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Gallbladder Agenesis

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Key Words
Gallbladder agenesis · Biliary colic · Conservative management · Sphincterotomy · Magnetic resonance cholangiopancreatography

Abstract
Gallbladder agenesis is a rare entity with an estimated incidence of 10–65 per 100,000. Females are more commonly affected (ratio 3:1), typically presenting in the 2nd or 3rd decade of life. Despite an absent gallbladder, half of patients present with symptoms similar to biliary colic, which is poorly understood. Clinicians should have a strong index of suspicion if nonvisualization is suggested by an ultrasound. HIDA scans are typically not helpful since nonvisualization of the gallbladder remains typical of cystic duct obstruction as well as of agenesis. While there are no specific guidelines for management of gallbladder agenesis, conservative management with smooth muscle relaxants is preferred. Sphincterotomy also has been reported in severe cases. Here, we report a case of a 21-year-old woman who presented with recurrent biliary colic and was diagnosed to have gallbladder agenesis on magnetic resonance cholangiopancreatography. A comparison with other cases and a review of the literature are presented.

Introduction

Gallbladder agenesis is a rare entity with an estimated incidence of 10–65 per 100,000. Females are more commonly affected (ratio 3:1), typically presenting in the 2nd or 3rd decade of life. Despite an absent gallbladder, half of patients present with symptoms similar to biliary colic, which is poorly understood. Here, we report a case of a 21-year-old woman who presented with recurrent biliary colic and was diagnosed to have gallbladder agenesis on magnetic resonance cholangiopancreatography (MRCP). A comparison with other cases and a review of the literature are presented.

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Case Presentation

A 21-year-old woman presented to the hospital with right upper quadrant pain. She was in her usual state of health until 6 weeks prior when she developed abdominal pain. The pain was located in her right upper quadrant, dull, aching in quality, sudden in onset, colicky in nature, and radiated to her right scapula. Associated symptoms included nausea, vomiting, and inability to tolerate anything by mouth. These symptoms were worsened by meals and particularly by fatty food. The episodes of pain would last for 45–90 min following each meal. As a consequence of the post-prandial pain, she developed sitophobia and lost 12 pounds over a 6-week period.

Her past medical history was notable for a benign ovarian cyst. She had no prior surgical history. She was taking oral contraceptive pills and had no known drug allergies. Her social history was notable for lack of tobacco, alcohol or illicit drug use. With respect to her family history, both her parents had had cholecystectomies; her father at the age of 45 due to gallstone disease and her mother at the age of 39 (noted to have cholesterolosis). Family history was also significant for hemochromatosis in her father; her mother had not been tested.

The patient presented to the emergency department 4 weeks after symptom onset and given concerns for the biliary nature of her pain, she was evaluated by the surgical service. She had an ultrasound of her abdomen which showed prominence of her common bile duct (7 mm) without intrahepatic biliary dilatation, and nonvisualization of her gallbladder. She subsequently underwent a HIDA scan, which was read as concerning for possible acute cholecystitis given the lack of gallbladder filling. She was discharged after symptomatic management with plans to be evaluated by gastrointestinal surgery for possible laparoscopic cholecystectomy in 4–6 weeks.

In the interim, she had recurrence of her symptoms and presented again to the emergency department. At this time, her exam revealed a nontoxic appearance with normal vital signs and mild tenderness to palpation in her right upper and bilateral lower quadrants without rebound or guarding. Her laboratory testing was notable for an unremarkable basic metabolic panel, CBC and liver enzymes. A CT scan was obtained and was read by the radiologist as 'status post cholecystectomy.' Given nonvisualization of the gallbladder on ultrasound as well as CT scan, an MRCP was ordered which revealed a 4-mm cystic lesion seen adjacent to the proximal common hepatic duct with apparent communication via a diminutive duct with the right hepatic duct, consistent with gallbladder agenesis/hypoplasia (**fig. 1**). At this point, a gastroenterology consult was called for assistance with further management.

Discussion

Gallbladder agenesis is a rare entity with an estimated incidence of 10–65 per 100,000 [1, 2]. The incidence is noted to be higher (up to 90 per 100,000) in studies based on autopsy reports [3]. The first reports of cases of gallbladder agenesis date back to 1701 and 1702 by Lemery and Bergman [1, 2, 4]. The pathogenesis is related to embryonic development due to failure of the gallbladder and cystic duct to bud off from the common bile duct during the fifth week of gestation [1].

Table 1 summarizes a list of cases reported on gallbladder agenesis including the demographics of patients affected, their initial clinical presentation, mode of diagnosis and their outcomes. Females are more commonly affected (in a 3:1 ratio) and typically present in the 2nd or 3rd decade of life [5]. For unclear reasons, despite the absence of a gallbladder, up to 50% of patients present with symptoms similar to biliary colic [6]. Some postulate that an associated sphincter of Oddi dysfunction may be the cause of biliary colic in these patients [7]. In other cases, associated development of common bile duct stones may be the cause [2].

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Prior authors have classified patients into three groups. The first group consists of asymptomatic anatomical abnormalities seen incidentally on autopsy. The second group presents with symptoms of biliary colic (54%), dyspepsia (34%) and/or jaundice (27%), and the third presents in childhood with other associated severe fetal anomalies [2, 4].

The exact prevalence of each of the three groups is variable based on published reports. It is thought that approximately 70% of cases are usually isolated anomalies, although some cases appear to be familial and are associated with more severe anomalies [5, 8, 9]. In an interesting series of 34 cases (29 children and 5 adults) of congenital gallbladder agenesis, the most common anomalies associated were involving the genitourinary tract followed by gastrointestinal and cardiovascular malformations. Family history was negative in all, suggesting a sporadic occurrence [10].

Historically, all cases were identified intraoperatively. In a review of 9 cases by Cho et al. [11], all patients underwent a laparotomy, which failed to identify the gallbladder. However, now with the increased frequency of advanced imaging, cases are being diagnosed more often and, more importantly, before any surgical intervention.

However, given that patients with gallbladder agenesis tend to present symptoms suggestive of biliary colic, a number of them are still diagnosed intraoperatively. Due to a lack of awareness of the diagnosis, this entity remains a diagnostic challenge [2, 12]. In those cases which are diagnosed intraoperatively, patients often are exposed to complications from prolonged exploration [13], and it is suggested to abort the procedure rather than complete further exploration if a gallbladder is not found on laparoscopy since open exploration for possible ectopic gallbladder increases the risk of complications [14]. Intraoperative ultrasound can demonstrate an ectopic gallbladder but is not always available [13]. A follow-up with more advanced imaging techniques should be the next option to truly identify gallbladder agenesis as the sole abnormality to guide management further.

It is therefore important to consider the presence of this unusual entity when the nonvisualization of the gallbladder is suggested on ultrasound [15]. However, as is known, ultrasound is highly dependent not only on the operator but also on other factors such as body habitus or presence of bowel gas obscuring visualization. Cases of gallbladder agenesis have been reported as 'contracted/fibrotic gallbladder' on ultrasound [14].

HIDA scans, which are also usually performed in patients with cholecystitis, in this case are unhelpful since nonvisualization of the gallbladder remains typical of cystic duct obstruction, as well as of agenesis [13, 16–18].

MRCP is considered the test of choice if there is suspicion. It is also helpful in demonstrating an ectopic gallbladder along with other possible anomalies of the biliary tract system [8, 19].

In terms of treatment, there are no specific guidelines on how to manage these cases. An algorithm published by Malde [2] is presented in figure 2. Interestingly, one author notes that 98% of patients had resolution of symptoms after exploratory, nontherapeutic surgery [5]. It is unclear how these patients would have had symptom

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resolution in the absence of exploration. This was also noted to be the case in 2 cases reported by Waisberg et al. [20] and some of the other reports (see table 1).

In this case, the patient was started on hyoscyamine extended release tablets twice daily, which did help alleviate her symptoms and has prevented any recurrence of symptoms or hospitalization during a 5-month follow-up.

She was also noted to be heterozygous for C282Y mutation for hereditary hemochromatosis. Whether the gene for gallbladder development is associated with hemochromatosis is not known, and we did not come across studies associating it with gallbladder agenesis.

Conclusions

Gallbladder agenesis presents as a significant diagnostic challenge. With the advances in imaging, more cases of gallbladder agenesis are being diagnosed incidentally and outside of the operating room. Clinicians should have a strong index of suspicion if nonvisualization is suggested by an ultrasound. A positive HIDA scan can be seen in the presence of gallbladder agenesis in the absence of cholecystitis. MRCP is considered the test of choice if there is suspicion. It is also helpful in demonstrating an ectopic gallbladder along with other possible anomalies of the biliary tract system. Management is usually conservative with smooth muscle relaxants.

Acknowledgements

We are deeply indebted to the patient for allowing us to present her information as a case report. Special thanks to Dr. Sachin Malde [2] for giving us the permission to include the algorithm (**fig. 2**) in our paper.

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Table 1. Summary of cases reported on gallbladder agenesis and demographics of patients affected, their clinical presentation, mode of diagnosis and their outcomes

	Paper	Case	Presentation	Diagnosis on	Management/comments
1	Mittal et al. [1]	45-year-old woman	Biliary colic/ choledocholithiasis	CT/laparotomy	Choledocholithotomy with choledochoduodenostomy
2	Malde [2]	79-year-old man	Choledocholithiasis/ fatty food intolerance/weight loss	Laparotomy	Open CBD exploration and removal of CBD stones
3	Stephenson et al. [5]	23-year-old woman	Biliary colic	Laparotomy	Interestingly revealed hepatic hemangiomas mimicking as gallstones. No intervention
4	Fiaschetti et al. [8]	44-year-old man	Abdominal pain/ dyspepsia	MRCP	Conservative management; clinical history revealed familial gallbladder agenesis in two paternal aunts during laparoscopic surgery
5	Gupta et al. [12]	28-year-old woman	Abdominal pain/ dyspepsia	Laparotomy	Conservative management
6	Demir et al. [9]	47-year-old man	Biliary colic/dyspepsia	MRI/MRCP	Conservative management; associated congenital short and annular pancreas, and splenic malrotation were also noted
7	Balakrishnan et al. [14]	30-year-old woman	Biliary colic/dyspepsia	Laparoscopy	Conservative management
8	Balakrishnan et al. [14]	55-year-old man	Admitted for splenomegaly	CTA/ERCP	Noted to have other associated biliary anomalies and portal vein thrombosis; management not reported in detail
9	Peloponissios et al. [13]	34-year-old man	Abdominal pain/ bloating	Laparoscopy converted to laparotomy	A branch of the right hepatic duct was also noted to have been injured. The segmental biliary duct was ligated and the area drained
10	Peloponissios et al. [13]	76-year-old man	Presentation was for a renal tumor	CT/laparotomy	In place of the gallbladder, a small fibrous structure was found and excised. Right nephrectomy was also done at the same time
11	Waisberg et al. [20]	68-year-old man	Colicky abdominal pain for 10 years	Laparotomy	Was operated upon, but no intervention done; patient remains asymptomatic
12	Waisberg et al. [20]	50-year-old woman	Biliary colic	Laparoscopy	Was operated upon, but no intervention done; patient remains asymptomatic
13	Vijay et al. [17]	50-year-old woman	Chronic right upper quadrant pain/ dyspepsia	Laparotomy	No intervention done intraoperatively; associated renal cysts noted

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14	Cho et al. [11]	9 cases were reviewed	Jaundice noted in 5, epigastric pain in 4, 5 had right upper quadrant pain (1 had symptoms typical for a biliary colic)	All cases underwent laparotomy; in only 1 case CT had suggested gallbladder agenesis	Specific outcomes not stated in the paper
15	Hershman et al. [6]	23-year-old man	Recurrent biliary colic	Laparoscopy	No intervention done intraoperatively; patient also had Gilbert's disease
16	Dickinson et al. [18]	69-year-old man	Abdominal pain/ dyspepsia	Laparotomy	No intervention was done, patient remained asymptomatic
17	Turkel et al. [10]	Necropsy study: 34 cases (29 children and 5 adults); of the adults, 4 were males and 1 was female	–	–	–
18	Wright et al. [7]	50-year-old woman	Biliary colic	Laparotomy	No intervention was done, patient remained asymptomatic
19	Monroe et al. [3]	46-year-old man	Abdominal pain	Patient was scheduled for cholecystectomy; diagnosis revealed on autopsy	Patient apparently died from 'pulmonary problems' before he was to be operated upon
20	Beuran et al. [21]	23-year-old woman	Biliary colic	Laparoscopy	No intervention was done, patient remained asymptomatic
21	Beuran et al. [21]	52-year-old woman	Right upper quadrant pain	Laparotomy	No intervention was done, patient remained asymptomatic
22	Ishida et al. [22]	84-year-old woman	Abdominal pain/ choledocholithiasis	Laparotomy	Impacted stone removed; t-tube placed
23	Gotohda et al. [23]	29-year-old man	Right upper quadrant pain/vomiting	Laparoscopy	No intervention was done, patient remained asymptomatic

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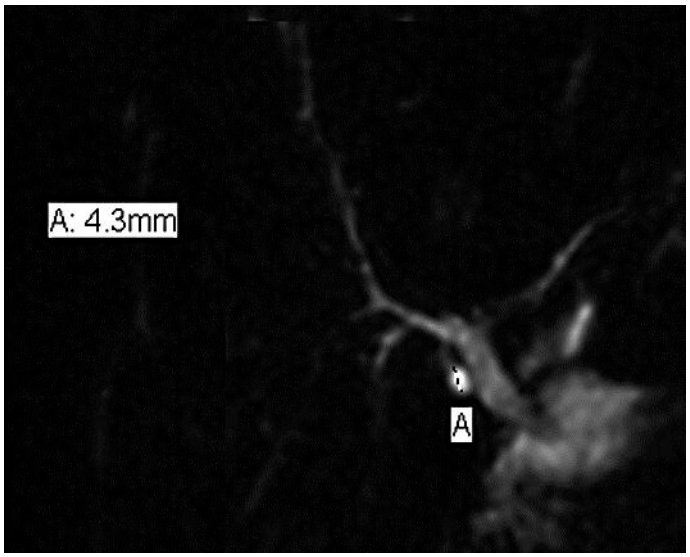

Fig. 1. MRCP showing a 4-mm cystic lesion adjacent to the proximal common hepatic duct with apparent communication through a tiny duct with the right hepatic duct, representing a hypoplastic gallbladder. MRCP is considered the test of choice if there is suspicion of a hypoplastic gallbladder. It is also helpful in demonstrating an ectopic gallbladder along with other possible anomalies of the biliary tract system.

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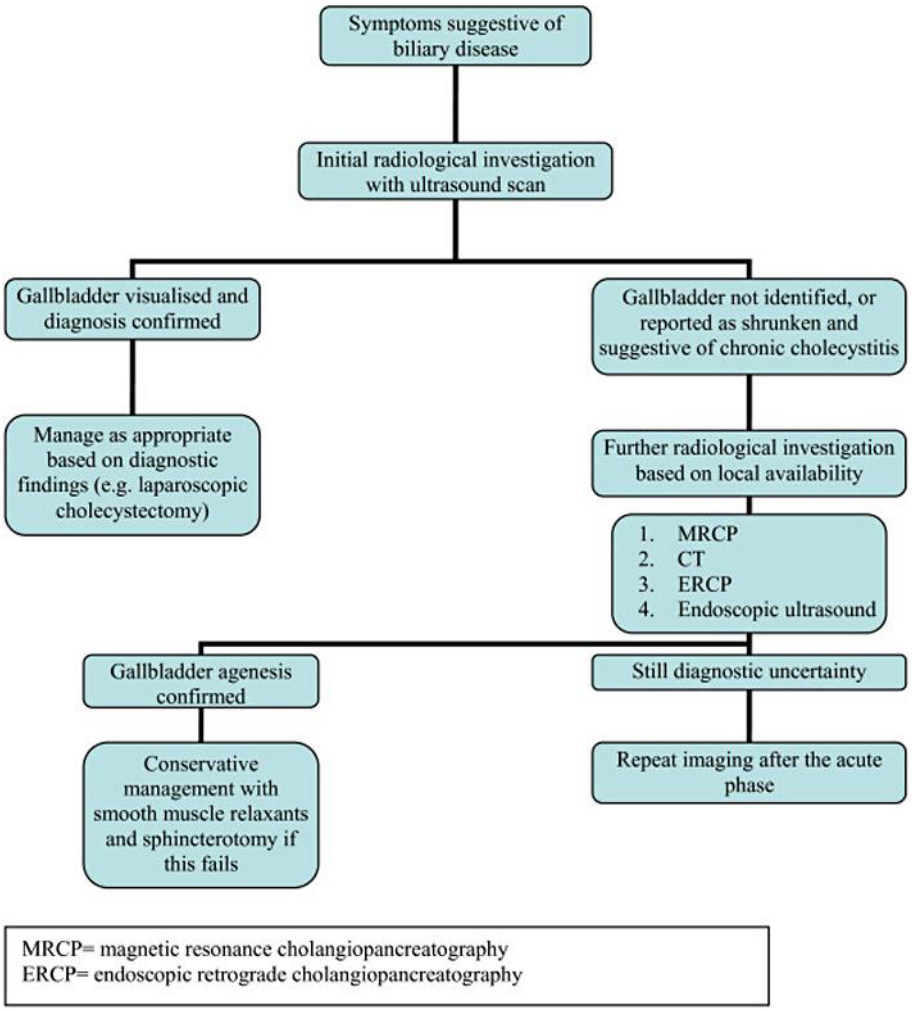

Fig. 2. Algorithm for workup and management of gallbladder agenesis as suggested by Malde [2]. As noted, while there are no specific guidelines for management of gallbladder agenesis, conservative management with smooth muscle relaxants is preferred. Sphincterotomy also has been reported in severe cases. (Permission to use under creative contributions open access license from http://www.biomedcentral.com; permission also obtained from the author.)

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