



Duodenal Stenosis Due to Carcinoma of the Lower Bile Duct: A Case Report

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ABSTRACT: An 83-year-old man was referred to our hospital for a detailed evaluation for vomiting. Esophagogastroduodenoscopy and abdominal computed tomography showed duodenal stenosis with wall thickness. Biopsy including endoscopic ultrasound-guided fine-needle aspiration of the thickened wall showed inflammation without malignancy. During the clinical course, wall thickening of the distal bile duct appeared. Biopsy under endoscopic retrograde cholangiography showed papillary adenocarcinoma. Surgery revealed that the tumor had widely invaded the duodenal wall from the outside; therefore, only gastrojejunostomy was performed. It was hypothesized that the cholangiocarcinoma had progressed to the serosal side, disseminated in the peritoneum, infiltrated the duodenal serosa, and caused duodenal stenosis.

KEYWORDS: Cholangiocarcinoma, duodenal stenosis, peritonitis carcinomatosa

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Introduction

Cholangiocarcinomas tend to cause bile duct stenosis, and jaundice is often the initial symptom. As the cancer progresses, it infiltrates the surrounding organs and may cause various types of organ damage. In this communication, we herein report a case of distal cholangiocarcinoma in which the first symptom consisted of vomiting due to duodenal stenosis. Although pancreatic malignant tumors tend to cause duodenal stenosis, malignant tumors originating in the bile duct and manifesting first with symptoms of duodenal stenosis are rare and have virtually not been reported thus far.

Case Report

An 83-year-old man with a history of cerebral infarction consulted his previous doctor for vomiting. Esophagogastroduodenoscopy (EGD) revealed a circumferential edematous stenosis of the descending portion of the duodenum and duodenal papilla, extending toward the anal side. Abdominal computed tomography revealed a circumferential stenosis of the duodenum. A biopsy of the stenosed part of the duodenum was performed, and the findings showed no malignancy. Magnetic resonance cholangiopancreatography (MRCP) revealed no bile duct stenosis. In addition, there was no accumulation in the duodenum, bile duct, and pancreas on positron emission tomography with 2-deoxy-2-[fluorine-18] fluoro-D-glucose integrated with computed tomography (18F-FDG PET/CT). The patient was hospitalized and treated for 1 month, but the symptoms showed no improvement. Oral ingestion was impossible, and he

was transferred to our hospital for further examination and treatment.

Blood tests revealed slightly increased blood levels of biliary and liver function enzymes, and levels of the tumor markers CEA and CA-19-9 were within normal limits (Table 1). Abdominal contrast-enhanced CT revealed a circumferential stenosis of the duodenum and an extremely mild thickening of the lower bile duct wall (Figure 1A and B). EGD showed that the papilla of Vater was mildly enlarged and that the anal side of the papilla of Vater in the descending portion of the duodenum showed a circumferential edematous stenosis (Figure 2A and B). The mucosa at the site of the stenosis was relatively soft, with no erosion or ulceration. The EGD scope (GIF-HQ290, Olympus Co, 10.2 mm in diameter of the distal end) could pass through the stenotic site, but the contrast agent did not flow toward the anal side; therefore, he was diagnosed with type III duodenal stenosis (Figure 2C). At the same time, a biopsy of the papilla of Vater and the stenosed part of the duodenum was performed. The findings showed only an active inflammation infiltrated by neutrophils and eosinophils, and no granulomatous lesion, amyloid deposition, or neoplastic lesion was observed. Endoscopic ultrasonography (EUS) revealed a thickening of the duodenal mucosal layer (Figure 2D), and no stenosis/wall thickness of the common bile duct (Figure 2E). EUS-guided fine-needle aspiration (EUS-FNA) of the papilla of Vater and enlarged lymph nodes were performed (Figure 2F), but the findings showed no malignancy. Subsequently, biopsy of the mucosa of the stenosed part of the duodenum was performed twice, but the findings showed only



Table 1. The patient's laboratory data.

	ON ADMISSION	ONE MONTH AFTER DISCHARGE
Biochemistry		
AST (U/L)	45	22
ALT (U/L)	53	22
LDH (U/L)	171	145
ALP (U/L)	343	283
γ-GTP (U/L)	122	101
T-Bil (mg/dL)	0.6	0.9
D-Bil (mg/dL)	0.2	0.3
AMY (U/L)	35	46
LIP (U/L)	28	23
TP (g/dL)	6.2	6.1
ALB (g/dL)	3.0	3.4
BUN (mg/dL)	13.4	13.7
Cre (mg/dL)	0.70	0.92
Na (mmol/L)	135	143
Cl (mmol/L)	100	104
K (mmol/L)	4.5	4.8
eGFR (mL/min/1.73 m ²)	80.6	59.8
CRP (mg/dL)	1.21	0.15
Hematology		
WBC (/μL)	4770	6560
RBC (×10 ⁴ /μL)	425	338
Hb (g/dL)	14.9	11.4
Plt (×10 ⁴ /μL)	19.9	21.3
Tumor marker		
CEA (ng/mL)	2.3	2.7
CA19-9 (U/mL)	13.2	14.0

Abbreviations: ALB, albumin; ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST: aspartate aminotransferase; BUN, blood urea nitrogen; Cl, chloride; Cre, creatinine; D-bil, direct bilirubin; eGFR, estimated glomerular filtration rate; Hb: hemoglobin; HBs Ag, hepatitis B core antigen; HCV Ab, hepatitis C virus core antigen; K, potassium; Na, sodium; Plt, platelets, PT; prothrombin time; RBC, red blood cells; T-bil, total bilirubin; TP, total protein; WBC, white blood cells; γ-GTP: gamma-glutamyl transpeptidase.

a mild inflammation. The cause of the stenosis could not be identified, but because oral feeding was possible, the patient was followed up in an outpatient setting.

Abdominal CT was performed 1 month after discharge from our department, and no significant lesion was found in the

stenosed part of the duodenum. However, the findings showed an exacerbation of the thickening of the distal bile duct wall (Figure 3A). The blood levels of the hepatobiliary enzymes and tumor markers were within normal limits (Table 1). EUS revealed a smooth wall thickening of the lower bile duct (Figure 3B); however, it was difficult to detect the lower bile duct which was located near by the ampulla due to stenosis of duodenal second portion. The endoscopic retrograde cholangiopancreatography (ERCP) image showed a smooth stenosis in the lower bile duct (Figure 3C). In addition, there were no abnormal findings (mass, dilated pancreatic duct) of the pancreas on EUS/MRCP (Figure 3D and E). A biopsy of the stenosed bile duct under ERCP revealed a well-differentiated adenocarcinoma (Figure 4A and B). He was diagnosed with T2 N0 M0 stage II distal cholangiocarcinoma and was indicated for surgery. At the same time, he was also diagnosed with early-stage esophageal cancer, and an initial endoscopic submucosal dissection of the lesion was performed. Four months later, pancreaticoduodenectomy was carried out based on the diagnosis of distal cholangiocarcinoma. After laparotomy, palpation revealed an extrahepatic bile duct tumor extending from the distal bile duct to the cystic duct. The tumor had invaded the transverse colon from the descending portion of the duodenum and had caused a stenosis of the duodenum. A peritoneal nodule was subjected to an intraoperative rapid pathological diagnosis, and the findings revealed a poorly differentiated adenocarcinoma partially mixed with a signet-ring cell, carcinoma-like component (Figure 4C and D). Immunohistochemistry showed positive cytokeratin 7 (CK7), and negative cytokeratin 20 (CK20) (Figure 4E to H). It is difficult to discriminate between biliary and pancreatic cancer from histological examination. From clinical imaging examination, he was diagnosed with T3 NX M stage IV extrahepatic bile duct cancer infiltrating a broad area ranging from the duodenum to the colon. Therefore, surgery was terminated after gastrojejunostomy was completed. The postoperative course was uneventful, but the patient was transferred to another hospital for continuation of medical treatment.

Discussion

We report a case of circumscribed duodenal stenosis due to infiltration of a distal cholangiocarcinoma. Duodenal stenosis developed before the thickening of the distal bile duct wall, and the symptoms of stenosis appeared as initial symptoms, making diagnosis difficult.

Benign diseases that cause duodenal stenosis include inflammatory bowel diseases such as Crohn disease,¹ duodenal ulcers, chronic/recurrent pancreatitis,² among others. Malignancies that cause duodenal stenosis include duodenal tumors and direct tumor invasions to the surrounding organs. In our case, the differential diagnosis of localized stenosis of the gastrointestinal tract included inflammatory bowel disease, vasculitis, ischemic changes, and eosinophilic gastroenteritis. However, in this case, the cause of the duodenal stenosis could not be

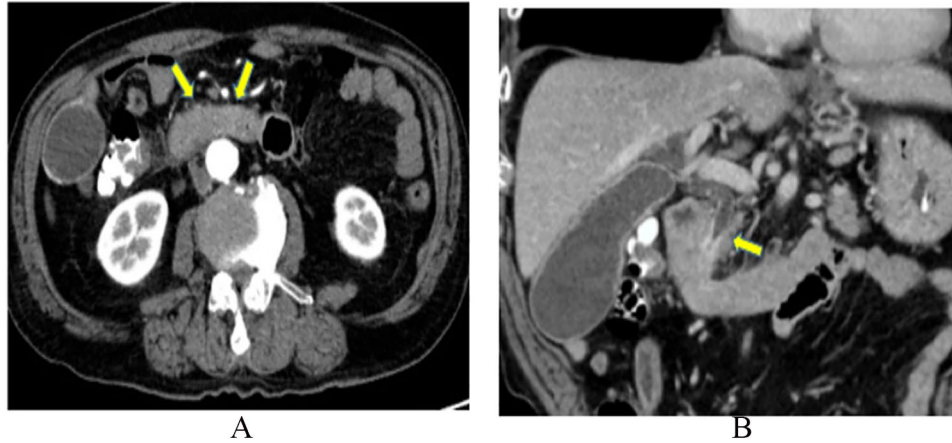


Figure 1. (A). Abdominal contrast-enhanced CT revealed a circumferential stenosis of the duodenum (arrows). (B). An extremely mild thickening of the lower bile duct wall (arrow).

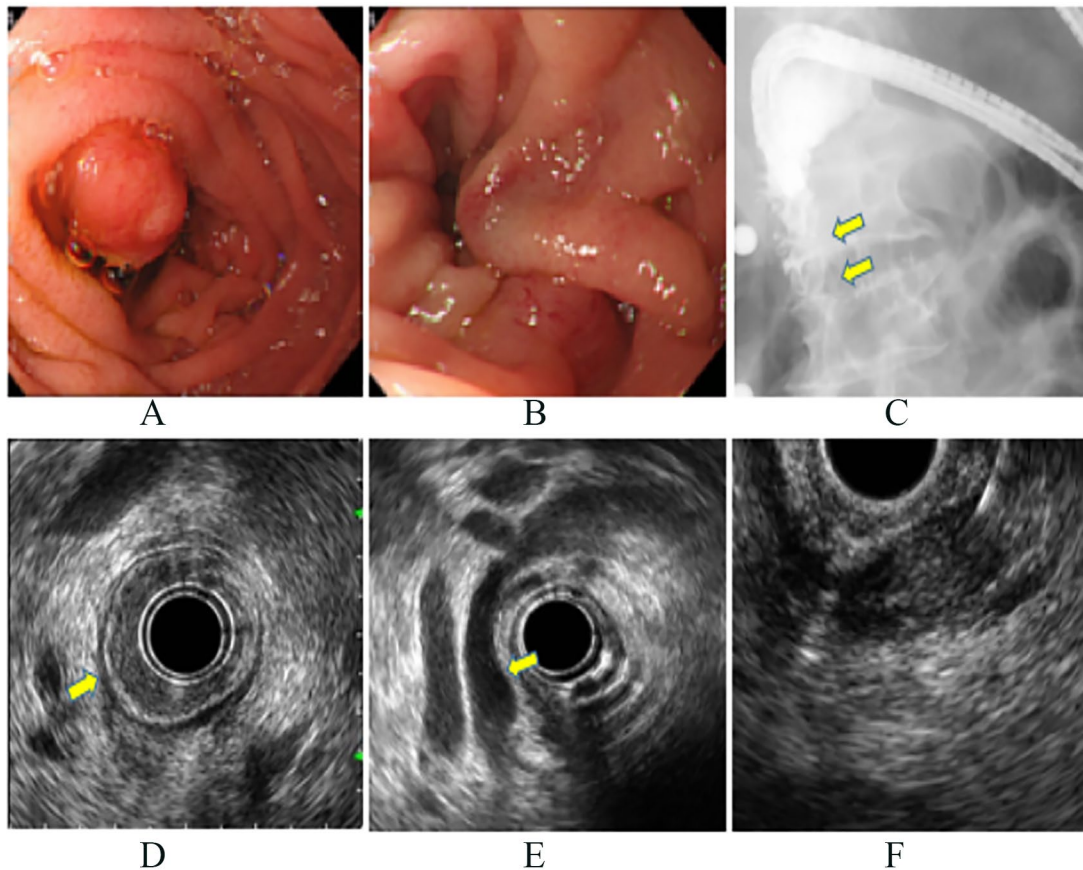


Figure 2. (A & B). EGD showed that the papilla of Vater was mildly enlarged and that the anal side of the papilla of Vater in the descending portion of the duodenum showed a circumferential edematous stenosis. (C). Contrast agent did not flow toward the anal side; therefore, he was diagnosed with type III duodenal stenosis (arrows). (D). EUS revealed a thickening of the duodenal mucosal layer (arrow). (E). EUS showed no stenosis/wall thickness of the common bile duct (arrow). (F). EUS-FNA of the enlarged papilla of Vater was performed. EGD indicates esophagogastroduodenoscopy; EUS, endoscopic ultrasonography; EUS-FNA, EUS-guided fine-needle aspiration.

identified on the basis of the various imaging tests, blood tests, or pathological tests that were conducted on biopsy and EUS-FNA specimens. Three months after the emergence of vomiting as a symptom due to duodenal stenosis, abdominal computed tomography findings revealed an exacerbation of the distal bile duct wall thickening. Findings from a bile duct biopsy under

ERCP led to the diagnosis of a well-differentiated adenocarcinoma, and pancreaticoduodenectomy was planned based on the diagnosis of distal cholangiocarcinoma (T2 N0 M0 c stage II). A peritoneal nodule that was a poorly differentiated adenocarcinoma partially mixed with a signet-ring cell, and carcinoma-like component was subsequently discovered. It was estimated

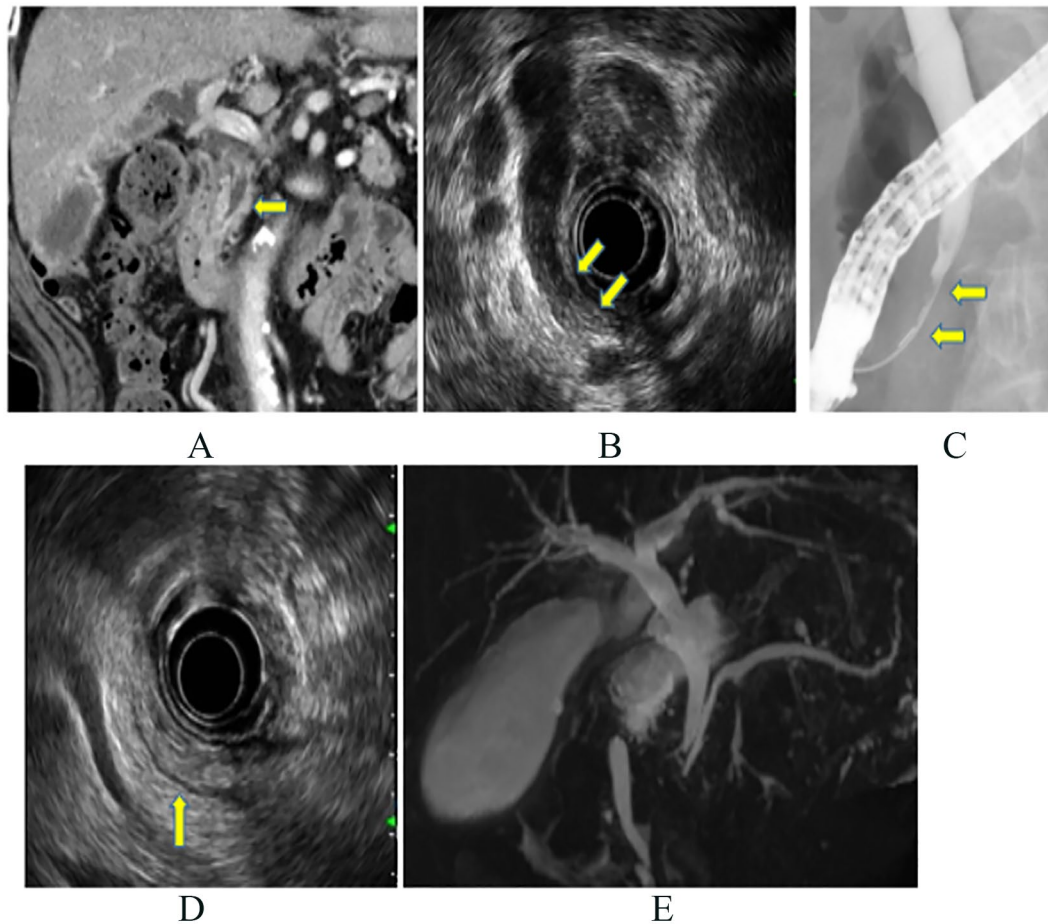


Figure 3. (A). Abdominal CT was performed 1 month after discharge from our department, the findings showed an exacerbation of the thickening of the distal bile duct wall (arrow). (B). EUS revealed a smooth wall thickening from the papilla of Vater to the lower bile duct (arrow). (C). ERCP image showed a smooth stenosis in the lower bile duct (arrows). (D). There was no dilation of the main pancreatic duct, 1.6mm in diameter, on EUS (arrow). (E). There was no dilation of the main pancreatic duct on MRCP. EUS indicates endoscopic ultrasonography; ERCP, endoscopic retrograde cholangiopancreatography; MRCP, magnetic resonance cholangiopancreatography.

that there had been a period of 4 months from diagnosis of a well-differentiated adenocarcinoma to surgery, and that it had changed to a poor differentiation type during this course or the tumors had a mix of well-differentiated and poorly differentiated distal cholangiocarcinoma at the time of diagnosis.

Generally, cholangiocarcinomas have a tendency to invade the digestive lumen, and jaundice due to bile duct stenosis is often the initial symptom.³ In our case, vomiting was the initial symptom and was due to duodenal stenosis. Lee et al⁴ and Kwon et al⁵ reported a case of enlargement of the papilla of Vater due to invasion by a signet-ring cell carcinoma originating from the distal bile duct. Welsh et al⁶ reported a case of stenosis of the horizontal part of the duodenum due to invasion by a bile duct signet-ring cell carcinoma. In our case, the duodenal stenosis should have developed early from an invasion by a cholangiocarcinoma. However, because the bile duct findings themselves (bile duct stenosis and bile duct wall thickening) were poorer than those of duodenal stenosis, the possibility of duodenal stenosis due to cholangiocarcinoma was not considered likely. Tumor cells were not identified

from the biopsy and EUS-FNA of the stenosed part of the duodenum and duodenal papilla. We hypothesize that the cholangiocarcinoma had infiltrated the serosa, which led to the development of the disseminated peritoneal metastasis. The infiltration by the disseminated metastases could have started from the surface of the duodenal serosa, and tumor cells could have then invaded the duodenal mucosa diffusely, leading to development of fibrosis of the duodenal mucosa due to cancer-associated fibroblasts (CAF).⁷ Duodenal stenosis may have resulted from the fibrosis, and the biopsy and EUS-FNA might have not detected the tumor cells that had disseminated across the lesion. On the contrary, it is considered that the cause of duodenal stenosis might have been related not only to fibrosis but also to inflammation in this case, and it is presumed that the duodenal stenosis improved slightly with time as the inflammation gradually improved although the fibrosis progressed.

The limitation in our case was that we could not completely rule out the possibility that pancreatic cancer may have been the primary cancer. We had conducted a biopsy of the distal bile duct

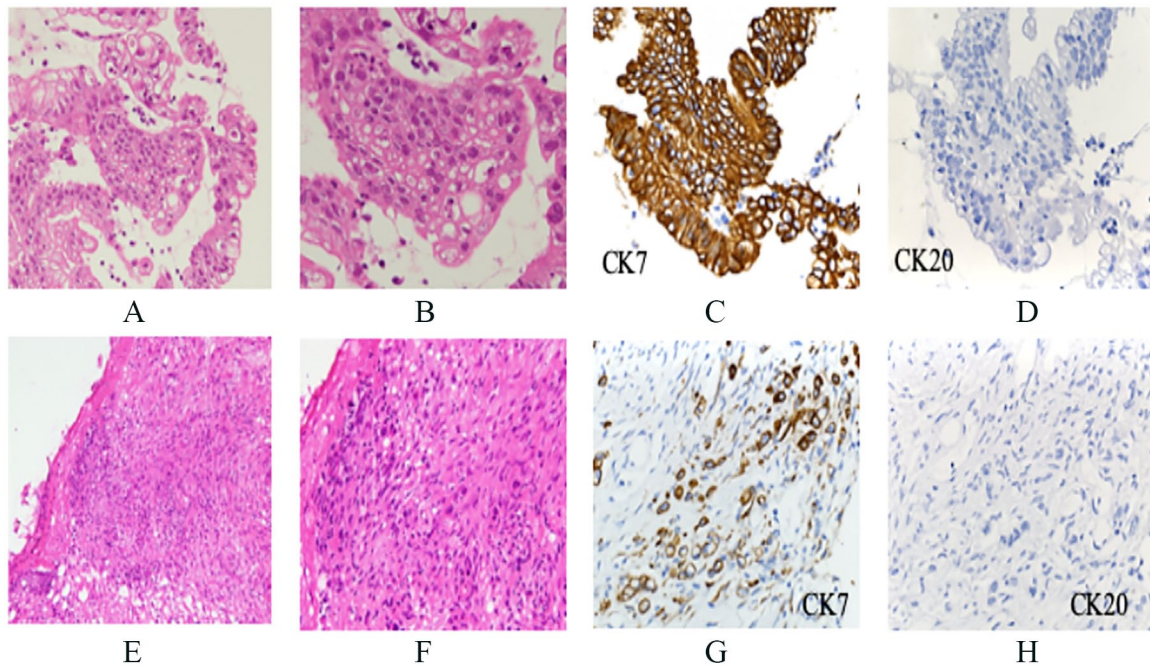


Figure 4. (A & B). A biopsy of the stenosed bile duct under ERCP revealed a well-differentiated adenocarcinoma (HE, 100 \times , 200 \times). (C & D). Immunostaining of CK7 and CK20 for the stenosed bile duct. Positive for CK7 and negative for CK20 were identified (100 \times). (E & F). A peritoneal nodule was subjected to an intraoperative rapid pathological diagnosis, and the findings revealed a poorly differentiated adenocarcinoma partially mixed with a signet-ring cell, carcinoma-like component (HE, 100 \times , 200 \times). (G & H). Immunostaining of CK7 and CK20 for a peritoneal nodule. Positive for CK7 and negative for CK20 were identified (\times 100).

under ERCP and found adenocarcinoma cells, consequently leading to a diagnosis of distal cholangiocarcinoma. Distal bile duct stenosis can also develop in the case of a bile duct invasion by a pancreatic cancer. However, because most pancreatic cancers are ischemic tumors, the bile duct wall is not enhanced by contrast-enhanced CT in the case of bile duct wall thickening due to bile duct invasion by a pancreatic cancer. Furthermore, in our case, a well-differentiated adenocarcinoma was found in the bile duct epithelium. However, in cases where bile duct invasion is due to a pancreatic cancer, undifferentiated cancers would usually be detected. Moreover, we considered that the absence of dilation of the main pancreatic duct by EUS/MRCP was an important finding that denies pancreatic cancer. In addition, immunohistochemistry of the specimens of bile duct and peritoneal nodule showed positive CK7 and negative CK20 in any specimen. Duval et al⁸ demonstrated carcinomas of the extrahepatic biliary tract and pancreas are strongly positive for CK7 and negative for CK20, and the CK7/CK20 immunostaining profile will not identify the site of origin for tumors with extensive growth in the porta hepatis region. Although it was difficult to discriminate between biliary and pancreatic cancer by immunohistological examination, considering the above comprehensively, the primary cancer in our case report may have been a distal cholangiocarcinoma. However, detailed testing could not be performed because of the absence of a resected specimen; hence, we could not reach a definite conclusion.

In cholangiocarcinoma, surgery is the only treatment that provides radical cure. In our case, the stage was preoperatively diagnosed as T2, and tumor protrusion into the bile duct lumen was mild. Therefore, treatment of the esophageal cancer was conducted as a priority before surgery was carried out as a treatment for cholangiocarcinoma. However, the duodenal stenosis was also due to the tumor invasion; thus, the condition was inoperable. There was a possibility that tumoral infiltration into the surrounding would have been small if surgery had been performed when the diagnosis of a well-differentiated adenocarcinoma in the lower bile duct was made by biopsy. However, assuming that the duodenal narrowing was due to serosal invasion of cholangiocarcinoma and its accompanying peritoneal disseminated metastasis, infiltration into the surrounding organs would seem to have occurred at the time of duodenal stenosis. Even if the tumor had shown less protrusion into the bile duct lumen, cholangiocarcinoma can be highly infiltrating and the mass may have had an indistinct morphology. Therefore, careful attention is required when assessing the depth of invasion.

Author Contributions

Maki T and Irisawa A: writing and revision of the paper; Notohara K: supervision for the description of pathology; Shibukawa G, Sato A, Yamabe A, Yoshida Y, Yamamoto S: collection and making the data and/or figures; Soeta N, Saito T: supervision for the description of surgery.

Disclosures and Ethics

The authors have read and confirmed their agreement with the ICMJE authorship and conflict of interest criteria. The authors have also confirmed that this article is unique and not under consideration or published in any other publication, and that we have permission from rights holders to reproduce any copyrighted material. Any disclosures are made in this section. The external blind peer reviewers report no conflicts of interest.

Patient Consent Confirmation Statement

The patient consent has been secured to publish the findings of this case study.

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