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Agenesis of gallbladder-series of four cases - why it is difficult to diagnose preoperatively?

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ABSTRACT

Agenesis of gallbladder (AGB) is a rare clinical entity first reported by Bergman in 1702. The incidence is about in 10–65 cases/1,00,000 population. It is seen in 1/6th cases of biliary atresia. It is of unknown etiology and is believed to be due to abnormal embryonic development. Nearly 70% cases are sporadic. AGB may be associated with other congenital abnormalities including the biliary system. The majority (nearly 50%) of the patients are symptomatic with misinterpreted signs and symptoms of cholecystitis and lands up to unnecessary surgery. Our series of four cases have male: female ratio of 3:1. Two of the cases underwent laparoscopic surgery. Among the other two, one had biliary pancreatitis due to primary calculous in the common bile duct (CBD) with upstream dilation. Other cases had chronic pancreatitis with dilated pancreatic duct and a proximal calculous close to ampulla causing proximal dilation of CBD. Two operated cases were postoperatively diagnosed by magnetic resonance cholangiopancreatography (MRCP) and the non-operated patients were also diagnosed by MRCP. Symptomatic AGB is often wrongly interpreted as cholecystitis with cystic duct obstruction or as sclero-atrophic gallbladder, therefore leading to pointless surgical interventions. In case of false-positive ultrasonography (USG) of AGB, it has been suggested that either a loop of gas-containing bowel located in the gallbladder fossa or periportal tissue and subhepatic peritoneal folds impersonate a contracted gallbladder containing gallstones. When USG reveals such reports or in cases of non-visualization in other imaging modalities, the need of additional preoperative imaging investigation must be in the surgeon's mind such as MRCP to avoid surgery which is not at all required.

Key words: Agenesis; Gallbladder; Bile duct

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INTRODUCTION

Anatomic anomalies of the biliary tract are not uncommon, but gallbladder and cystic duct agenesis are rare. It is often discovered incidentally and is usually asymptomatic.[4] It was reported for the 1st time in humans by Bergman back in 1702. It has since been described several times in case reports. Courvoisier collected 25 such cases in 1890.[1] The etiology of agenesis of gall bladder (AGB) is unknown; in nearly 70% cases, it is sporadic in nature with no clear causes.[2,8] AGB can be observed in both children and adults, with a mean age of 46 years at the time of the diagnosis.[5] It is often a casual finding during abdominal surgery or at autopsy. The agenesis is attributed to an abnormality in the embryonic development, so most cases of gallbladder agenesis are associated with other congenital abnormalities, including those of the biliary system. The gallbladder develops from the caudal part of the hepatic diverticulum in the 4th week of prenatal life. There are two theories regarding non-development of the gallbladder.[8] According to one theory, the hepatic diverticular bud of the foregut fails to develop properly into the gallbladder and cystic duct. The other theory holds that, following solid-phase development, there is a failure of recanalization of the cystic duct and gallbladder. AGB has been reported to be associated with many other gastrointestinal, skeletal,

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cardiovascular, and genitourinary malformations, such as ventricular septal defect, imperforate anus, duodenal atresia, malrotation of the gut, pancreas divisum, hypoplasia of the right hepatic lobe, duplication cysts of the hepatic flexure, renal agenesis, undescended testes, and syndactyly.[9] It is present in 1/6 of cases of biliary atresia; the isolated absence of the gallbladder and cystic duct is rare.[2] Symptomatic presentation of patients in 50% of cases, and AGB will almost always be misinterpreted as cholecystitis with cystic duct obstruction or as scleroatrophic gallbladder, therefore leading to unnecessary surgery.[3,9,12]

Aims and objectives

The objective of our present study of this rare anomaly is to find out the reasons for the misinterpretation in diagnosis to avoid unnecessary surgery.

CASE PRESENTATION

In our series of four cases of AGB were detected, between June 2014 and October 2021 among nearly 18,000 diagnosed gall stone disease patients. All were adult patients of age between 26 years and 55 years. Three patients were male and one female. Two were diagnosed preoperatively of whom one had chronic pancreatitis with dilated pancreatic duct (PD) with proximal calculous and the other presented with biliary pancreatitis and jaundice due to primary common bile duct (CBD) calculous. Two patients underwent laparoscopic surgery for misinterpreted clinical and investigative findings.

Case 1

A 55-year-old male patient attended hospital with pain in the upper abdomen with anorexia and yellowish discoloration of urine for 2 weeks. His liver function test (LFT) was deranged with increased bilirubin and amylase, lipase. He was known diabetic and hypertensive. His ultrasonography (USG) revealed contracted gallbladder with dilated biliary ducts (Figure 1). Magnetic resonance cholangiopancreatography (MRCP) revealed AGB and dilated biliary system with lower CBD calculous (Figure 2). As the GB was absent, so it was primary CBD calculus. Following recovery from the biliary pancreatitis, he underwent endoscopic retrograde cholangio-pancreatography (ERCP) and CBD stone extraction.

Case 2

The 49-year-old male patient had features of chronic pancreatitis (non-alcoholic). His USG report (plate was not taken by the patient to reduce expenditure) revealed contracted gallbladder and dilated PD and CBD with a calculous in the proximal PD. His MRCP confirmed

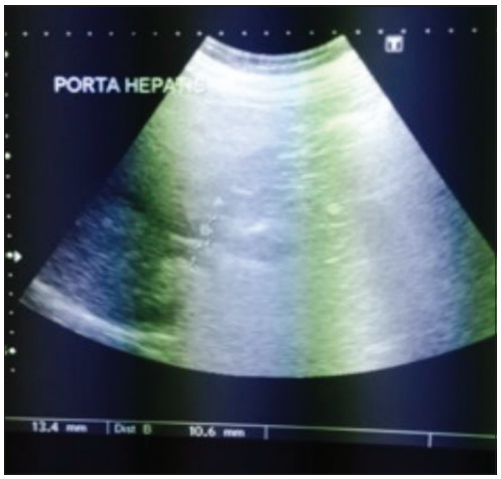

Figure 1: Ultrasonography whole abdomen of the patient with biliary pancreatitis due to lower common bile duct calculi

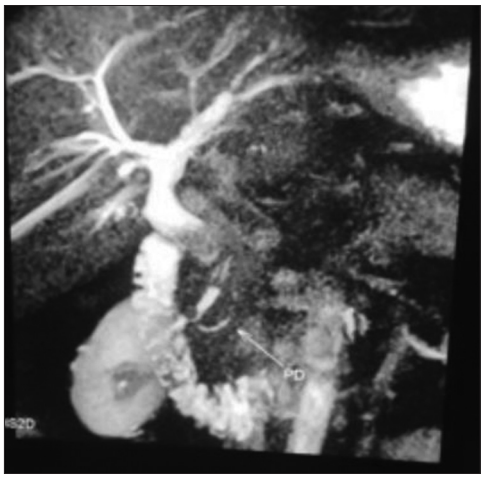

Figure 2: Magnetic resonance cholangiopancreatography shows agenesis of gall bladder and dilated bile ducts with lower common bile duct calculus

AGB and chronic pancreatitis with dilated biliopancreatic ductal system. A calculous near ampulla in PD was present compressing the CBD (Figures 3 and 4). He also underwent ERCP and extraction of the PD calculous.

Case 3 and Case 4

The two operated patients – (a) one 26–year-old female presented with dyspepsia, intolerance to fatty foods with mild epigastric pain occasionally for 3 months. The USG abdomen revealed gallbladder with multiple calculi with acoustic shadow and Grade II fatty liver (Figure 5). LFT and all other relevant investigations were within acceptable limits. (b) A 49–year-old male presented with flatulence dyspepsia and occasional discomfort in the epigastrium for more than 7–8 months. On investigation (USG), his gallbladder was found to be contracted and contained calculi (Figure 6). Other investigations were within normal limits. Both were planned for laparoscopic cholecystectomy under general anesthesia. In both cases, the gallbladder

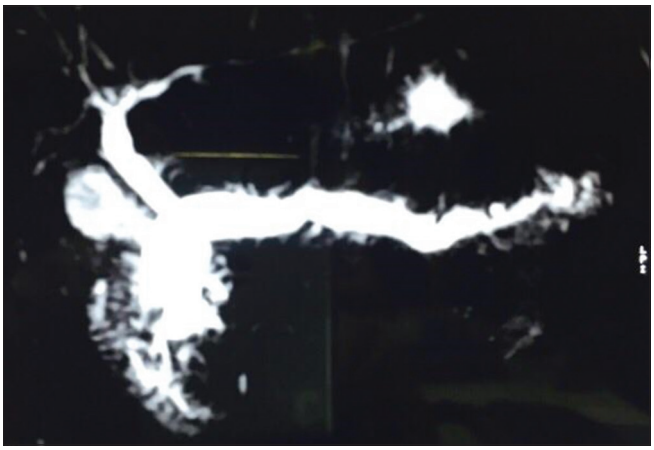

Figure 3: Magnetic resonance cholangiopancreatography of showing the proximal calculous at ampulla in pancreatic duct (PD) dilating both PD and common bile duct

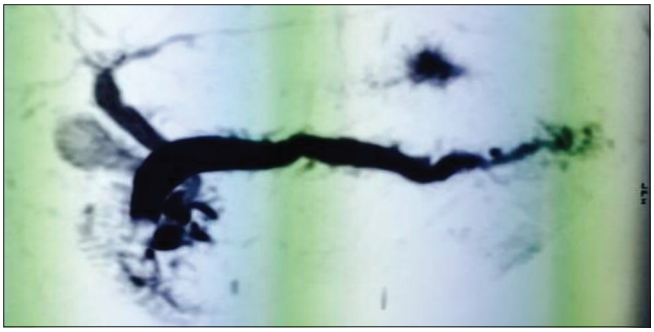

Figure 4: Contrast magnetic resonance cholangiopancreatography of showing the proximal calculous at ampulla in pancreatic duct (PD) dilating both PD and common bile

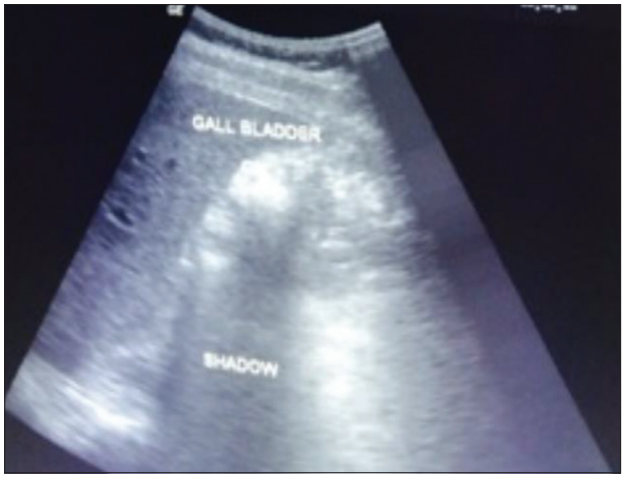

Figure 5: Ultrasonography whole abdomen of the operated female patient showing acoustic shadow of gall stones

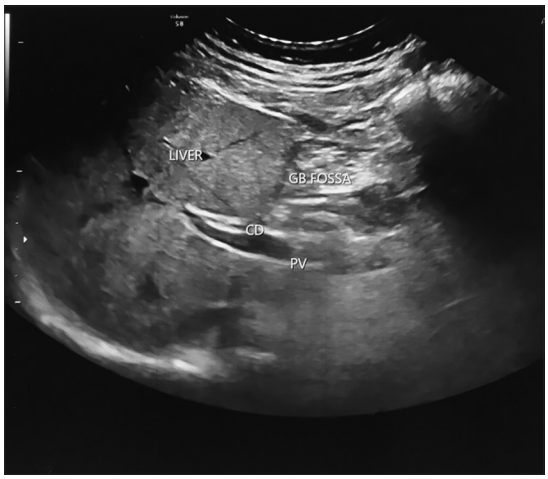

Figure 6: Ultrasonography whole abdomen of the operated male patient gall bladder fossa

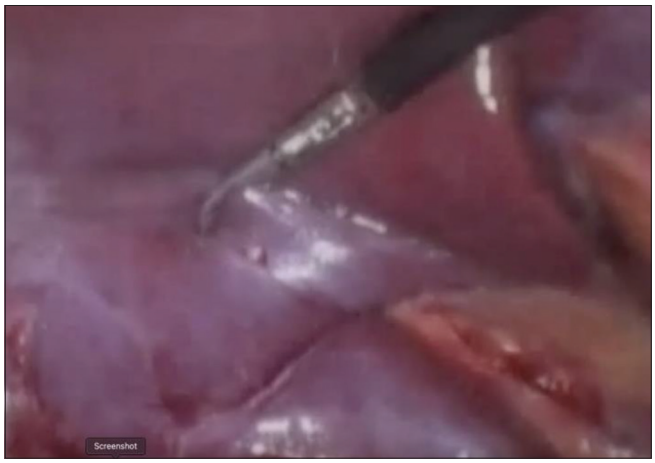

Figure 7: Screenshot of the operative Video of the female patient showing agenesis of gall bladder

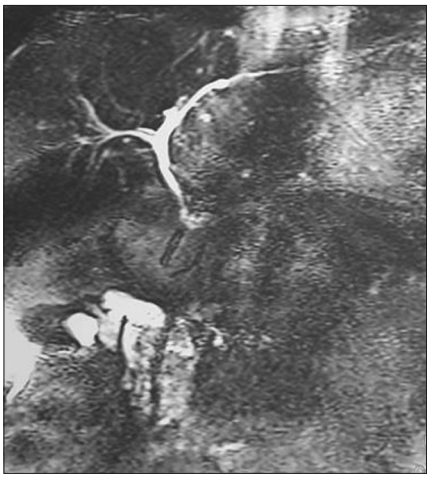

Figure 8: Magnetic resonance cholangiopancreatography of the operated male patient showing agenesis of gall bladder

was absent along with the cystic duct (Figures 7 and 8). The CBD was traced upward in search of the cystic duct so that the gallbladder could be traced if it was intra-hepatic. Other possible sites of ectopic gallbladder were not examined to avoid any major trauma. In either case, the facility of Intraoperative USG and/or near infrared fluorescence cholangiography (NIRFC) were not available to detect the gallbladder intra-operatively. Intraoperative cholangiography was not attempted as the cystic duct was

not traceable. The procedure in both cases was abandoned after discussion with the patients' relatives and their consent.

In all cases, MRCP was advised (postoperatively in the operated cases). In the operated cases, we wanted to confirm AGB. In all cases, MRCP revealed AGB (Figures 9 and 10 of the operated patients). All four patients recovered uneventfully. Two operated patients were discharged after confirmation of AGB by MRCP a day after the operation. CBD calculous patient was discharged 2 days after ERCP. The fourth patient (Calculous in PD) was discharged 4 days post-ERCP as he was having pain abdomen. All patients were followed up for 4 months and were doing well.

DISCUSSION

The prevalence range of AGB is 0.007–0.13%. The incidence of this malformation is slightly lower in the surgical cholecystectomy series (0.007–0.027%) than that in autopsy reports.[6] AGB diagnosed during surgery has a female predominance of 3: 1, while cases found in autopsies have an equal sex ratio.[7] In our series, male-to-female ratio among patients who underwent surgery was equal.

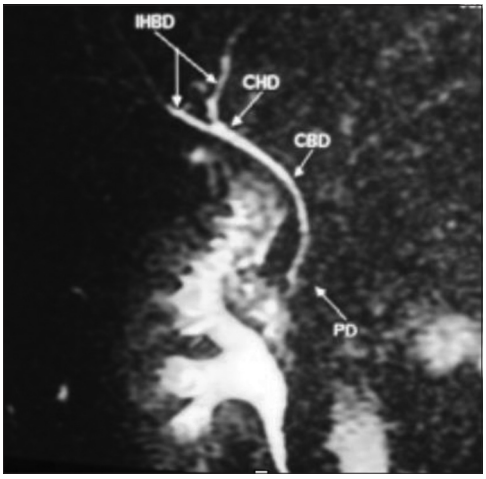

Figure 9: Magnetic resonance cholangiopancreatography of the operated female patient showing agenesis of gall bladder

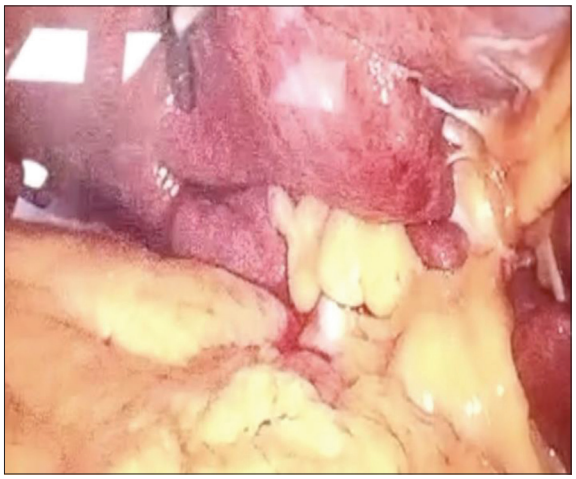

Figure 10: Screenshot of the operative video of the male patient showing agenesis of gall bladder

AGB itself has no characteristic symptomatology.[9] Clinically, three groups of AGB presentation were reported by Bennion et al., in 1988[5]: (1) multiple fetal anomalies (15–16%): These patients invariably die in the perinatal period due to associated anomalies and AGB was only recognized at autopsy. Most frequently encountered were cardiovascular, gastrointestinal, genitourinary, anterior abdominal wall, and central nervous system anomalies. In this group, AGB is only a trivial anomaly. (2) Asymptomatic group (35%): AGB was discovered either at autopsy, at laparotomy for unrelated diagnosis, or by screening the family members of patients known to have AGB. These patients do not have symptoms of the biliary tract. (3) Symptomatic group (50%): this major group presents in the 4th or 5th decades (three of our patients were in this age group) and this is usually an isolated anomaly. In the symptomatic group, common signs are chronic right upper quadrant pain (90%), dyspepsia (30%), nausea and vomiting (66%), fatty food intolerance (37%), and jaundice (35%).[10,11] Two of our AGB patients had symptoms related to CBD and PD calculous with one patient having jaundice. The operated patients had symptoms of fatty food intolerance and flatulence. The female patient also had Grade II fatty liver. The symptoms lead to false interpretation of cholecystitis, thus making the diagnosis of AGB difficult. The possible mechanisms of these symptoms include primary duct stone (in one of our cases), biliary dyskinesia, or non-biliary disorders. Biliary dyskinesia may be due to a spasm of the sphincter of Oddi and is associated with increased pressure in the CBD.[6] This may lead to pancreatitis. Possible causes of pain epigastrium as a symptom in AGB include biliary dyskinesia, adhesions in the gallbladder fossa, or periportal adhesions. The lysis of these adhesions at operation is the main cause that this pain is resolved postoperatively.[12] The jaundice is due to associated choledocholithiasis with or without ascending cholangitis[13] (found in one of our cases).

It has been suggested that gallbladder agenesis mirrors the post-cholecystectomy condition,[14] which predisposes patients to biliary dyskinesia. Furthermore, this biliary dyskinesia, which occurs from a greater retrograde ampullary sphincteric musculature contraction compared with normal subjects, promotes the dilation of the CBD and biliary stasis.[15] This condition predisposes patients to the development of biliary calculi.

The preoperative diagnosis of gallbladder agenesis has been considered to be difficult, and most diagnoses are

made at laparotomy or during attempted laparoscopic cholecystectomy.[9,16] If the diagnosis of AGB is made during operation, the surgeon must prove AGB by thorough investigation of the most common sites for ectopic gallbladders, which are intrahepatic, retrohepatic, on the left side or within the leaves of the lesser omentum or within the falciform ligament and retroperitoneal.[8,16,17] Some surgeons even reported the need to convert to open access, to establish an accurate diagnosis of AGB.[18,29] Excessive dissection is required to fulfill Frey's criteria for AGB,[19,20] because of the great danger of injuries in the hepatobiliary tract, this procedure must be avoided. It is not wise to convert a laparoscopic to an open-access procedure. It is better to remain at the level of a simple laparoscopy and to establish the accurate diagnosis of AGB postoperatively by imaging modalities, mainly by MRCP.[20,21] This necessitates proper patient and relative counseling because the procedure is abandoned due to pre-operative misinterpretation of the clinical and investigative findings.

The use of imaging modalities to diagnose AGB has some advantages and disadvantages that should be kept in mind: USG is the investigation of choice for the diagnosis of cholelithiasis[30] or CBD stones with a sensitivity of 95–98%. The usual ultrasonographic report in cases that were subsequently confirmed to be AGB is a shrunken gallbladder containing gallstones. In case of false-positive USG of AGB, it has been suggested that either a loop of gas-containing bowel located in the gallbladder fossa[16] or periportal tissue[12] and subhepatic peritoneal folds[5,11] mimic a shrunken gallbladder containing gallstones as in our first case. Sometimes, in the place of an absent gallbladder, there may be a liver hemangioma,[22] a great lipoma,[23] or migrated liver tissue in the fossa of the gallbladder[24] that creates diagnostic problems not only on USG but also in the interpretation of other imaging modalities such as computed tomography scan.

If the diagnosis of gallbladder agenesis is made preoperatively, patients who have choledocholithiasis should undergo ERCP stone extraction as in our second case.

MRCP is a non-invasive and well-demonstrated imaging method in the evaluation of the biliary tract. As it does not require contrast material to visualize the bile, it is not compromised by biliary stasis. It can then demonstrate an excluded and/or ectopic gallbladder.[6] Preoperative MRCP should be considered in cases, in which ultrasound suggests non-visualization of the gallbladder before any decision to operate.[25] In one case, MRCP was interpreted wrongly with the comment that "the gallbladder was difficult to identify but appeared to be contracted," but there was a large liver hemangioma in the gallbladder fossa.[21] Recently, per-operative indocyanine green has been used I/V for NIRFC, as a method of imaging to detect the gallbladder in AGB.[28] hepatobiliary iminodiacetic acid (HIDA) scan cannot diagnose AGB by mere non-visualization of the gallbladder. Non-visualization of gallbladder in HIDA scan may be due to obstruction of the cystic duct due to inflammation or calculous.[30]

There are some cases reported, in which AGB was diagnosed preoperatively and the operation was avoided.[16,26,27] However, it is extremely difficult to diagnose AGB preoperatively probably for the reasons discussed following review of literature.

CONCLUSION

The patients with AGB are usually operated because of "Misinterpreted" clinical and investigative findings. When USG reveals a "scleroatrophic" gallbladder or in cases of non-visualization in other imaging modalities, the need of further preoperative investigation must be in the surgeon's mind like MRCP which is most accurate non-invasive diagnostic tool to diagnose AGB.

When laparoscopic surgery is done, further surgical procedures should be abandoned to prevent injuries and the patients must undergo postoperative MRCP investigation. Further, the scope of the study to reduce surgery in AGB is possible by review of literature on pre- and post-MRCP era to consider MRCP as the diagnostic tool to avoid surgery in AGB.

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Authors Contribution:
BB- Concept and design of the study, preparation of manuscript, revision of manuscript; **AB-** Review of literature, preparation of first draft of manuscript; **SS**- Concept, coordination, and finalization of manuscript.

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