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Gallbladder Papillomatosis and Cholecystocolonic Fistula: A Rare Combination

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Conflict of interest: None declared

Patient: Female, 81
Final Diagnosis: Gallbladder papillomatosis
Symptoms: Epigastric pain
Medication: —
Clinical Procedure: —
Specialty: Gastroenterology and Hepatology

Objective: Rare disease

Background: Biliary papillomatosis (BP) with sole involvement of the gall bladder or gall bladder papillomatosis (GBP) is very rare. Biliary-enteric fistula, particularly the cholecystocolonic fistula (CCF) type, is also very rare. The combination of both types of lesions in a single patient has never previously been reported in the English literature.

Case Report: We report herein the case of an 81-year-old woman who was diagnosed with both disease entities, which occurred in a cause-and-effect relationship. She underwent resection of the gall bladder with closure of the fistula, and was discharged improved afterwards.

Conclusions: GBP is a premalignant condition that warrants extensive resection. An absent Murphy's sign or jaundice on physical examination should not rule out this disease or accompanying biliary tract infection because a biliary-enteric fistula may be present. Thorough review of the radiologic images should be performed, since subtle details could be easily missed or dismissed, thus affecting the postoperative course. A CCF should alert the physician that another disease entity is present.

MeSH Keywords: Biliary Fistula • Colonic Diseases • Gallbladder Neoplasms

Full-text PDF: http://www.amjcaserep.com/abstract/index/idArt/891190

Background

Biliary papillomatosis (BP) is a rare disease entity characterized by multiple mucin- or non-mucin-secreting papillary adenomata in the biliary tract, with significant risk of malignant transformation. Fewer than 200 cases have been reported in the English literature [1–3]. Cholecystocolonic fistula (CCF) is also a rare clinical entity. In an article by Costi et al., only 231 cases were confirmed from 160 manuscripts published from 1950 to 2006 [4]. Our case is unique since 2 relatively rare disease entities occurred via a cause-and-effect relationship in a single patient. After a thorough search in the English literature, this is the first report of a patient with gallbladder papillomatosis combined with a CCF.

Case Report

An 81-year-old Taiwanese woman was admitted to our hospital due to epigastric pain and fever for 2 days. She had hypertension and diabetes mellitus for more than 30 years, but did not smoke cigarettes or drink alcohol. The pain was nonradiating and was not related to eating or positional changes. She denied having similar symptoms in the past. On presentation, the patient was afebrile and normotensive. Her skin was not jaundiced but her sclera was slightly icteric. There was direct tenderness over the epigastric area, but Murphy's sign was negative. Her white cell count was 11 170 cells/uL, alkaline phosphatase was 124 U/L, aspartate aminotransferase was 758 U/L, alanine aminotransferase was 361 U/L, total bilirubin was 2.58 mg/dL, direct bilirubin was 1.36 mg/dL, and gamma-glutamyl transferase was 375 mU/mL. Serum amylase and lipase were within normal range and hepatitis B and C virus titers were negative. An abdominal ultrasonography revealed gallbladder (GB) wall thickening with sludge, fatty change of the liver, and common bile duct (CBD) dilatation of 1 cm. Cefazolin 1 gm IV every 8 h and metronidazole 500 mg IV every 12 h were started.

An abdominal computed tomographic (CT) scan showed GB wall thickening and distension (Figure 1), thus percutaneous transhepatic gallbladder drainage (PTGBD) with T-tube cholangiography was performed. Filling defects were noted at the GB outlet without opacification of the CBD, but contrast media was immediately visualized over the colon (Figure 2). A GB tumor combined with a cholecysto-colonic fistula was suspected. Surgery was deferred for 2 weeks to allow maturation of the fistulous tract.

Operative findings included: omental wrapping of the GB, GB wall thickening, GB tumor with cystic duct involvement, CBD dilatation, and cholecysto-colonic fistula involving the GB fundus and transverse colon. There were also minimal adhesions

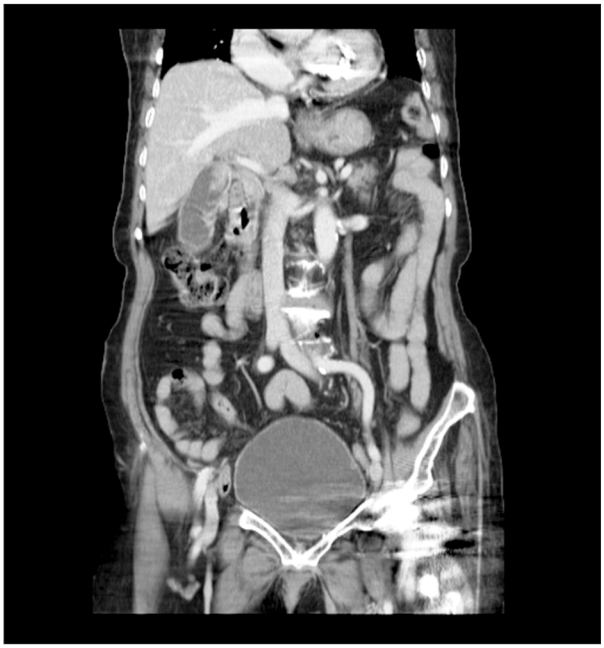

Figure 1. CT image of the patient, showing a distended gallbladder with thickened wall.

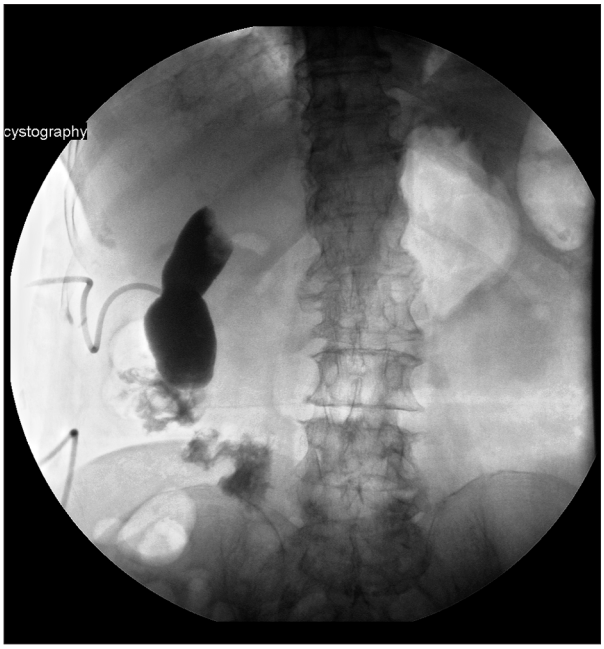

Figure 2. Percutaneous transhepatic gallbladder drainage showed filling defects over the GB outlet, and contrast media can be visualized over the colon.

noted between the GB fundus and the transverse colon. Further exploration did not reveal any other abnormalities. On gross examination, the GB mucosa was roughened, with a fibrotic wall and sludge was noted inside. Also, a papillary tumor measuring 5×3 cm was located at the GB neck just before the cystic duct, and the papillomatosis extended into the cystic

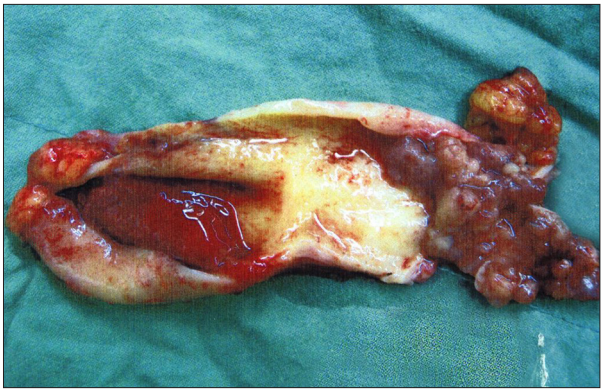

Figure 3. Gross specimen of the gallbladder, showing rough mucosa with a fibrotic wall. A papillary tumor measuring 5×3 cm was noted close to the cystic duct.

duct (Figure 3). Due to this finding, together with a mildly dilated CBD, possible involvement of the CBD was suspected. Therefore, the CBD was dissected and a scope was inserted for exploration. A small amount of muddy, paste-like substances or "muddy stones" were noted over the distal CBD and removed. The approximate size of the muddy substances when put together measured about 1–2 mm in diameter. The proximal and distal CBD was free of papillomatosis. The complete surgical procedure included cholecystectomy, closure of the biliary fistula, choledocholithotomy plus T-tube drainage, and intraoperative choledochoscopy. No complications were noted during or after the procedure. A T-tube cholangiogram performed 2 days after surgery showed a patent biliary tree with no filling defects.

Histopathologic examination showed the section of the main GB lesion had multiple papillary or villous-like projections over the GB wall on screening magnification (Figure 4). Foci of high-grade intraepithelial glandular lesions were noted, with enlarged pyknotic nuclei on high-power magnification (Figure 5). The cystic duct stump tissue submitted showed chronic inflammation and fibrosis with surgical margins that were free of papillomatosis (not shown). The colonic tissue showed a fistulous tract lined by fibrous and granulation tissues, and was also free of papillomatosis. The excised lymph nodes showed follicular hyperplasia. The patient was discharged improved 1 week after surgery and has been asymptomatic and well for 3 years, with regular follow-up at our hospital.

Discussion

BP usually involves the entire biliary tree and sole extrahepatic involvement occurs in about 27% of cases. However, sole GB involvement was reported to be even lower, at 3% [2]. If we include the study by Lee et al., [1] which did not involve the GB, the incidence would only be 1.8%. After 2004, the only

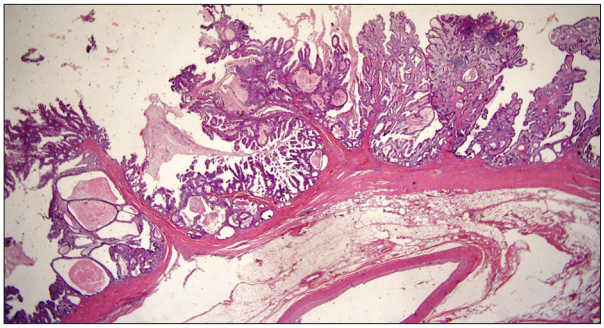

Figure 4. Representative section of the gallbladder wall, showing multiple papillary or villous-like projections (screening magnification, hematoxylin and eosin).

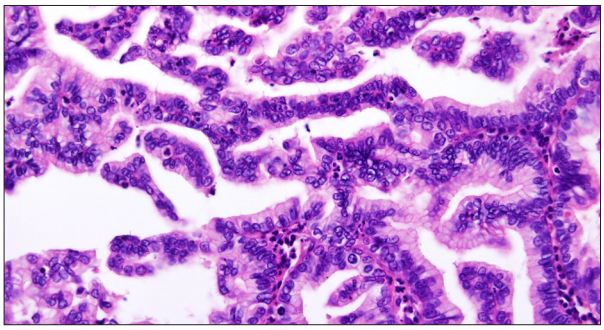

Figure 5. Foci of high-grade intraepithelial glandular lesions (HGIN) were noted with enlarged pyknotic nuclei (high-power magnification, hematoxylin and eosin, 400×).

study that analyzed patients with BP having more than 3 patients was published in 2008 [3]. In that series, none of the 18 patients had GB involvement. Twenty years ago, we reported 3 cases of BP and none of our patients had GB involvement [5]. These data indicate that sole involvement of the GB or GB papillomatosis (GBP) is extremely rare.

Since BP is a premalignant condition with a 25–50% risk of malignant transformation, extensive resection is usually recommended. Moreover, although sole extrahepatic involvement usually has a better prognosis, as most lesions can be excised completely, they tend to recur intrahepatically, and malignant changes have occurred in the background of a benign facade. Patients usually present with recurrent obstructive jaundice and cholangitis, but not all patients have jaundice when fistulous tracts are present to allow bile drainage, as in our case.

CCFs are rare complications of gallstones or GB disease, occurring in 0.06–0.14% of patients with biliary disease [6,7]. Other causes of CCF, including previous biliary tract surgeries, peptic ulcer disease, Crohn's disease, malignancies, and trauma, were all ruled out in this patient. Pneumobilia, chronic diarrhea, and vitamin K malabsorption are the pathognomonic triad of CCF [8]. However, some patients may be asymptomatic, like our patient, and these lesions may only be found during

surgery or during examinations not related to it. Biliary-enteric fistulas have been found in 0.9% of patients undergoing biliary tract surgery [9], with the most common site being cholecystoduodenal (70%), followed by cholecystocolonic (10–20%) and cholecystogastric sites. Finding cholecystocolonic fistulas during cholecystectomy is rare and has an incidence of only 0.5%. Identifying these lesions, particularly during surgery, is very important because an unsuspecting surgeon may injure or rupture the fistulous tract during manipulation, which can result in peritonitis when bowel contents spill into the peritoneum. Moreover, finding a CCF should alert the physician of other pathologies, as CCF is rarely primary.

It is postulated that acute inflammation of the GB with cystic duct obstruction may result in adhesion of the GB to the contiguous organs like the duodenum, which is nearest to it. Recurrent cholecystitis then results in ulceration and ischemia of the GB wall and the adjacent organs, resulting in further erosion and ultimate fistulation [6]. This was probably what happened in our patient since biliary obstruction at the level of the cystic duct from papillomatosis resulted in severe GB distension reaching up to the transverse colon. Then, inflammation from cholecystitis may have caused ulceration between the 2 proximate structures, resulting in a fistulous tract between them.

We cannot be absolutely certain of this theory because of the following. The patient and her family denied having previous episodes of epigastric and right upper quadrant pain, nausea, or vomiting, and there were only minimal adhesions noted between the 2 structures, suggesting that this may have been a recent event. There were also no solid or formed stones noted on preoperative CT scan and after dissection and exploration of both the GB and CBD. However, a small amount of sludge and "muddy" substance were found over the GB and distal CBD, respectively. Although minimal in amount, the presence of the "muddy" substance also complicates our claim since this may have been the cause of the biliary obstruction, which resulted in inflammation and fistula formation, instead of the papillomatosis. It also suggests that the papillomatosis was only partially obstructive, as it allowed the sludge to escape from the GB.

However, the CBD was only mildly dilated (1 cm), both intrahepatic ducts were normal, and the "muddy" or paste-like substance was spread over the circumference of the distal CBD. We believe that even after gathering the "muddy" substance together to a size of 1–2 mm, it could not have caused an obstruction. However, given that the patient has GB sludge and "muddy stone", we concede that the patient may have indeed previously passed a GB or CBD stone, and the GBP is only an incidental finding.

The main reason for thinking that the GBP was the proximate cause of the CCF was that both the papillary tumor and the papillomatosis, as seen on cut section, were crowding the neck of the GB and encroaching on the cystic duct. Although it initially caused minimal or no obstruction before, because it still allowed bile to flow inside or the sludge to escape outside, further enlargement of the tumor and progression of the papillomatosis later on may have worsened the obstruction. Then, the increasing weight of the bile-filled GB may have caused it to sag, creating acute angles at the neck, and further narrowing the already obstructed lumen. The resulting rise in pressure inside the GB would then result in ischemia and ulceration of its wall, affecting the surrounding structures and resulting in the fistula.

On the other hand, it is also equally plausible that the fistulous connection was older than we thought and that years of backflow of enteric contents from the colon into the GB may have led to inflammation and eventual papillomatosis. Whichever came first, the GBP or the CCF or vice versa in this case, will never be known. However, if the theory that the fistula causing the papillomatosis is true, it is still a cause-and-effect relationship, but in a reverse fashion. We strongly feel that the first scenario is more likely, because spontaneous biliary enteric fistula in itself, or even resulting in papillomatosis, is an even rarer occurrence and so much harder to explain.

There has been some debate as to the best treatment option in these patients. Some advocate the more invasive approach because these lesions are premalignant, while others opt for a more conservative or observational approach for patients who cannot tolerate surgery or when life expectancy is in question. Since the GB is usually the culprit for developing CCF, together with papillomatosis in the cystic duct and a dilated CBD, an open cholecystectomy with resection of the fistula, followed by choledocholithotomy and intraoperative choledochoscopy for CBD exploration, was the best treatment strategy in this patient.

After a thorough search of the English literature, there is only 1 reported case of BP resulting in a biliary-enteric fistula [10]. However, our case is slightly different from theirs, based on the location of the biliary and the enteric lesions. In our patient, the papillomatosis occurred solely in the GB, which is very rare, as opposed to their more common intraductal or diffuse type, and only 4 cases have been reported out of about 150 cases worldwide. Moreover, our patient had the much rarer cholecystocolonic fistula versus the more common cholecystoduodenal type, which occurred in their patient.

Conclusions

GBP, although very rare, is relatively easy to treat since it can be completely excised when diagnosed early and without other

intra- or extrahepatic involvement. An absent Murphy's sign or jaundice should not rule out this disease or accompanying infection since a biliary-enteric fistula may be present. Careful review of the radiologic images should be performed, since subtle and minute details like contrast medium draining into the colon could easily be missed or dismissed. This seemingly harmless detail may result in a complicated surgical procedure if the fistulous tract was accidentally injured or transected by an unsuspecting surgeon.

Statement

No financial support or conflicts of interest exist regarding this manuscript

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