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• *CASE REPORT* •

Agenesis of the gallbladder: A dangerously misdiagnosed malformation

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Abstract

Isolated agenesis of the gallbladder is a rare anomaly, often asymptomatic. However, one patient out of four presented with right upper abdominal pain, nausea, and fatty food intolerance. The condition is frequently mistaken with an excluded or sclero-atrophic gallbladder, regardless of the imaging modality used. Consequently, AG often leads to unnecessary and potentially dangerous laparoscopic surgery as described in a few case reports over the last 10 years. The aim of this study is to clarify the diagnostic and therapeutic approach of this unusual pathology. Two cases seen in our institutions were retrospectively reviewed, together with a review of the American and European literature. During laparoscopy, the absence of normal anatomical structures and the impossibility of pulling on the gallbladder to expose and dissect the triangle of Callot increases the risk of iatrogenic injury to biliary or portal structures. Depending on the experiment of the surgeon in laparoscopic procedure, this has to be taken into account to decide a conversion to laparotomy. A high index of suspicion is necessary when interpreting the radiological images. In case of doubt, a MRI-cholangiography is mandatory. Because of possible inherited transmission, relatives with a history of biliary symptoms should be investigated.

Key words: Gallbladder; Laparoscopy; Pathology

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INTRODUCTION

In animals, the absence of a gallbladder has been a subject of research since the Aristotelian era[1]. Present in 1/6 of cases of biliary atresia[2], the isolated absence of the gallbladder and cystic duct is rare. Patients become symptomatic in 23% of cases[3,4], and agenesis of the gallbladder (AG) will almost always be misinterpreted as cholecystitis with cystic duct obstruction or as a sclero-atrophic gallbladder, therefore leading to unnecessary surgery. Reported for the first time in human beings by Bergman in 1702[5], it has since been described several times in case reports. During laparoscopic surgery, it represents a pitfall for the surgeon[6,7]: the biliary or portal structures can easily be injured during dissection as one searches for a gallbladder that does not exist. The absence of normal anatomical structures and the inability to pull on the gallbladder to dissect the triangle of Callot represent a risk of iatrogenic injury.

This review is based on a Medline and PubMed search from 1960 to 2003. Keywords used were agenesis of the gallbladder, absence of gallbladder, congenital syndromes, ultrasound, cholangiography, hepatobiliary scintigraphy, endoscopic retrograde cholangiopancreatography, magnetic resonance cholangiography, biliary dyskinesia, postcholecystectomy syndrome, laparoscopic surgery. Relevant literature was selected from the abstracts and cross-references of the retrieved literature were used to complete the search.

Between 1992 and 1999, two cases of AG were reported in our two institutions (Centre Hospitalier Universitaire Vaudois and Centre Hospitalier Cantonal de Fribourg), which are briefly described.

CASE REPORT

Case one

A 34-year-old man was admitted for right upper abdominal pain and bloating after meals for the last 9 years. The ultrasonography showed a scleroatrophic gallbladder and the intravenous cholangiogram revealed a very narrow biliary tree without opacification of the gallbladder. Total bilirubin was slightly elevated, and the direct fraction was twice the normal value. Other laboratory results were within normal limits. During the laparoscopic procedure, no gallbladder could be identified. A branch of the right hepatic duct was injured. Laparoscopy was converted to a median laparotomy. Initial dissection was carried out on the vena portis thought to be an ectopic gallbladder. Neither the intraoperative cholangiogram performed through the accidentally divided segmental duct nor the surgical exploration could demonstrate a gallbladder. The segmental biliary duct was ligated and the area drained.

Case two

A 76-year-old asymptomatic man went to his physician for

a check-up. Ultrasonography revealed a tumor of the right kidney, which was confirmed by a CT scan. Both failed to identify the gallbladder, but showed an increased size of the common bile duct. A median laparotomy was decided in order to deal with both pathologies. In place of the gallbladder, a small fibrous structure (1.5 cm×1 cm) was found and excised. The intraoperative cholangiogram did not show an ectopic gallbladder. A choledocotomy with the extraction of two gallstones was realized and an abdominal right nephrectomy performed. The histopathological analysis did not demonstrate any gallbladder tissue.

DISCUSSION

AG can be observed in both children and adults, with a median age of 46 at the time of diagnosis[8]. It is almost always a fortuitous finding during abdominal surgery or at autopsy. The prevalence range is 0.007-0.13%. The incidence of this malformation is slightly lower in surgical cholecystectomy series (0.007-0.027%)[9,10] than that in autopsy reports (0.04-0.13%)[5,11-13]. The male to female ratio is equal in autopsy reports[11,14] but seems to reach the same ratio (2-3 women for 1 man) in the clinical group as other biliary tract diseases[15,16]. AG occurs in association with other malformations in 40-65% of cases[8,11,17]. It is then found above all in children[8,11,13], leading in most cases to death in the first year of life[8,13,18,19]. Two congenital syndromes with multiple anomalies including gallbladder agenesis have been described: cerebrotendinous xanthomatosis[20] and the G syndrome[18]. AG has been occasionally mentioned with trisomy 18 and the Klippel-Feil syndrome[8,21,22]. Some authors[23-25] reported this anomaly in children with congenital malformations caused by thalidomide (up to 10% in Männl's series)[24].

This anomaly is explained by an embryological disturbance occurring during the 3rd wk of gestation and concerning the caudal portion of the anterior diverticulum of the primitive gut. It is an anomaly of the development of vessels located on each side of the gallbladder bud (sinus venosus cordis, omphaloenteric, and umbilical veins)[26]. This may explain the association of this anomaly with cardiac, vascular, gastro-intestinal, and abdominal wall malformations observed in the multiple fetal anomaly group[18]. AG may be inherited, with several familial cases observed, including across two generations[4,15,19,27-29]. These series suggest a non-sex-linked heredity with variable penetration.

Patients with AG will become symptomatic in about 23% of cases[4,19,30,31]. In 1988, Bennion *et al*.[8], found 208 symptomatic cases of AG in the literature. 90.1% presented with right upper abdominal pain, 66.3% with nausea or vomiting and 37.5% with fatty food intolerance. Thirty-two percent of these patients presented with a common bile duct dilatation whereas only 27% had gallstones. In the literature, AG is associated with a dilatation of the common duct or gallstones in 25-50% of cases[15,31,32]. The symptomatology and the increased frequency of gallstones has been attributed, by some authors, to biliary dyskinesia[16,30-34] and compared by others to a postcholecystectomy syndrome[8]. According to Toouli *et al*.[35], and Meshkinpour *et al*.[36], the biliary dyskinesia may be due to a hypertonic muscular retrograde contraction of the Oddi sphincter leading to a common duct dilatation, biliary stasis and gallstone formation[35,37]. Tanaka *et al*.[38], showed in 1983 that induction of a spasm of the Oddi sphincter reproduced the same painful symptomatology as biliary dyskinesia, and was associated with increased pressure in the common bile duct. However, it does not explain why the majority of patients become asymptomatic postoperatively (94% of cases in Bennion's series)[8]. Furthermore, the presence and development of a sphincter regulating the bile flow seems to be related to the presence or absence of the gallbladder. Indeed in animals without a gallbladder, the sphincter is poorly developed[39]. According to Lindskog[40], common bile duct dilatation without stones may simply indicate that the calculi have passed. Nevertheless, when we compare the frequency of common duct stones after cholecystectomy (5%) with the frequency of stones in AG (23%), we must recognize that this condition predisposes to calculus formation. Ahlberg *et al*.[9], did not show any changes in the bile lipid composition of patients with AG. However, the small number of patients in this study does not allow any conclusions to be drawn. Similar studies were realized in postcholecystectomy patients with conflicting results due to differences in methodology and patient selection[9,41-44].

When reviewing the literature, with the exception of two cases of AG[27,33], the preoperative investigations carried out on symptomatic patients failed to demonstrate the diagnosis. Whatever the method was used, cholangiography, hepatobiliary scintigraphy, ultrasound (US) or even endoscopic retrograde cholangiopancreatography (ERCP), the diagnosis proposed was almost always cystic duct obstruction or a small contracted gallbladder[3,6,7,45-47].

Ultrasonography is actually the investigation method of choice for the diagnosis of common bile duct stones, with a sensitivity of 95-98%. Crade *et al*.[48], defined three categories of abnormal ultrasounds of the gallbladder. The only case of AG in this study came from the second category (as also seen in other numerous cases described in the literature[7,30,46,47,49]): (1) shadowy gravity-dependent opacities within the gallbladder, (2) nonvisualization of the gallbladder lumen, and (3) nonshadowy opacities within the gallbladder lumen. The accuracy of US in these three different categories is 100%, 96%, and 61%, respectively[48]. The great difficulty in visualizing a contracted gallbladder on stones is well known[48,50]. According to Hammond[51], there is always either a recognizable segment of wall or a thin rim of bile identifying the gallbladder. He bases his assertion on MacDonald's *et al*.[52], and Raptopoulos's *et al*.[53], reports, which described the WES triad (demonstration of the gallbladder wall, the echo of the stone, and the acoustic shadow) or the double arc shadow (two parallel arcuate echogenic lines separated by a thin anechoic space with distal acoustic shadowing). However, the examination conditions as well as the examiner's experience does not always permit such accurate appreciation. Shadowy opacities misdiagnosed as stones can be due to intestinal gas artefacts or to other structures in close proximity, such as a calcified hepatic lesion or a surgical clip[46,51].

The hepatobiliary scintigraphy with new ^{99m}Tc-IDA agents and quantification of function is increasingly giving results,

especially in the detection of gallbladder anomalies[54]. Nevertheless, the nonvisualization of the gallbladder remains typical of cystic duct obstruction, as well as AG[54].

ERCP has been used in addition to other diagnostic methods[6,27,33,55,56]. Again, the nonvisualization of the gallbladder was interpreted as an occlusion of the cystic duct.

Magnetic resonance cholangiography is a noninvasive and well demonstrated imaging method in the evaluation of the biliary tract[57–59]. As it does not require contrast administration to visualize the bile, it is not compromised by biliary stasis. It can then demonstrate an excluded and/or ectopic gallbladder. However, this technique is not readily available. It may not yet replace ultrasound as the gold standard of acute gallbladder imaging but it is an ideal complementary study to inconclusive sonographic studies[60].

Selective arteriography of the hepatic artery has been proposed to prove gallbladder agenesis[6,61], but remains a very invasive procedure.

Reviewing the recent literature[62-65] concerning the AG, we noticed that symptomatic patients are still unnecessarily operated. In only two cases, AG was demonstrated by nonoperative means[27,33]. It was the evocation of this disorder in the initial assessment (US and cholangiography), which led to diagnosis. An ERCP increased the suspicion and AG was confirmed in each case by repeated US and cholangioscintigraphy during follow-up in asymptomatic patients.

In conclusion, AG is an unusual anomaly, mimicking a biliary stone disease in 23% of cases. This condition must be kept in mind in the differential diagnosis of ultrasonographically undetected or scleroatrophic gallbladder. When the WES triad or double arc shadow are not present, this congenital malformation should be suspected. An ectopic location of the gallbladder should be excluded. In case of doubt a conservative approach involving repeat investigations, in asymptomatic patients or after the acute phase, will avoid unnecessary surgery.

When AG is a laparoscopical discovery, the possibility of iatrogenic injury, by dissecting the portal structures without normal anatomical landmarks, has to be taken into account to decide a conversion to laparotomy. An intraoperative cholangiography should be realized through the common duct. Intraoperative ultrasound can demonstrate an ectopic gallbladder but is not always available. The lesser omentum, the falciform ligament, and the liver must be palpated. The exploration will also include a Kocher maneuver to explore the posterior wall of the duodenum as well as the head of the pancreas. The scar tissue in the gallbladder bed and the portal area must be carefully explored.

Associated malformations need not be systematically sought in adults, but family heredity has to be taken into account. Relatives with past or repetitive biliary symptomatology should have at least an ultrasonography when asymptomatic.

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