Choledochoduodenal Fistula after the Placement of a Partially Covered Metal Stent for Unresectable Pancreatic Cancer

Daisuke Masuda, Takeshi Ogura, Akira Imoto, Saori Onda, Tatsushi Sano, Wataru Takagi, Atsushi Okuda, Toshihisa Takeuchi, Shinya Fukunishi, Takuya Inoue and Kazuhide Higuchi

Abstract

A 75-year-old Japanese man with type 2 diabetes mellitus suffered from unresectable pancreatic head cancer and was admitted to our institution due to acute cholangitis. A partially covered metal stent was placed at that time. 11 months later, he was readmitted for acute cholangitis. Upper endoscopy revealed complete stent distal migration and a small hole on the oral side of the ampulla. While attempting cannulation into the hole, an upstream biliary tract was revealed. Accordingly, we diagnosed the patient to have a choledochoduodenal fistula. After metal stent removal and balloon dilation, we placed two 7 Fr plastic stents, which successfully relieved the patient’s cholangitis.

Key words: choledochoduodenal fistula, biliary stricture, metal stent migration, acute cholangitis, unresectable pancreatic cancer


Introduction

Choledochoduodenal fistula (CDF) - a type of internal bilioenteric fistula - is an abnormal connection between the common bile duct and the duodenum (1). The primary causes of CDF are choledocholithiasis and a penetrating peptic ulcer (2, 3). CDF is also a relatively rare, delayed complication of metal stent placement, which has been reported to be caused by bile duct wall injury due to stent migration or the sharp end of the metal stent with a poor prognosis (4-9). We herein present a rare case of CDF after the placement of a partially covered metal stent for distal common bile duct obstruction in a patient with unresectable pancreatic cancer.

Case Report

In September 2008, a 75-year-old Japanese man with type 2 diabetes was referred and admitted to our institution due to a high fever and jaundice. On physical examination his conscious was clear, blood pressure was 98/56 mmHg, pulse was 125 beats/min, and body temperature was 40.2°C. His skin and eyes showed yellow pigmentation. Laboratory tests on admission revealed the following results: leukocyte count, 16,280/μL; C-reactive protein (CRP) level, 3.1 mg/dL; total bilirubin level, 4.0 mg/dL; aspartate aminotransferase (AST) level, 341 IU/L; alanine aminotransferase (ALT) level, 341 IU/L; alkaline phosphatase (ALP) level, 288 IU/L; lactate dehydrogenase (LDH) level, 288 IU/L; and gamma-glutamyl transpeptidase (GGT) level, 711 IU/L. Levels of cancer antigen (CA) 19-9, serum glucose, and hemoglobin A1c (HbA1c) were elevated at 2,484 IU/L, 394 mg/dL, and 9.5%, respectively. Renal dysfunction was not observed.

Ultrasoundography showed intrahepatic bile duct dilation and a hypoechoic lesion on the head of the pancreas. Dynamic computed tomography (CT) and magnetic resonance
imaging (MRI) further revealed a 40 mm, irregular, marginal, poorly enhanced mass on the head of the pancreas, which had invaded into the distal bile duct, superior mesenteric vein, and artery. Magnetic resonance cholangiopancreatography (MRCP) revealed an obstruction of the common bile and main pancreatic ducts. According to the laboratory results and imaging findings, acute cholangitis with sepsis due to a biliary tract obstruction was diagnosed. We performed urgent endoscopic retrograde cholangiopancreatography (ERCP) with successful selective biliary cannulation and endoscopic prosthesis. Blood and bile cultures revealed Gram-negative enteric bacteria. After an improvement of acute cholangitis, we performed ERCP again for biliary brush cytology, which revealed positive results. Therefore, we diagnosed the patient with unresectable pancreatic head cancer and placed a partially covered, self-expandable metal stent (SEMS) (10 mm×60 mm covered WALLSTENT; Boston Scientific Japan, Tokyo, Japan) in the distal bile duct. However, a few days after stent placement, the metal stent had proximally migrated. Thus, we inserted an additional SEMS through the previous SEMS, using the “stent through stent” method, which successfully relieved the patient’s acute cholangitis and jaundice.

Nine months later, cholangitis appeared again during chemotherapy (gemcitabine, 1,000 mg/m²). Conservative treatment was performed for acute cholangitis because enhanced CT revealed pneumobilia in the intrahepatic duct and we believed that the covered SEMS were not obstructed or had migrated (Fig. 1a). Eleven months after the first SEMS insertion, the enhanced CT revealed suspected stent migration to the duodenum and multiple liver metastases with pneumobilia in the intrahepatic duct (Fig. 1b, c). CT and MRCP showed an obstruction of the common bile and main pancreatic ducts, as well as a bar-shaped high intensity signal outside the biliary tract (Fig. 2). According to these findings, stent distal migration was suspected. Upper endoscopy confirmed that the covered WALLSTENT had completely migrated to the duodenum (Fig. 3a) and revealed a small hole on the oral side of the ampulla (Fig. 3b). Duodenal stenosis due to cancer invasion was also noted on the anal side of the small hole and around the ampulla. When we attempted to perform cannulation through the small hole, a proximal biliary tract was revealed (Fig. 4). Therefore, we diagnosed the patient having a CDF, which had a negative biopsy result, and identified that the orifice of the CDF was connected to the proximal edge of the biliary stricture. We removed the covered SEMS using biopsy forceps and a retrieval basket and placed two 7 Fr double-pigtail plastic stents through the CDF after balloon dilation of the CDF (Fig. 5) without any adverse events. The patient’s cholangitis
This force and the sharp end of the stent are thought to in-
a high axial force tends to kink at the proximal edge of the
straightening of a WALLSTENT; therefore, a bile duct with
axial force, which is the recovery force that leads to
"stent through stent" method. The WALLSTENT has a high
stent for 1 case, and the Niti-S uncovered stent for 1 case,
at the descending portion of the duodenum. The inserted
present case are shown in Table. Five CDFs were located at
reference cases). The characteristics of these 6 cases and the
present case are shown in Table. Five CDFs were located in
the bile duct without migration 3 months after the first insertion, however, 9 months later the SEMS migrated to the duodenum, and the size of the primary pancreatic cancer was gradually reduced.

Discussion

Various etiologies of CDF have been reported, such a
penetrating peptic ulcer (1), cholelithiasis (2), hepatobili-
ary (5, 8, 9) and pancreatic cancer (6, 7), and iatrogenic
injury, including that by an endoscopic prosthesis (4-9).
CDF is a relatively rare, delayed complication of metal stent
placement, which is related to bile duct wall injury due to
stent migration or the sharp end of the metal stent (9). CDF
cases associated with SEMS were identified in the PubMed
database using the search terms “choledochoduodenal fis-
tula” and “self-expandable metallic stent,” or “metal stent,”
and 6 additional cases were found (hereafter referred to as
reference cases). The characteristics of these 6 cases and the
present case are shown in Table. Five CDFs were located at
the bulbus with a large ulcer, however, only 2 cases of small
CDF occurred, including the present case, and were located
at the descending portion of the duodenum. The inserted
stents were a WALLSTENT for 2 cases and the WallFlex
stent for 1 case, and the Niti-S uncovered stent for 1 case,
in addition to our present case, which were inserted by the
“stent through stent” method. The WALLSTENT has a high
axial force, which is the recovery force that leads to
straightening of a WALLSTENT; therefore, a bile duct with
a high axial force tends to kink at the proximal edge of the
straightening stent (10, 11), and this stent has a sharp end.
This force and the sharp end of the stent are thought to in-
jure the bile duct at the proximal edge of the stent and form
a CDF. Indeed, in this present case, the CDF connected to
the bile duct around the proximal edge. Moreover, the in-
serted stents in present case completely migrated distally,
and many investigators have reported covered metal stent
migration. Nakai et al. (11) reported that chemotherapy and
a covered SEMS with a low radial force were significant
risk factors for covered metallic stent migration in patients
with a distal malignant biliary obstruction due to pancreatic
cancer. Although the WALLSTENT also has a high radial
force, in addition to a high axial force, chemotherapy was
thought to reduce the size of the primary pancreatic cancer
lesion because of necrosis and reduction of extra compres-
sion to the biliary tract from primary pancreatic cancer
(Fig. 6), which may have resulted in radial force reduction.

Chemotherapy was also reported to be a factor of forming
a CDF (6). According to the reference cases, chemotherapy
was performed for 3 of 6 cases, in addition to the present
case. Chemotherapy was thought to result in necrosis of the
primary pancreatic cancer lesion and around invasive tissues
and organs, thus the bile duct wall was also vulnerable be-
cause of invasion. Cancer invasion to the common bile duct
and duodenum is another factor for the formation of a CDF.
The association between CDF and cancer, including ampul-
ary, duodenal, gallbladder, biliary, and pancreatic cancers, is
rare (12). For 1 of the 6 reference cases, the result of a bi-
opsy at the CDF was positive. In the present case, pancre-
atic cancer directly invaded both the duodenum on the anal
side of the ampulla and the distal biliary tract, and the CDF
was connected to the proximal edge of the distal bile duct
obstruction, however, the biopsy of the duodenum at the
CDF was negative. Although chemotherapy might influence
the formation of a CDF, cancer invasion was not speculated
to be a factor due to the negative biopsy results in the pre-
sent case.

Increased intraductal pressure of the biliary tract is an-
other factor of forming a CDF. Severe cholangitis, espe-
cially, caused from a bile duct obstruction due to distal mi-
gration of a covered SEMS influenced vulnerable bile duct
d wars by increasing the intraductal biliary pressure. Accord-
ing to Lee et al. (9), the formation and rupture of a cystic
lesion between the common bile duct and the duodenum fol-
owing a bile duct obstruction could create a CDF. Although
those findings could not be observed with CT, the biliary
pressure was speculated to be increased because of severe
acute cholangitis due to the migration of a covered SEMS in
the present case. The mechanism of forming a CDF could
not be verified, however, bile duct injury due to a high axial
force and sharp end of a SEMS, chemotherapy, and acute
cholangitis due to SEMS migration were likely involved in
the present case.

It is difficult to diagnose and detect a CDF, and it is typi-
cally detected incidentally on endoscopy. Abdominal pain, a
high fever, jaundice, nausea, and vomiting can be symptoms,
however, many cases of CDF will present with no or non-
specific symptoms. According to the reference cases and our

Figure 2. Magnetic resonance cholangiopancreatography shows obstruction of the common bile and main pancreatic ducts, as well as a bar-shaped high intensity signal (red arrows) outside the biliary tract. The CDF cannot be seen, however, it is indicated by the yellow arrow and line.

Figure 3. (a) An upper endoscopic image shows that the covered SEMS completely migrated from the bulb to the descending portion of the duodenum. The ampulla of Vater is indicated by the white circles. (b) An upper endoscopic image after SEMS removal shows a small hole (white arrow) on the oral side of the ampulla and bile juice flowing from the hole.

Figure 4. Endoscopic (a) (b) images and fluoroscopic (c) image during ERCP. (a) A small hole (white arrow) on the oral side of the ampulla is seen and the ampulla of Vater is recognized on the anal side of the small hole (green arrow). (b) (c) Following cannulation of the small hole under fluoroscopic guidance, cholangiography was revealed.

In the present case, cholangitis and bleeding from a CDF as initial symptoms was observed for 3 cases each; 3 cases had ‘tarry stool’, ‘hematemesis’ and ‘melena’ as symptoms of bleeding in large CDF at the bulbus; and 1 case of large CDF and 2 cases of small CDF had cholangitis. CT revealed pneumobilia in some cases of CDF (13, 14) due to a connection be-
Figure 5. Endoscopic (a) and fluoroscopic (b) images during stent placement. Two double pig-tail type plastic stents are placed after balloon dilation of the CDF.

Figure 6. Change in the CT images of the SEMS inserted on the first admission, 3 months later, and 9 months later. The primary pancreatic cancer is indicated with red arrows. CT images show the SEMS inserted on the first admission, 3 months later, and 9 months later. The SEMS is seen in the bile duct 3 months after insertion, but it is outside of the bile duct 9 months later. The size of the primary pancreatic cancer is reduced.

In the 6 reference cases, pneumobilia was observed for 1 large CDF case, not including the present case.

Conventionally, surgical treatment has generally been performed for large symptomatic CDFs (1). However, following a report by Tanaka et al. in 1983, endoscopic treatment has become the first choice (2). Endoscopic treatment is performed to prevent acute cholangitis (15, 16), usually if the CDF can be healed with re-insertion of a covered metal stent (15) or through endoscopic closure (17). In cases of both duodenal and biliary obstruction caused by pancreatic
cancer, the use of a double stent method has been recently reported (18-20). Mutignani et al. (18) classified three types of bilio-duodenal obstruction according to the duodenal stricture in relation to the papilla. According to these criteria, the present case was thought to be compatible with type II, which affects the second part of the duodenum with involvement of the papilla. Approaching the papilla by inserting a duodenoscope through the duodenal stent and biliary cannulation and inserting the delivery system of SEMS through the mesh of the duodenal stent are necessary following duodenal stenting under fluoroscopic guidance for the placement of a biliary metal stent in cases of type II bilio-duodenal stricture, however, these procedures are generally difficult through the mesh of the stent. Among the reference cases, the cases of large CDF at the bulbus were treated with EMS exchange from the ampulla, insertion of a duodenal stent, or embolization of the feeding artery for bleeding, however, the CDFs remained. The small CDF case at the duodenal descending portion was treated with ENBD, which resulted in the disappearance of the CDF. None of the reference cases of CDF had duodenal obstruction. Double metal stenting has been recently performed for duodenal and biliary obstruction and is another treatment option for a CDF. However, we previously did not select a metal stent for use except in cases of malignant biliary stricture, including CDF. Furthermore, CDF cases associated with SEMS placement in advanced cancer have a poor prognosis (4-6), and a long-term survival is not expected. As long stent patency was not needed, we inserted 2 plastic stents from the CDF with the successful relief of cholangitis. Indeed, the prognosis of CDF associated with EMS was poor for 3 cases because all cases were unresectable pancreatic cancer, biliary cancer, or other organ metastatic cancer. Three of the 5 cases of large CDF at the bulbus and the present case of small CDF ultimately died due to bleeding, hepatorenal syndrome, or cancer progression. Our case died due to the progression of primary pancreatic cancer 2 months after re-intervention.

In conclusion, CDF is a rare complication after metal stent placement, and a small CDF at the duodenal descending portion is especially rare with successful relief of acute cholangitis. Endoscopic stent placement through the CDF may be the first choice of treatment for acute cholangitis.

The authors state that they have no Conflict of Interest (COI).

References


Table. Characteristics of CDF Cases Associated with SEMS.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Age</th>
<th>Gender</th>
<th>Primary cancer (Chemotherapy)</th>
<th>Location</th>
<th>Size (Diameter)</th>
<th>Symptom</th>
<th>Cancer invasion to CDF</th>
<th>Previous stent migration</th>
<th>Treatment (Effect to CDF)</th>
<th>Prognosis (From treating CDF)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>68</td>
<td>Male</td>
<td>Rectum (Yes)</td>
<td>Bulbus</td>
<td>Nd</td>
<td>Tarry stool</td>
<td>None</td>
<td>None</td>
<td>Conservative (None)</td>
<td>Death (16 days later)</td>
</tr>
<tr>
<td>5</td>
<td>76</td>
<td>Male</td>
<td>Bile duct (None)</td>
<td>Bulbus</td>
<td>Large (Nd)</td>
<td>Hematemesis</td>
<td>None</td>
<td>None</td>
<td>Conservative (None)</td>
<td>Death (Nd)</td>
</tr>
<tr>
<td>6</td>
<td>56</td>
<td>Male</td>
<td>Pancreas (Yes)</td>
<td>Bulbus</td>
<td>Large (Nd)</td>
<td>Melena</td>
<td>Nd</td>
<td>None</td>
<td>Embolize feeding artery (None)</td>
<td>Death (Nd)</td>
</tr>
<tr>
<td>7</td>
<td>66</td>
<td>Male</td>
<td>Pancreas (Yes)</td>
<td>Bulbus</td>
<td>Large (50mm)</td>
<td>Cholangitis</td>
<td>Nd</td>
<td>Proximal</td>
<td>EMS exchange (None)</td>
<td>Nd</td>
</tr>
<tr>
<td>8</td>
<td>85</td>
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<td>Bile duct (None)</td>
<td>Bulbus</td>
<td>Large (70mm)</td>
<td>None</td>
<td>Yes</td>
<td>None</td>
<td>EMS exchange Duodenal stent (Nd)</td>
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</tr>
<tr>
<td>9</td>
<td>76</td>
<td>Female</td>
<td>Ampulla (None)</td>
<td>Descending portion</td>
<td>Small (Nd)</td>
<td>Cholangitis</td>
<td>None</td>
<td>None</td>
<td>ENBD (Effective)</td>
<td>Alive</td>
</tr>
<tr>
<td>Present case</td>
<td>79</td>
<td>Male</td>
<td>Pancreas (Yes)</td>
<td>Descending portion</td>
<td>Small (&lt;5mm)</td>
<td>Cholangitis</td>
<td>None</td>
<td>Distal</td>
<td>EBS from CDF (None)</td>
<td>Death (2 months later)</td>
</tr>
</tbody>
</table>

Nd: not description