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WORD COUNT 1610
TIME SUBMITTED 15-NOV-2023 05:32PM
PAPER ID 104266537

Name of Journal: *World Journal of Clinical Cases*

Manuscript NO: 87833

Manuscript Type: CASE REPORT

Persistent vomiting and diarrhea in a patient with advanced gallbladder cancer: A case report and review of literature

Wang CY *et al*. Gallbladder cancer persistent vomiting and diarrhea

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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, colonoscopy, and magnetic resonance cholangiopancreatography; the results of these tests confirmed a diagnosis of synchronous CDF and CCF. The patient underwent a Roux-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

Wang CY, Chiu SH, Chang WC, Ho MH, Chang PY. Persistent vomiting and diarrhea in a patient with advanced gallbladder cancer: A case report and review of literature. *World J Clin Cases* 2023; In press

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.

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.

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 ℃, 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 x 10^3/uL (normal range: 150-400 × 10^3), 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 GBC-related 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, colonoscopy, 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 established 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 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.

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