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ABOUT COVER

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WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

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CASE REPORT

Cholecystoenteric fistula in a patient with advanced gallbladder cancer: A case report and review of literature

Chun-Yu Wang, Sung-Hua Chiu, Wei-Chou Chang, Meng-Hsing Ho, Ping-Ying Chang

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Abstract

BACKGROUND

Cholecystoenteric fistula (CEF) involves the formation of a spontaneous anomalous tract between the gallbladder and the adjacent gastrointestinal tract. Chronic gallbladder inflammation can lead to tissue necrosis, perforation, and fistulogenesis. The most prevalent cause of CEF is chronic cholelithiasis, which rarely results from malignancy. Because the symptoms and laboratory findings associated with CEF are nonspecific, the condition is often misdiagnosed, presenting a challenge to the surgeon when detected intraoperatively. Therefore, a preoperative diagnosis of CEF is crucial.

CASE SUMMARY

We present the case of a 57-year-old male with advanced gallbladder cancer (GBC) who arrived at the emergency room with persistent vomiting, abdominal pain, and diarrhea. An abdominopelvic computed tomography scan revealed a contracted gallbladder with bubbles in the fundus connected to the second portion of the duodenum and transverse colon. We suspected that GBC had invaded the adjacent gastrointestinal tract through a cholecystoduodenal fistula (CDF) or a cholecystocolonic fistula (CCF). He underwent multiple examinations, including esophagogastroduodenoscopy, an upper gastrointestinal series, colo-noscopy, and magnetic resonance cholangiopancreatography; the results of these tests confirmed a diagnosis of synchronous CDF and CCF. The patient underwent a Roux-



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en-Y gastrojejunostomy and loop ileostomy to address the severe adhesions that were previously observed to cover the second portion of the duodenum and hepatic flexure of the colon. His symptoms improved with supportive treatment while hospitalized. He initiated oral targeted therapy with lenvatinib for further anticancer treatment.

CONCLUSION

The combination of imaging and surgery can enhance preoperative diagnosis and alleviate symptoms in patients with GBC complicated by CEF.

Key Words: Cholecystoenteric fistula; Biliary enteric fistula; Cholecystoduodenal fistula; Cholecystocolonic fistula; Gallbladder neoplasms; Case report

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Core Tip: Cholecystoenteric fistulas are rarely associated with malignancy, and synchronous cholecystoduodenal and cholecystocolonic fistulas are even rarer. We present the case of a 57-year-old male with advanced gallbladder cancer complicated by synchronous cholecystoduodenal and cholecystocolonic fistulas. He presented with persistent vomiting, abdominal pain, and diarrhea. We also review 30 cases of gallbladder cancer-related cholecystoenteric fistulas published between 1973 and 2023. We performed a statistical analysis of clinical symptoms, imaging findings, and management. Our aim is to share our experience with diagnosis and surgical treatment of this condition and offer our insights to guide future clinical decision-making.

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INTRODUCTION

Gallbladder cancer (GBC) is a lethal disease typically diagnosed at an advanced stage, leading to a grim prognosis[1]. Cholecystoenteric fistula (CEF) is an uncommon complication of biliary disease that results from an abnormal connection between the gallbladder and the adjacent gastrointestinal tract. CEF occurs in only 3%-5% of patients with cholelithiasis and 0.15%-4.8% of those undergoing biliary surgery[2]. The most prevalent type of CEF is the cholecystoduodenal fistula (CDF), accounting for 70% of cases, followed by the cholecystocolonic fistula (CCF) at 20%[2,3]. CEF can be attributed to various factors, including cholelithiasis, peptic ulcer disease, and malignant neoplasms[2,4]. However, malignancy is associated with CEF in only 3%-14% of cases[5-8]. The coexistence of CDF and CCF is exceedingly rare, with reported incidences ranging from 1.5% to 5%[5,9-11].

We present the case of a 57-year-old male with advanced GBC complicated by synchronous CDF and CCF, who presented with persistent vomiting, abdominal pain, and watery diarrhea.

CASE PRESENTATION

Chief complaints

A 57-year-old Taiwanese male presented to our emergency department in November 2022 with a 3-d history of vomiting, abdominal pain, and watery diarrhea.

History of present illness

The patient reported experiencing postprandial vomiting, epigastric abdominal pain, and watery diarrhea more than 10 times daily for 3 d.

History of past illness

His past medical history was significant for gallstones, for which he received conservative treatment. In April 2022, he was diagnosed with poorly differentiated gallbladder adenocarcinoma, cT3N1M1, stage IVB, with liver metastases. He underwent 3 mo of palliative chemotherapy with cisplatin and gemcitabine. While the primary tumor exhibited a partial response, the hepatic tumor progressed. He subsequently underwent 3 mo of treatment with gemcitabine, high-dose 5-fluorouracil, and leucovorin.

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Personal and family history

The patient denied any family history of malignant tumors.

Physical examination

A physical examination revealed generalized abdominal tenderness but no Murphy's sign or rebound abdominal tenderness. His body temperature was 36.0 °C, blood pressure 130/90 mmHg, heart rate 103 beats per minute, and respiratory rate 18 breaths per minute.

Laboratory examinations

Laboratory blood tests revealed a white blood cell count of 10990/L (normal range: 4500-11000), hemoglobin level of 8.0 g/dL (normal range: 13.5-18.0), platelet count of $466 \times 10^3/\mu$ L (normal range: 150-400 × 10³), creatinine level of 1.1 mg/dL (normal range: 0.7-1.2), aspartate aminotransferase 10 U/L (normal range: < 40), alanine aminotransferase 5 U/L (normal range: < 40), C-reactive protein 18.09 mg/dL (normal range: < 0.8), and lipase < 3 U/L (normal range: 11-82).

Imaging examinations

Abdominopelvic computed tomography (CT) displayed a gallstone in the gallbladder and a contracted gallbladder with bubbles in the fundus connected to the second portion of the duodenum and transverse colon (Figure 1). We suspected GBC invasion of the adjacent gastrointestinal tract through a CDF or a CCF. A subsequent esophagogastroduodenoscopy (EGD) and upper gastrointestinal (UGI) series identified a CDF in the second portion of the duodenum (Figure 2). A colonoscopy revealed a fistula-like lesion in the transverse colon near the hepatic flexure region. Magnetic resonance cholangiopancreatography (MRCP) confirmed the diagnoses of CDF and CCF.

FINAL DIAGNOSIS

Considering the patient's medical history, we arrived at a final diagnosis of advanced GBC complicating synchronous CDF with CCF.

TREATMENT

The patient was administered empiric antibiotic treatment for his intra-abdominal infection and parenteral nutrition. Nevertheless, the postprandial vomiting and watery diarrhea persisted, leading us to consider that his symptoms were the result of the synchronous CDF and CCF. We referred the patient to a general surgeon for palliative surgery to improve his quality of life. During the exploratory laparotomy, we identified GBC with invasion of the duodenum and transverse colon, resulting in CDF and CCF. Furthermore, severe adhesions over the second portion of the duodenum and hepatic flexure of the colon posed challenges for fistulectomy, fistula closure, and stent placement. As a result, we performed a Roux-en-Y gastrojejunostomy and loop ileostomy.

OUTCOME AND FOLLOW-UP

Following surgery, his symptoms improved, and he resumed oral intake. On day 50, he was discharged and commenced oral targeted therapy with lenvatinib for ongoing anticancer treatment.

DISCUSSION

While most CEFs arise as late complications of gallstone disease, they can also develop when GBC invades the adjacent gastrointestinal tract, as reported in several studies (Table 1). Adenocarcinoma is the predominant cancer type (68.7%). The incidence of CCF is similar to CDF, with rates of 45.2% and 38.7%, respectively. Synchronous CCF and CDF occur in 12.9% of all patients, typically within the hepatic flexure (72.2%) and transverse colon (28.8%). Gallstones and recurrent gallbladder inflammation preceding GBC invasion may contribute to CEF development[12]. Direct GBC invasion into the duodenal and colonic walls likely contributed to our case's fistula formation.

The primary clinical manifestations of CEF include abdominal pain (typically in the right upper quadrant), nausea, vomiting, weight loss, and diarrhea[2,5]. Our review of the literature found that the most common symptoms of GBCrelated CDF are abdominal pain (68.8%), nausea or vomiting (62.5%), and weight loss (25%). These symptoms resemble GBC-related CCF (abdominal pain: 88.9%, nausea or vomiting: 33.3%, and weight loss: 33.3%). Only 16.7% of patients with GBC-related CCF experience diarrhea. Due to its nonspecific symptoms, signs, and laboratory investigations, preoperative diagnosis of CEF can be challenging (reported rates of 31%-58.6% in recent research)[2,5,9]. Furthermore, distinguishing GBC-related CEF from GBC alone can be difficult due to their overlapping symptoms[1]. Failing to diagnose CEF before surgery can complicate surgery, potentially necessitating a more complex procedure and leading to additional complications. Various diagnostic imaging techniques, including abdominal ultrasound, barium studies, EGD, colo-



Table 1 Summary data of gallbladder cancer related cholecystoenteric fistula							
Ref.	Sex/age(yr)	Clinical symptoms	Image modalities and findings	Type of GBC	Type of CEF	Management	
[4]	M/68	Abdomen pain, anorexia, weight loss	CT, colonoscopy: GBC, HF colon fistula	Adenocarcinoma	CCF	Diverting loop ileostomy	
[15]	F/64	Right abdomen pain, weight loss, fever, jaundice	CT: GBC, HF colon fistula	Carcinoma	CCF	Palliative treatment	
[<mark>16</mark>]	F/78	Nausea, vomiting	EGD, CT: GBC, duodenal fistula	Adenocarcinoma	CDF	Cholecystectomy, left hepatic lobectomy, antrectomy, resection of first portion of duodenum, reconstruction with a Roux-en-Y gastrojejunostomy	
[17]	F/81	Right upper abdomen pain, anorexia, fever	EGD, CT, MRI, gastrografin: GBC, duodenal fistula, HF colon fistula	SqCC	CDF, CCF	EGD and colonoscopy with endoscopic fistula closure	
[18]	F/59	Nausea, vomiting	CT, ERCP: GBC, duodenal fistula	Adenocarcinoma	CDF	Endobiliary RFA with stents placement	
[19]	F/80	Right upper abdomen pain	CT: Transverse colon fistula	SqCC	CCF	Cholecystectomy, partial colectomy	
[20]	M/68	Right upper abdomen pain, weight loss	CT: Duodenal fistula	SqCC	CDF	Palliative chemotherapy, targeted therapy, and radiotherapy	
[<mark>21</mark>]	M/68	None	PET CT, MRI, EGD: porcelain gallbladder, suspected GBC, duodenal fistula	Adenocarcinoma	CDF	Subtotal stomach-preserving pancreatoduodenectomy, radical cholecystectomy	
[22]	M/59	Abdomen pain, vomiting	CT: HF colon fistula, a gallstone in the left colon	Carcinoma	CCF	Colostomy	
[23]	M/74	Right upper abdomen pain, weight loss	CT: Duodenal fistula	Adenocarcinoma	CDF	Unknown	
[24]	F/67	Upper abdomen pain, nausea, diarrhea, weight loss	CT: GBC	SGCC	CCF	Cholecystectomy, bisegmentectomy IVb-V, right hemicolectomy	
[25]	M/87	Abdomen pain	CT: Transverse colon fistula	Carcinosarcoma	CCF	Cholecystectomy with partial transverse colectomy	
[<mark>6</mark>]	F/62	None	CT: Gallstone, suspected HF colon cancer	Adenocarcinoma	CCF	Cholecystectomy, right hemicolectomy	
[<mark>26</mark>]	F/81	Upper abdomen pain, fever	PTC: GBC, transverse colon fistula	Papillomatosis	CCF	Cholecystectomy, fistula closure, choledocholithotomy with T-tube drainage	
[<mark>27</mark>]	M/66	Right upper abdomen pain, nausea, vomiting	CT, EGD: Duodenal fistula	SqCC	CDF	Palliative treatment	
[28]	F/48	Right upper abdomen pain, jaundice, melena	US, CT: GBC, HF colon fistula	Adenocarcinoma	CCF	Chemotherapy, radiotherapy	
[29]	F/81	Upper abdomen pain,	CT: Duodenal fistula	Adenocarcinoma	CDF	Cholecystectomy, fistula closure, gastrojejunostomy, choledochojejunostomy	

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		vomiting				
[<mark>30</mark>]	F/75	Abdomen pain, vomiting, diarrhea	CT: Air-filled thickened-walled gallbladder	Adenocarcinoma	Unknow	Laparotomy with stone extraction, palliative treatment
[31]	F/80	Anorexia	EGD: Duodenal fistula	Adenocarcinoma	CDF	Cholecystectomy, fistula closure, choledocholithotomy with T-tube drainage
[32]	F/46	Right upper abdomen pain, weight loss	US, CT: GBC, gallstone	Adenocarcinoma	CCF	Cholecystectomy with partial hepatic segments resection (IV and V), fistulectomy, right hemicolectomy
[<mark>33</mark>]	F/76	Right upper abdomen pain, vomiting	CT: Air-filled thickened-walled gallbladder, duodenal fistula	Carcinoma	CDF	Enterotomy with stone extraction
[34]	M/84	Coffee ground emesis	EGD, CT: Gallstone, duodenal fistula	Adenocarcinoma	CDF	Cholecystectomy, duodenum repair
[35]	F/60	Right upper abdomen pain, fever, nausea, vomiting	US, PTC, MRI: GBC, gallstone, HF colon fistula	Adenocarcinoma	CCF	Laparotomy, right hemicolectomy, primary anastomosis
[<mark>36</mark>]	F/67	Right upper abdomen pain, anorexia	CT, gastrografin: Gastric fistula	Adenocarcinoma	CGF	Cholecystectomy, liver wedge resection, and gastric antrectomy including the fistula, gastroduodenal anastomosis
[37]	F/70	Abdomen pain, nausea, vomiting, weight loss	US, gastrografin: HF colon fistula	SqCC	CCF	Extended right hemicolectomy, subtotal excision of the gallbladder
[38]	F/72	Upper abdomen pain, nausea, vomiting	Gastrografin, EGD: Gallstone in duodenum	Metastatic breast carcinoma	CDF	Laparotomy with stone extraction
[3 9]	F/75	Abdomen pain, nausea, diarrhea, weight loss	US, gastrografin, EGD: Gallstone, gastric outlet obstruction	Adenocarcinoma	CDF	Enterostomy with stone extraction, cholecystectomy with fistula excision
[40]	M/55	Right upper abdomen pain, diarrhea, weight loss	Gastrografin, colonoscopy, EGD: duodenal fistula, transverse colon fistula	Adenocarcinoma	CDF, CCF	Radical cholecystectomy, partial gastrectomy, vagotomy, duodenectomy, proximal pancreatectomy, right hemicolectomy, resection of the proximal jejunum, anticolic antiperistaltic gastrojejunostomy (Polya), end-to-side choledochojejunostomy, ileotransverse colostomy
[41]	F/51	Right upper abdomen pain, fever, vomiting	Gastrografin: Leakage from the duodenum	Adenocarcinoma	CDF, CCF	Diagnostic laparotomy, palliative treatment
[41]	M/63	Right upper abdomen pain, melena	None	Adenocarcinoma	CCF	Palliative treatment
Our case	M/57	Abdomen pain, vomiting, diarrhea	CT, EGD, colonoscopy, gastrografin, MRCP: GBC, gallstone, duodenal fistula, transverse colon fistula	Adenocarcinoma	CDF, CCF	Roux-en-Y gastrojejunostomy, loop ileostomy

M: Male; F: Female; GBC: Gallbladder cancer; CEF: Cholecystoenteric fistula; CT: Computed tomography; HF: Hepatic flexure; CCF: Cholecystocolonic fistula; EGD: Esophagogastroduodenoscopy; CDF: Cholecystoduodenal fistula; MRI: Magnetic resonance imaging; SqCC: Squamous cell carcinoma; ERCP: Endoscopic retrograde cholangiopancreatography; RFA: Radiofrequency ablation; PET: Positron emission tomography; SGCC: Spindle and giant cell type undifferentiated carcinoma; PTC: Percutaneous transhepatic cholangiography; US: Ultrasonography; CGF: Cholecystogastric fistula; MRCP: Magnetic resonance cholangiopancreatography. Wang CY et al. Gallbladder cancer persistent vomiting and diarrhea



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Figure 1 Abdominopelvic computed tomography. Coronal contrast-enhanced abdominal computed tomography reveals a contracted gallbladder (white arrowhead) in close contact with the second portion of the duodenum (orange arrowhead), with a compromised fat plane between these two structures (white dotted line). A soft-tissue density (white arrow) connects the contracted gallbladder and transverse colon (asterisk).



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Figure 2 Barium upper gastrointestinal series. The examination reveals a contrast-filling sac-like structure in the right lower guadrant of the abdomen (orange arrowhead) connected to the second portion of the duodenum (white arrowhead).

noscopy, abdominopelvic CT, MRCP, and endoscopic retrograde cholangiopancreatography, have been used to diagnose CEF[2,4,9]. In most cases, the fistulous tract lesion was detectable in imaging studies (75%; Table 1). In our case, abdominopelvic CT suggested the presence of CCF; however, a colonoscopy could not confirm it. CDF was suspected via EGD and confirmed by the UGI series and MRCP. The diagnosis of synchronous CDF and CCF was ultimately esta-blished during laparotomy. Advances in imaging technology have improved our ability to detect CEF, and combining various imaging techniques can improve the likelihood of an accurate preoperative diagnosis.

Conventional surgery for CEF involves cholecystectomy and fistula closure, performed as an open or laparoscopic procedure based on the surgeon's experience and the patient's condition[2,5,9,11,13]. However, few cases are suitable for resection, and palliative chemotherapy with gemcitabine and cisplatin is the current standard of care for patients with advanced-stage GBC[1,14]. Therefore, surgical closure of fistulas, stent placement therapy, and bypass surgery may be



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considered. Our patient underwent an exploratory laparotomy for palliative purposes. Further palliative treatment, such as chemotherapy, radiation therapy, or targeted therapy, is indicated. Due to the failure of previous standard chemotherapy and malnutrition, our patient received lenvatinib as an oral targeted therapy.

CONCLUSION

Clinicians should consider CEF in patients with GBC who present with persistent vomiting or diarrhea. Use of multiple imaging modalities can increase the likelihood of detecting CEF before surgery. Despite its grim prognosis and 5-year survival rate of < 5%, surgery remains a viable option for alleviating GBC symptoms and enhancing quality of life.

FOOTNOTES

Author contributions: Wang CY contributed to manuscript writing, editing, and data collection; Chiu SH and Chang WC prepared the figures; Ho MH completed the surgery; Chang PY were responsible for manuscript modification; all authors have read and approved the final manuscript.

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