laparoscopic technique, the gallbladder was not appreciated. The right lobe of the liver was elevated but the gallbladder was not visualized (Figure 2). Additional dissection was performed in order to clear the liver plate but still no gallbladder was seen (Figure 3). No surgical clips or signs of prior surgery in the right upper quadrant were identified. Close inspection of both lobes of the liver as well as the falciform ligament was performed but no aberrant location of the gallbladder was identified. At this point the procedure was terminated. A magnetic resonance cholangiopancreatography (MRCP) was performed to evaluate the patient's anatomy in an outpatient setting that confirmed the absence of the gallbladder (Figure 4). The patient was discharged home and recovered as expected. She continues to experience intermittent right upper quadrant pain similar to that which she experienced prior to surgery.

DISCUSSION

Gallbladder agenesis is an uncommon congenital entity. The prevalence ranges from 0.007 to 0.013 percent [4]. While autopsy reports have not shown a difference in frequency between females and males, the incidental cases of GA found during surgical procedures have been reported to have a 3:1 female predominance [5]. Gallbladder agenesis was first reported in the medical literature in 1702 by Bergman [6]. Formed in the fourth week of intrauterine life, the gallbladder arises from the caudal bud of the hepatic diverticulum along with the cystic duct and the ventral pancreas [7]. Although the exact pathogenesis of GA is unknown, there are two main hypotheses. The first hypothesis postulates that the superior division of the caudal bud of the hepatic diverticulum fails to develop into the cystic duct and gallbladder, likely secondary to an aberration in the development of the vessels surrounding the caudal bud [8]. Consequently, GA is frequently found in patients with other gastrointestinal and cardiovascular abnormalities [9]. The second theory states that GA occurs secondary to a failure of recanalization of the gallbladder and cystic duct after their formation and this offers explanation for cases with isolated GA but no additional associated congenital anomalies [5].

The presentation of GA is varied. In 1988, Bennion *et al.* classified GA patients according to their presentation. The first group consisted of patients where their GA was associated with multiple fetal anomalies and in which all the patients died secondarily to their other congenital defects. The second group consisted of those who were asymptomatic and in whom GA was diagnosed postmortem. A third group consisted of patients presenting with gastrointestinal symptoms which resulted in the intraoperative diagnosis of GA [1]. Amongst patients with GA, 50 to 70 percent are asymptomatic [2,3]. The remaining patients usually present with symptoms of chronic right upper quadrant pain, dyspepsia, jaundice, and fatty food intolerance, all of which are similar to symptoms experienced in acute cholecystitis or biliary colic [10]. It has additionally been proposed that these symptoms occur because patients with GA can have associated Sphincter of Oddi dysfunction explained by the common embryologic origin of the sphincter and gallbladder. Sphincter of Oddi dysfunction may predispose to biliary stasis resulting in patient jaundice, elevated liver functions tests, and even common bile duct stones [11].

Diagnosing GA before patients undergo unnecessary surgery can be challenging. In fact, a significant proportion of patients with GA are only diagnosed intraoperatively [9,12-14]. Surgery in this patient population is not without risk. If the gallbladder is not found in its normal anatomic location upon entry into the abdominal cavity, especially in patients where there is a high index of sus-

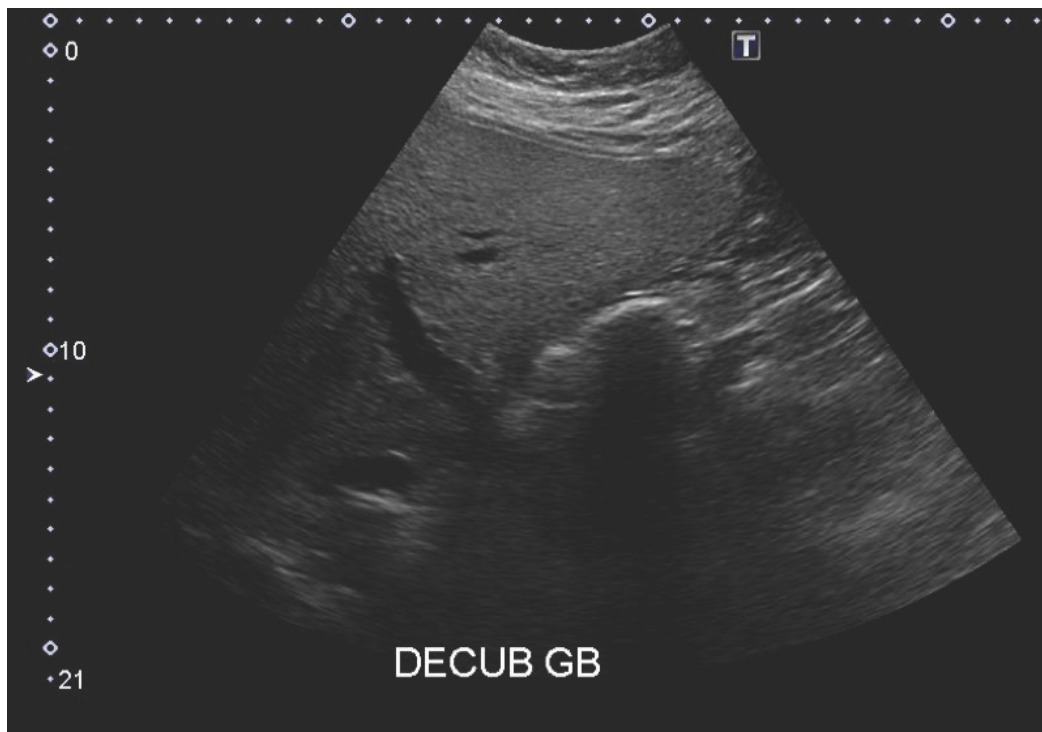


Figure 1. Pre-operative ultrasound with equivocal visualization of the gallbladder.

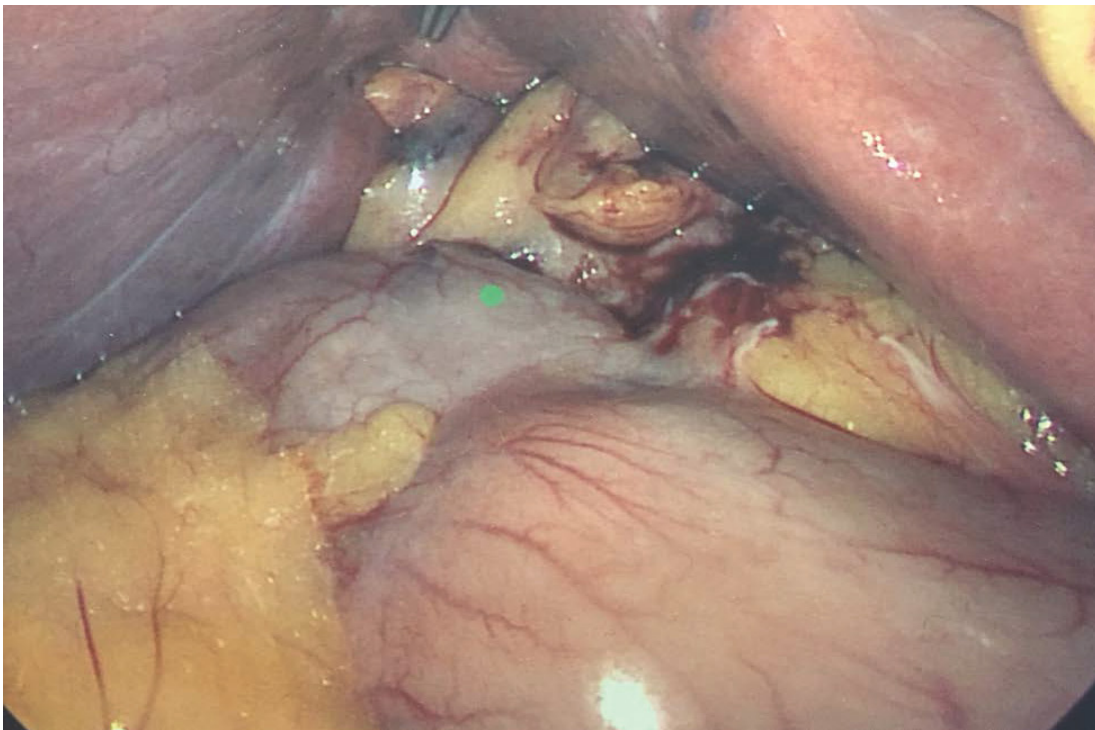


Figure 2. Intra-operative photograph demonstrating non-visualization of the gallbladder upon liver elevation.



Figure 3. Intra-operative photograph demonstrating absence of the gallbladder after dissection of the gallbladder bed and liver plate.

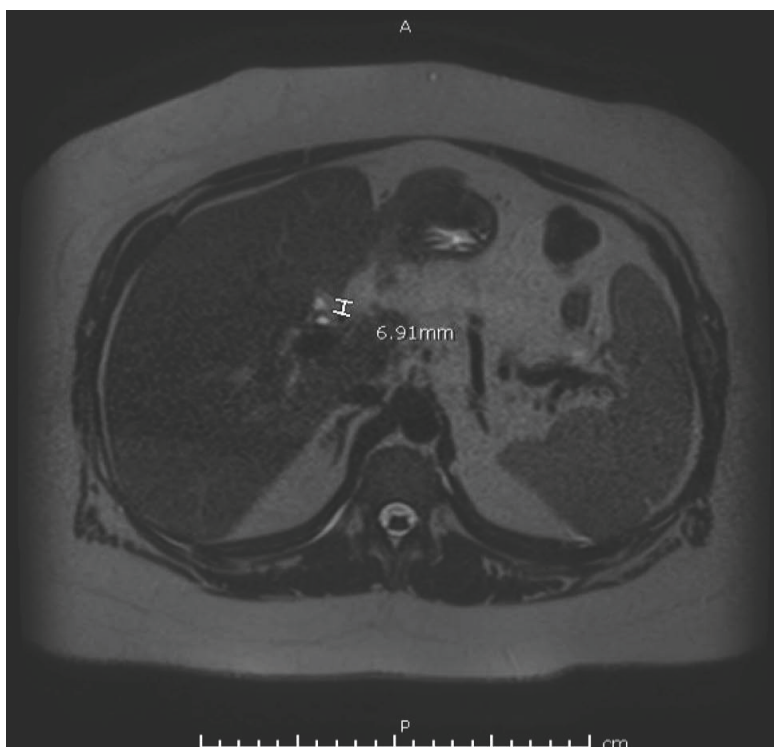


Figure 4. Magnetic resonance cholangiopancreatography showing absence of the gallbladder. Remnant of cystic duct measured.

picion for biliary disease, ectopic locations need to be explored. The falciform ligament must be taken down and the leaves of the lesser omentum [4] as well as intrahepatic and retrohepatic locations must be inspected. It is easy to imagine how damage to the liver, biliary tree, small bowel, and hepatic vessels could result from this dissection. Intraoperative ultrasound and cholangiography can be employed to aid in localization of an ectopic gallbladder. While US remains the preferred initial diagnostic method for patients presenting with symptoms suggestive of gallstone disease, US can be a misleading imaging tool in the evaluation of patients with GA [15]. Patients with GA are often misdiagnosed by US as instead having a contracted gallbladder [16]. Hepatobiliary iminodiacetic acid (HIDA) scan and endoscopic retrograde cholangio-pancreatography (ERCP) can also be misleading in the setting of GA [17,18]. This is because non-visualization of the gallbladder is more likely to be interpreted as obstruction of the cystic duct, consistent with a diagnosis of cholecystitis, rather than as absence of the gallbladder [12]. MRCP, on the other hand, can diagnose patients with GA prior to surgery [5,19]. Because it does not rely on the passage of contrast for visualization of the biliary tree, it is not affected by biliary stasis. Therefore, MRCP should be considered when the diagnosis is uncertain.

CONCLUSIONS

Gallbladder agenesis is a rare condition that can present with symptoms that mimic those of common surgical entities like cholecystitis and symptomatic cholelithiasis. Because surgery is not without risk and offers no therapeutic benefit in patients with GA, it is important for clinicians to keep this entity on their list of differential diagnoses, especially if the gallbladder is not clearly delineated on pre-operative US. In patients where pre-operative US imaging is equivocal an MRCP should be obtained prior to proceeding to the OR for exclusion of GA.

REFERENCES

1. Bennion RS, Thompson JE Jr, Tompkins RK. Agenesis of the gallbladder without extrahepatic biliary atresia. *Arch Surg*. 1988;123(10):1257–60.
2. Nadeau LA, Cloutier WA, Konecki JT, Morin G, Taylor RW. Hereditary gallbladder agenesis: twelve cases in the same family. *J Maine Med Assoc*. 1972;63(1):1–4.
3. Hershman MJ, Southern SJ, Rosin RD. Gallbladder agenesis diagnosed at laparoscopy. *J R Soc Med*. 1992;85(11):702–3.
4. Peloponissios N, Gillet M, Cavin R, Halkic N. Agenesis of the gallbladder: A dangerously misdiagnosed malformation. *World J Gastroenterol*. 2005;11(39):6228–31.
5. Fiaschetti V, Calabrese G, Viarani S, Bazzocchi G, Simonetti G. Gallbladder Agenesis and Cystic Duct Absence in an Adult Patient Diagnosed by Magnetic Resonance Cholangiography: Report of a Case and Review of the Literature. *Case Rep Med*. 2009;2009:674768.
6. Latimer EO, Mendez FL, Hage WJ. Congenital Absence of Gallbladder: Report of Three Cases. *Ann Surg*. 1947;126(2):229–42.
7. Ando H. Embryology of the Biliary Tract. *Dig Surg*. 2010;27(2):87–9.
8. Blechschmidt CM. Agenesis of the gallbladder—borderline-case of normality? *Anat Anz*. 1982;151(3):281–5.
9. Turkel SB, Swanson V, Chandrasoma P. Malformations associated with congenital absence of the gall bladder. *J Med Genet*. 1983;20(6):445.
10. Kasi PM, Ramirez R, Rogal SS, Littleton K, Fasanello KE. Gallbladder Agenesis. *Case Rep Gastroenterol*. 2011;5(3):654–62.
11. Wright E, Madore P. Congenital Absence of the Gallbladder. *Can Med Assoc J*. 1965;93(3):123–5.
12. Rajkumar A, Piya A. Gall Bladder Agenesis: A Rare Embryonic Cause of Recurrent Biliary Colic. *Am J Case Rep*. 2017;18:334–8.
13. Amaral JF, Ferland R. Agenesis of the gallbladder: laparoscopic diagnosis. *Surg Laparosc Endosc*. 1993;3(4):337–41.
14. Cabajo Caballero MA, Martin del Olmo JC, Blanco Alvarez JI, Atienza Sanchez R. Gallbladder and cystic duct absence. An infrequent malformation in laparoscopic surgery. *Surg Endosc*. 1997;11(5):483–4.
15. Serour F, Klin B, Strauss S, Vinograd I. False-positive ultrasonography in agenesis of the gallbladder: a pitfall in the laparoscopic cholecystectomy approach. *Surg Laparosc Endosc*. 1993;3(2):144–6.
16. Crade M, Taylor KJ, Rosenfield AT, de Graaff CS, Miniham P. Surgical and pathologic correlation of cholecystosonography and cholecystography. *AJR Am J Roentgenol*. 1978;131(2):227–9.
17. Dickinson CZ, Powers TA, Sandler MP, Partain CL. Congenital absence of the gallbladder: another cause of false-positive hepatobiliary image. *J Nucl Med*. 1984;25(1):70–2.
18. O'Sullivan J, O'Brien PA, MacFeely L, Whelton MJ. Congenital absence of the gallbladder and cystic duct: nonoperative diagnosis. *Am J Gastroenterol*. 1987;82(11):1190–2.
19. Fulcher AS, Turner MA, Capps GW. MR cholangiography: technical advances and clinical applications. *Radiographics*. 1999;19(1):25–41; discussion 4.