

Gallbladder Cancer Manifesting as Recurrent Common Bile Duct Stone and Duodenal Ulcer Bleeding

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Gallbladder cancer (GBC) is an uncommon disease and is usually asymptomatic. Poor prognosis and high mortality rate have been noted in patients with delayed diagnosis. We report a case of locally advanced GBC with duodenum and colon invasion manifesting as bleeding duodenal ulcer and recurrent common bile duct (CBD) stones. The patient was successfully treated with extended surgery. In patients who have multiple recurrence of CBD stones without common risk factors, concomitant biliary tract malignancy should be included in the differential diagnosis. [*J Chin Med Assoc* 2009; 72(8):434–437]

Key Words: choledocholithiasis, gallbladder neoplasm, gastrointestinal hemorrhage

Introduction

Gallbladder cancer (GBC) is a rare and highly lethal disease.^{1,2} With no specific clinical symptoms or signs, GBC is usually unexpected preoperatively. Most patients have right upper abdominal pain at presentation, and have advanced disease when diagnosed. The minority of GBCs are first diagnosed on microscopic examination at the time of routine cholecystectomy for biliary colic and cholelithiasis.³ Cholelithiasis is the best known risk factor for GBC.³ Only 0.5–3% of patients with gallstones develop GBC, and 20% of patients with GBC do not have stones.^{2–6} The most common symptoms of GBC are pain, followed by anorexia, nausea, or vomiting.⁷ However, patients with early invasive GBC are often asymptomatic. The management and prognosis of GBC depend on the initial tumor stage at diagnosis. Poor prognosis and high mortality rate have been noted in patients with delayed diagnosis. We report a case of locally advanced GBC with duodenum and colon invasion that manifested as bleeding duodenal ulcer and recurrent common bile duct (CBD) stones. The patient was successfully treated with extended surgery.

Case Report

A 78-year-old male retired soldier was admitted to Kaohsiung Veterans General Hospital with the chief complaints of intermittent fever, right upper abdominal pain, and progressive yellowish discoloration of the skin for 1 week. The patient had received abdominal surgery due to intestinal obstruction by a large bezoar 7 months previously.

On this admission, total bilirubin was 12.4 mg/dL (normal, <1.6 mg/dL), alkaline phosphatase was 188 U/dL (normal, <128 U/dL), and alanine aminotransferase was 18 U/dL (normal, <40 U/dL). Abdominal sonography during this admission revealed a 0.8-cm stone in the gallbladder, and other detailed images were blocked by gas (Figure 1A). Abdominal computed tomography (CT) showed stones in the gallbladder and CBD with dilatation of the intrahepatic ducts (Figures 1B and 1C). Endoscopic retrograde cholangiopancreatography (ERCP) confirmed the clinical diagnosis of CBD stones, but the gallbladder was not visualized. No juxta papillary diverticulum was seen. The CBD was 1.3 cm in diameter, without angulation. Endoscopic balloon dilation was performed, and some



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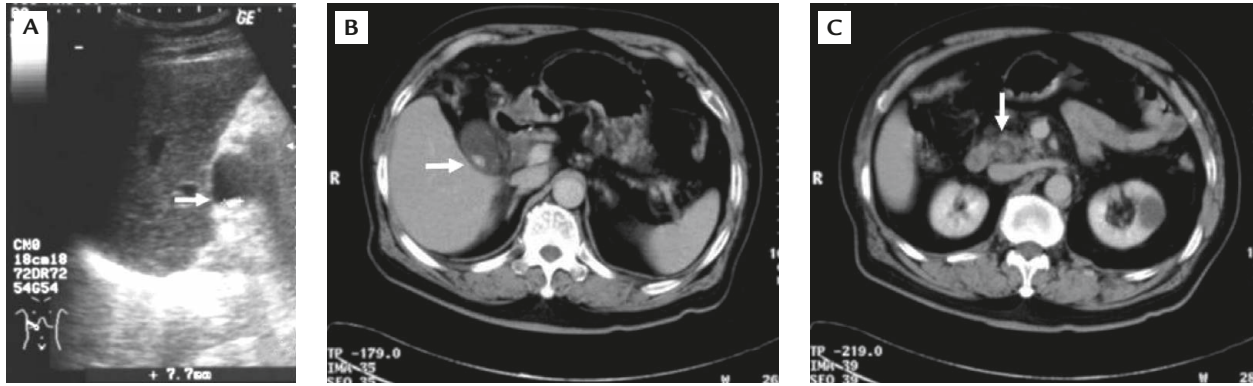


Figure 1. (A) Abdominal sonography before the first endoscopic retrograde cholangiopancreatography shows a hyperechoic lesion in the gallbladder with acoustic shadow (arrow). Computed tomography shows: (B) stones in the gallbladder (arrow); and (C) common bile duct stones (arrow).

yellow stones were removed smoothly. After complete clearance of the CBD, fever and jaundice subsided gradually. The patient refused elective cholecystectomy and was followed-up at our special clinic.

After normalization of liver function, quantitative cholescintigraphy was performed half a year later for evaluation of biliary emptying, and marked delay in bile duct clearance was noted.⁸ Repeated ERCP showed CBD stones and an ulcer with adherent blood clot at the duodenal bulb. Some yellowish muddy stones were removed by Dormia basket. A drop in hemoglobin level from 12.9 g/dL to 11.3 g/dL was found at that time. The patient was admitted for close observation, and proton pump inhibitor was given. He was discharged in a stable condition 3 days later.

Another quantitative cholescintigraphy was done 3 months later, and again showed marked delay in bile duct clearance. ERCP showed recurrent CBD stones, and stone extraction was done at the same time. During ERCP, a 0.8-cm polypoid lesion in the previously detected ulcer was found at the duodenal bulb (Figure 2). Biopsy revealed adenoma with high-grade dysplasia (Figure 3). Surgical intervention was suggested, but the patient refused.

The patient developed intermittent epigastric pain, poor appetite, progressive body weight loss, and blood-tinged stool 1 month later. Abdominal CT revealed a mass lesion measuring 7 cm over the hepatic flexure and gallbladder fossa (Figure 4), with adjacent transverse colon, stomach, and liver invasion. Some enlarged lymph nodes at the para-aortic and liver hilum were also noted. Gallbladder cancer with invasion to the intestine was impressed.

Colonoscopy showed narrowing of the lumen at the hepatic flexure with some scatter nodules and cauliflower-like mass lesion at the hepatic flexure. Pathology showed adenocarcinoma. Exploratory laparotomy showed a



Figure 2. A polypoid lesion measuring 0.8 cm in the previously detected ulcer is seen at the duodenal bulb.

tumor mass, about 9 × 6 cm in size, at the gallbladder fossa with invasion to the duodenum and colon. The tumor originated from the gallbladder wall, with a 2-cm indurated mass at the fundus of the gallbladder. No gallstone was found. The cystic duct and CBD were normal in gross appearance. Right hemicolectomy, cholecystectomy, partial hepatectomy, hemigastrectomy, partial duodenectomy preserving the ampulla of Vater, and lymph node dissections were done. Five groups of lymph nodes were dissected. Pathology revealed moderately differentiated adenocarcinoma of the gallbladder with duodenum and colon invasion, without lymph node involvement. Wound infection and fistula formation developed after operation, and the patient underwent surgical debridement 7 times. Finally, the patient recovered after the extended surgery. Over the next 5 years, he has been well, without detectable tumor recurrence.

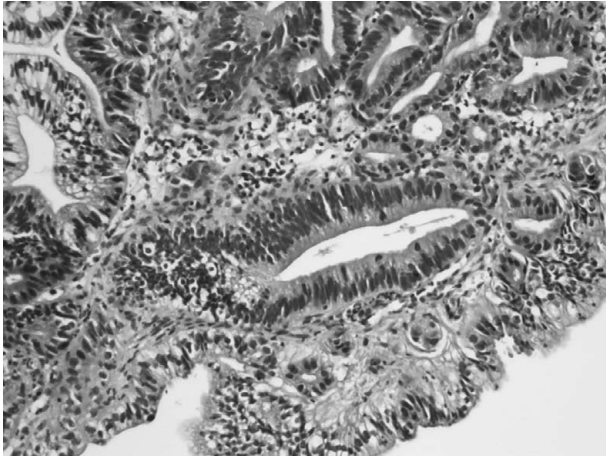


Figure 3. Biopsy from the duodenal bulb shows papillary protruding of the mucosa with stratified and hyperchromatic nuclei (hematoxylin & eosin, 200 \times).



Figure 4. Abdominal computed tomography 9 months after the first endoscopic retrograde cholangiopancreatography shows a mass lesion (arrow) at the gallbladder fossa with stomach and duodenum invasion (arrowheads).

Discussion

Piehler and Crichlow divided the symptoms of GBC into 5 groups: (1) acute cholecystitis; (2) chronic cholecystitis; (3) biliary tract disease; (4) malignant tumors outside the biliary tract; and (5) benign manifestation outside the biliary tract, like upper gastrointestinal bleeding and obstruction.² In a Taiwan study, gallstones were found in 62.2% and CBD stones were found in 30.4% of patients with GBC.⁹ Early diagnosis of GBC and evaluating the extent of the tumor are warranted. A multidisciplinary approach is required. Abdominal sonography is the most widely used technique for initial evaluation. It has a sensitivity of 85%

and accuracy of 80% for the diagnosis of GBC.¹⁰ Color Doppler ultrasonography and endoscopic ultrasound are other approaches and may improve the diagnosis. CT has been widely used in the diagnosis of GBC for the primary tumor, for its extent, and for staging. Recently developed multidetector CT allows for faster and accurate evaluation of the tumor extent and for staging. It has a sensitivity of 85–93% for the detection of peritoneal metastases, which is the limitation of traditional CT.³ Magnetic resonance imaging is particularly useful for visualizing invasion of the hepato-duodenal ligament, portal vein encasement, and lymph node involvement. Magnetic resonance imaging in combination with magnetic resonance cholangiopancreatography and magnetic resonance angiography is an attractive option to determine tumor resectability. Fluorodeoxyglucose positron emission tomography is useful in the evaluation of localized or metastatic GBC, with 75% sensitivity, 87.5% specificity, and 81.3% accuracy.³ In our case, the GBC was not detected on the first abdominal sonogram and CT scan, probably due to the tumor being located at the fundus with extraluminal growth. It was easily misinterpreted as the partial volume of the intestine.

This patient had recurrent CBD stone 6 months after endoscopic treatment. The known risk factors of recurrent CBD stones after endoscopic treatment are a dilated CBD, perampullary diverticulum, prior biliary surgery, and CBD angulation on cholangiography.¹¹ Although our patient had a dilated CBD (1.3 cm), continuous passage of stones from the gallbladder may also have been the cause of the recurrent CBD stones.

The incidence of GBC with duodenal invasion is about 11–17%,^{9,12} but upper gastrointestinal bleeding caused by GBC invasion is rare. Sharon et al reported that 8 of 859 (0.9%, 8/859) patients presenting with upper gastrointestinal bleeding had duodenal neoplasms on endoscopy, including primary duodenal neoplasm (3), metastatic involvement (2), and pancreatic tumor invasion (3).¹³ The etiology of duodenal ulcer should be carefully evaluated, especially in patients with refractory ulcer lesion or abnormal appearance of the ulcer margin and base.

The tumor stage of our patient was T4N0M0, stage III, by UICC/AJCC TNM classification.¹⁴ According to the National Cancer Database, the 5-year survival rate for GBC is 60% for stage 0, 39% for stage I, 15% for stage II, 5% for stage III, and only 1% for stage IV.¹⁵ However, extensive surgical resection of GBC with adjacent organ invasion should be attempted to increase the rate of survival.¹² In our case, the patient remained disease-free 5 years following extensive surgery, indicating successful treatment.

Gallstones are present in about 70–90% of patients with GBC.¹⁶ In patients with cholelithiasis, the overall risk of GBC is about 0.5–3%.² There is little literature on the association between GBC and recurrent CBD stones. In our previous study, delayed biliary emptying in quantitative cholescintigraphy was a predictor for recurrent CBD stones.¹⁷ Quantitative cholescintigraphy is a useful noninvasive test for biliary motility in patients after endoscopic treatment. The intact gallbladder with a patent cystic duct and organic lesion such as stone or tumors may influence the results of quantitative cholescintigraphy, and those conditions must be excluded by further tests such as ERCP for clinical interpretation. Whether the cancer growth around the bile duct in our patient affected biliary emptying or not remains unknown. Physicians should pay attention to patients who have multiple recurrence of CBD stones without the previously mentioned common risk factors, and concomitant biliary tract malignancy should be considered in their differential diagnosis. If ERCP shows poor or no visualization of the gallbladder, further regular follow-up with sonography or other imaging studies is advised, especially in patients with gallstones.

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