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Jin-Lei Wang  
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Dear Editor:

My coauthors and I wish to thank you for allowing us to revise our case report. We also wish to thank the reviewers for their positive and constructive suggestions regarding the manuscript. We have amended the manuscript in accordance with the reviewer's comments, and have responded to those comments in a point-by-point manner in this letter. We hope that our revisions and explanations are suitable for publication of this paper in your journal.

All words or paragraphs that were revised or had any change were marked blue in this version of manuscript, and we believe this would be more convenient for you to review our paper again.

We have stated in the first page of the manuscript that this report was not supported by any grant or agency, so we did not upload an Approved Grant Application Form or Funding Agency Copy of any Approval Document.

Thank you for your time in reviewing our re-submission. I look forward to hearing from you.

Yours sincerely,

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## **Reviewer's comments:**

### **Reviewer #1(code 03727100):**

**Comment 1)** This is a good report about endoscopic treatment for a bile duct polyp. Could you let me know whether a bile duct polyp can be resected without a duodenal fistula?

#### **Answer:**

Bile duct polyps can be resected by open abdominal surgery or snare polypectomy using choledochoscopy via the T-tube sinus tract without a duodenal fistula. However, these methods both require opening the abdomen and cutting into the bile duct to place the "T" tube. Regarding snare polypectomy, this method can only be used for pedunculated polyps, not for flat polyps. Because of these limitations, we developed a new and minimally invasive method of endoscopic mucosal resection (EMR) through the fistula for the resection of both flat and pedunculated bile duct polyps. Also, EMR is safe and effective, causes minimal pain, enables rapid rehabilitation, and has low cost. For additional details, please refer to the last two paragraphs in the Discussion section of the manuscript.

### **Reviewer #2(code 01213502):**

**Question 1)** How to explain the formation of choledochoduodenal fistula? Was there pancreaticobiliary maljunction?

#### **Answer:**

There are various causes of choledochoduodenal fistula (CDF); the most common causes are cholelithiasis, duodenal ulcer, and tumors <sup>[1,2]</sup>. In this case, the patient had a 28-year history of cholangiolithiasis, but showed no sign of duodenal ulcer or gastrointestinal tumors. Based on the patient's history of illness and the mechanisms underlying formation of CDF, we think that the fistula in this patient was mainly due to long-term compression of stones on the bile duct wall and duodenal wall <sup>[1,2]</sup>. Such compression caused necrosis and perforation of both bile duct wall and duodenal wall, finally leading to CDF. The relevant content had been added into the manuscript as the first paragraph of the Discussion part.

Regarding the pancreaticobiliary maljunction, we attempted to observe the lower

portion of the pancreatic duct and bile duct by MRI and endoscopic cholangiography through the fistula. However, pneumatosis of bile duct can be observed in almost half of the patients who suffered with CDF [2-4]. And in this case, pneumatosis severely interfered with the observation of the lower part of the pancreatic duct and bile duct as we mentioned in the gastroscopy examination section in the manuscript. But no pancreaticobiliary maljunction was found as far as we can see on images of MRI or cholangiography.

This paragraph was added into the manuscript as the first paragraph of the Discussion part.

“Among many causes of CDF, the most common causes are cholelithiasis, duodenal ulcer, and tumors [12,13]. In this case, the patient had a 28-year history of cholangiolithiasis, but showed no duodenal ulcer or gastrointestinal tumors. Therefore, the CDF in this patient was likely caused by the compression of stones on the bile duct wall and duodenal wall. This long-term compression could lead to necrosis and perforation of both bile duct wall and duodenal wall, resulting in CDF [12,13]. Epigastric pain, fever, and jaundice are common symptoms of CDF, depending on its location, whereas vomiting and diarrhea are relatively rare symptoms [12,13]. Pneumatosis of the bile duct on plain abdominal films and regurgitation of contrast on the upper gastrointestinal series can be observed in some patients [13-15]. In addition, fistulas can be found by CT and MRI in some cases. The fistulous orifice can be observed directly by gastroscopy and the CDF can be further confirmed by cholangiography. Notably, CDF patients with no symptoms or mild symptoms do not require treatment, whereas surgery is needed for those who experience repeated pain, fever, and jaundice [12,16].”

**Question 2)** The flat polyp seemed too small to the caliber of CBD, that seemed not the reason to cause choledocholithiasis and choledochoduodenal fistula.

**Answer:**

There are many causes of choledocholithiasis; the most common causes are biliary infection, foreign body in the biliary tract, and biliary obstruction. In the subsection describing the patient's history of illness, we mentioned that this patient was diagnosed with choledocholithiasis in 1991 and 2017, and that she had cholangiolithotomy twice (1991 and 2017). However, even in the operation record of cholangiolithotomy in 2017, no bile duct polyps were found during the intraoperative exploration of bile ducts; this observation suggested that the flat bile duct polyp was newly formed. So we do not think and did not conclude that the newly formed bile duct polyp could be the cause of choledocholithiasis that had been present in the patient over a period of 26 years. However, if this flat polyp had continued growing without our resection, it may have blocked the bile duct and promoted the formation of increasingly severe choledocholithiasis in the future.

Furthermore, we presume that the bile duct polyp might be caused by long-term stimulation of cholangiolithiasis [5].

Regarding the cause of choledochoduodenal fistula formation, please check our response to question 1 from Reviewer 2 again. And we concluded that the main cause of choledochoduodenal fistula in this patient was the compression of stone.

**Question 3)** How long was the length of biliary-pancreatic common channel?

**Answer:**

As we mentioned in the response to question 1 from Reviewer 2, pneumatosis greatly interfered with the observation of pancreatic duct and bile duct even when we tried the MRI examination and endoscopic cholangiography through the fistula. We checked the radiography images, but could not measure the exact length of the biliary-pancreatic common channel. We wish to note that endoscopic cholangiography through the fistula, magnetic resonance cholangiopancreatography (MRCP), and endoscopic retrograde cholangiopancreatography (ERCP) can all be used to measure the length of the biliary-pancreatic common channel, or to determine whether a pancreaticobiliary maljunction is presented, but only under the condition that the patient exhibits no pneumatosis in the pancreatic duct and bile duct.

**Question 4)** CT and MRI revealed a communication between the common bile duct and the duodenal bulb, and a high-density shadow inside the communication. Suggest the authors present the pictures in the text.

**Answer:**

We thank the reviewer for this suggestion. We have added the axial T2 weighted image (T2WI) as Figure 1A and the axial T1 weighted image contrast enhanced (T1WI +C) as Figure 1B in the revised manuscript. These two MRI images clearly demonstrate the communication which represents the fistula, and the shadow which represents the stone. We have also rewritten the imaging examination portion of the manuscript with the aid of the Department of Radiology to provide a more precise description of the images. Regarding the CT examination, we reviewed the CT examination report in the discharge note from another hospital where the patient had been hospitalized (discharged 4 days before she presented to our hospital); therefore, we included that CT report in the manuscript. We recently contacted the patient, but she had lost the CT film. Unfortunately, we cannot include the CT images in the figures, but the MRI images are high-quality and we presume that they provide sufficient support for the diagnosis in this case.

Changes in the case summary section in the abstract.

“Computed tomography (CT) and magnetic resonance imaging reported a

communication between the bile duct and duodenal bulb. Inside the communication, CT showed a high-density shadow which was a hypointense lesion in T2 weighted image. The lesion showed no enhancement in T1 weighted image contrast enhanced."

Changes in the imaging examination section in the manuscript.

"A CT report from the other hospital that the patient previously visited described a communication between the bile duct and the duodenal bulb, as well as a high-density shadow inside the communication. On MRI, axial T2 weighted image (Figure 1A) showed dilatation of the bile duct, as well as a fistula connecting the bile duct and duodenal bulb. Inside the fistula, there was a hypointense lesion. Axial T1 weighted image contrast enhanced (Figure 1B) showed no enhancement of the lesion."

**Question 5)** The explanation of words in legend should show in the picture with arrow(s).

**Answer:**

Revisions have been made in the figures, in accordance with the reviewer's comment. Additionally, we have added arrows in the figures and rewritten the figure legends.

Changes in the figure legends section.

"Figure 1. Magnetic Resonance Imaging. A: Axial T2 weighted image showing a fistula connecting the bile duct (Green arrow) and the duodenal bulb (Red arrow) which had a gas-liquid plane inside. Inside the fistula, there was a hypointense lesion (Yellow arrow). B: Axial T1 weighted image contrast enhanced showing no enhancement of the bile duct (Green arrow), duodenal bulb (Red arrow), or lesion (Yellow arrow).

Figure 2. Gastroscopy images. A: The incarcerated stone (Green arrow). B: The fistula (Yellow arrow) was observed in the duodenal bulb after the stone was removed.

Figure 3. Gastroscopy images of the bile duct. A: The image of hilar bile duct showing the left hepatic duct (Red arrow), right anterior hepatic duct (Yellow Arrow), and right posterior hepatic duct (Green arrow). B: The terminal part (Green arrow) of the common bile duct.

Figure 4. Gastroscopy images of the protruding lesion in the common bile duct. A: The lesion under white light (Green arrow). B: The lesion under narrow band imaging (Yellow arrow).

Figure 5. Endoscopic mucosal resection of the lesion in the common bile duct. A: The submucosal injection. B: The snare polypectomy of the polyp. C: Image collected after snare polypectomy.

Figure 6. Histopathology. Histological section showing an inflammatory fibroid polyp (hematoxylin and eosin staining; magnification, 200×).”

#### REFERENCES

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3. **Dadzan E, Akhondi H.** Choledochoduodenal fistula presenting with pneumobilia in a patient with gallbladder cancer: a case report. *J Med Case Rep* 2012; 6: 61. [PMID: 22333461 DOI: 10.1186/1752-1947-6-61]
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