

Endoscopic transpapillary pancreatic stenting for internal pancreatic fistula with the  
disruption of the pancreatic ductal system

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Short title: Endoscopic stenting for internal pancreatic fistula

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## **Abstract**

### [Background]

Internal pancreatic fistula (IPF) is a well-recognized complication of pancreatic diseases. Although there have been many reports concerning IPF, the therapy for IPF still remains controversial. We herein report our experiences with endoscopic transpapillary pancreatic stent therapy for IPF and evaluate its validity.

### [Method]

Six patients with IPF who presented at our department and received endoscopic transpapillary pancreatic stent therapy were investigated, focusing on the clinical and imaging features as well as treatment strategies, the response to therapy and the outcome.

### [Results]

All patients were complicated with stenosis or obstruction of the main pancreatic duct, and in these cases the pancreatic ductal disruption developed distal to the areas of pancreatic stricture. The sites of pancreatic ductal disruption were the pancreatic body in five patients and the pancreatic tail in one patient. All patients received endoscopic stent placement over the stenosis site of the pancreatic duct, and three patients improved completely and one patient improved temporarily. Finally, three patients underwent

surgical treatment for IPF. All patients have maintained a good course without recurrence of IPF.

[Conclusion]

Endoscopic transpapillary pancreatic stent therapy may be an appropriate first-line treatment to be considered before surgical treatment. The point of stenting for IPF is to place a stent over the stenosis site of the pancreatic duct to reduce the pancreatic ductal pressure and the pseudocyst's pressure.

**Key words:** internal pancreatic fistula, endoscopic transpapillary pancreatic stent, alcoholic chronic pancreatitis

## Introduction

Internal pancreatic fistula (IPF) is a rare clinical entity, but it is a well-known serious complication of acute and chronic pancreatitis or pancreatic trauma<sup>1-3)</sup> and is associated with significant morbidity and mortality<sup>3-6)</sup>. IPF is caused by the disruption of the pancreatic duct due to the associated disease. An inflammation or traumatic disruption of the pancreatic duct leads to the leakage of pancreatic exocrine secretions. If the duct is disrupted anteriorly, the disruption leads to pancreatic ascites. If the duct is disrupted posteriorly, the disruption may lead to the tracking of pancreatic fluid into the mediastinum along the path of least resistance through the aortic and esophageal hiatus, thus resulting in mediastinal pseudocyst or pleural fistula with amylase-rich pleural effusion<sup>3, 7-11)</sup>.

The traditional treatments for IPF include conservative medical therapy or surgery. However, these treatments have had limited success<sup>6, 12, 13)</sup>. The conservative therapy fails in approximately half the cases while surgical treatment is associated with significant morbidity<sup>14)</sup>. Although endoscopic transpapillary pancreatic stent therapy for IPF has been reported to be useful as an alternative treatment modality, the treatment strategy for IPF remains controversial. We herein report our experience with endoscopic transpapillary pancreatic stent therapy for IPF and evaluate its validity.

## **Methods**

### **Treatment strategy for IPF in our department**

Figure 1 shows a schema of the treatment strategy for IPF in our department.

After IPF was identified using various modalities such as ultrasonography (US), helical computed tomography (CT), and MR-cholangiopancreatography (MRCP), the pancreatic ductal system was investigated in detail in all cases using endoscopic retrograde cholangiopancreatography (ERCP). At the same time as ERCP, endoscopic transpapillary pancreatic stent placement was performed over the stenosis site of the pancreatic duct and endoscopic sphincterotomy was not performed at same time. Figure 2 shows the schema of endoscopic transpapillary pancreatic stent placement of our treatment strategy for IPF. The size of the stent was selected to be either 5 or 7 Fr (Cook Endoscopy, Winston, USA). Although the 7Fr stent was tried to place at first, the 5Fr stent was adapted to the cases which were difficult for the 7Fr stent to place. The exchange interval for the stent was set to be every four months, and the total placement period of the stent was one year. When a symptom worsened or stenting was not effective, surgical procedures were considered.

### **Patients**

Six patients with IPF who presented in the Department of Surgery at Nagasaki

University Hospital between July 2007 and November 2011 were included in this study.

The clinical and imaging records were reviewed and compared among the patients.

Imaging studies included US, CT, MRCP, and ERCP. In addition, parameters related to the treatment for IPF such as the stent size, interval for stenting, response to therapy, and long-term outcome were evaluated.

## Results

The clinical features of six patients with IPF are summarized in Table 1. All patients were men with a mean age of 64 years (range, 58 to 71 years). Five patients showed pancreatic ascites and one patient showed a mediastinal pseudocyst. As the main symptoms, three patients showed back pain, two patients showed abdominal pain, and one patient showed epigastralgia and abdominal distension. The underlying disease associated with IPF included alcohol-related chronic pancreatitis in all patients. The serum amylase and C-reactive protein (CRP) levels were  $238\pm 401$  (IU/l) and  $7.9\pm 9.9$  (mg/dl), respectively. The white blood cell count was  $10,900\pm 3,482$  (/mm<sup>3</sup>). The fluid amylase level within ascites or pseudocysts was  $46,890\pm 2,2921$  (IU/l). Four patients presented IPF after the acute aggravation of chronic pancreatitis.

Table 2 shows the imaging features of the patients. All patients received US, enhanced-CT, MRCP and ERCP. According to these modalities, the sites of pancreatic ductal disruption were the pancreatic body in five patients and the pancreatic tail in one patient. All patients were complicated with stenosis or obstruction of the main pancreatic duct and the pancreatic ductal disruption developed distal to the areas of the pancreatic structure. Four patients were complicated with pancreatic calculi; these were located in the whole pancreas in two patients, the head and body of pancreas in one

patient and only the head of pancreas in one patient. Five patients were complicated with pancreatic pseudocysts. Two patients were complicated with retroperitoneal abscesses.

Table 3 shows the results of endoscopic transpapillary pancreatic stent therapy for IPF. All patients received endoscopic transpapillary stent therapy according to our treatment strategy for IPF and the success rate of stent placement was 100%. Three patients became asymptomatic by stenting for IPF and did not have a recurrence after the stent was withdrawn. Figure 3 shows a successful case of endoscopic transpapillary pancreatic stent therapy for IPF; the pancreatic effusion disappeared after the stent therapy. Although two patients received the stent therapy, Case 4 continued to suffer from continuous pain and Case 5 was complicated with intracystic bleeding. Case 6 had become asymptomatic through stenting therapy and had been free of continuous pain for 13 months after the stent was removed. However, the symptoms recurred, and the replacement of the stent was not effective enough to improve the symptoms in Case 6. Finally, Case 4, 5, and 6 underwent surgical treatment and became asymptomatic afterwards. All patients have maintained a good course without the recurrence of IPF for a mean observation period of 3.2 years (range 1.1 years to 5.4 years).

## Discussion

IPF is rare clinical entity and Chebli et al reported that the incidence has been 11 patients (7.3%) of 150 patients with chronic pancreatitis from 1995 to 2003<sup>15)</sup>. Because of the low incidence, the treatment strategy for IPF remains controversial. However, endoscopic transpapillary pancreatic stent therapy for IPF has been reported to be useful as an alternative treatment modality. Our treatment strategy for IPF was used in all patients, and the validity of our strategy was evaluated. Furthermore, the important point of this study was to treat the patients with IPF using endoscopic stenting according to our original strategy. In this study, all patients had received endoscopic transpapillary pancreatic stent therapy during ERCP, and three patients showed complete improvement without recurrence. On the other hand, three patients finally required surgical intervention. We directed the operative procedures to control intracystic bleeding and to relieve continuous pain, thus resulting in favorable outcomes.

IPF with pancreatic ascites and pleural effusion shares a common pathophysiology. The disruption of the pancreatic duct results in the formation of internal fistula communicating with peritoneal or pleural cavities, which result in ascites or pleural effusion, respectively<sup>5, 16)</sup>. In most cases, IPF has been reported to develop

secondary to alcoholic chronic pancreatitis<sup>17-21</sup>). In the present study, all patients presented pancreatic ascites or pleural effusion. Moreover, in all patients IPF developed secondary to alcoholic chronic pancreatitis and four patients presented with IPF after an acute aggravation of chronic pancreatitis.

The diagnosis of IPF generally relies on imaging. Some reports have shown that the diagnostic sensitivity of MRCP is almost the same as that of ERCP and is higher than that of CT<sup>21-23</sup>). Our previous report found that a precise assessment of the pancreatic ductal system is essential for effectively managing patients with IPF; MRCP can be a promising tool for evaluating the pancreatic duct system, and it is also helpful for selecting the optimal treatment strategy<sup>24</sup>). The previous reports showed that ERCP is the most specific modality for identifying the pancreatic duct anatomy and the site of disruption. The reported advantage of ERCP is that it offers the opportunity for definitive therapy using an endoscopic stent, sphincterotomy, or nasopancreatic drainage<sup>25, 26</sup>).

The available treatment modalities for IPF are 1) conservative medical therapy, 2) surgery, and 3) endoscopic transpapillary pancreatic stent therapy. The aim of medical therapy is to reduce pancreatic exocrine secretions<sup>27</sup>). However, several reports have shown that the therapeutic rates of somatostatin or octreotide and parenteral

were 25-60% lower<sup>3, 4, 6, 12, 13)</sup>. Moreover, medical therapy is expensive and, requires prolonged hospitalization, and failure to respond for more than four weeks is associated with mortality rates ranging from 1-25%<sup>5, 13)</sup>. In this study, medical therapy such as somatostatin or octreotide was not used for any cases. On the other hand, the main indications for surgery are the failure of other treatments, obstruction of the pancreatic duct, intracystic bleeding, and cases in which symptoms did not improve. Surgical treatment includes either some form of pancreatic resection or enter-pancreatic anastomosis at the site of pancreatic duct leakage or the pseudocyst<sup>28)</sup>. However, surgical treatment has the disadvantages of the potential for complications and the occurrence of death in 1-20%<sup>4, 5, 17)</sup>. Whereas, the aim of endoscopic transpapillary pancreatic stent therapy is to reduce the main pancreatic ductal pressure and the pseudocyst's pressure<sup>29-31)</sup>. Complications of endoscopic stenting include perforation, bleeding, exacerbation of pain due to acute pancreatitis, infection of associated fluid collections, alterations in ductal morphology following stenting and death. Adverse events have been reported in 0-9%<sup>32)</sup>. The most important objective of stent therapy is to place the stent over the stenosis site of the pancreatic duct. Our previous report also found that a sufficient decompression of pancreatic stricture is mandatory for the treatment of patients with IPF<sup>24)</sup>. Therefore, there is also the report that combined

endoscopic and percutaneous rendezvous technique is the efficient method to reduce the pressure in cases of failure of endoscopic stenting<sup>33)</sup>. Although stent therapy has been reported to be more invasive and carries a greater risk than medical therapy, it has been reported to be safer than surgical treatment<sup>25, 26)</sup>.

In conclusion, it may be useful to consider endoscopic stent therapy before surgical treatment. Because the cause of IPF is stenosis of the pancreatic duct, it is important to remove this stenosis in order to resolve the condition. However, since there were few cases in this study, it is required to accumulate and examine IPF cases, cooperating with other institutions

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### **Figure Legends**

Figure 1: Treatment strategy for IPF in our department

After IPF was identified using various modalities such as US, enhanced-CT, and MRCP, in all cases the pancreatic ductal system was investigated in detail using ERCP. At the same time as ERCP, endoscopic transpapillary pancreatic stent placement was performed over the stenosis site of the pancreatic duct. The size of the stent was selected to be either 5 or 7 Fr (Cook Endoscopy, Winston, USA). The exchange interval for the stent was set to be every four months, and the total placement period of the stent was one year. When a symptom worsened or stenting was not effective, surgical procedures were considered.

Figure2: Schema of endoscopic transpapillary pancreatic stent placement

In order to reduce the main pancreatic ductal pressure and the pseudocyst's pressure, it is important to place the stent over the stenosis site.

Figure 3: A case of endoscopic transpapillary pancreatic stent therapy

The stent was placed over the site of the stenosis (white arrow).

Figure 1 Treatment strategy for IPF in our department

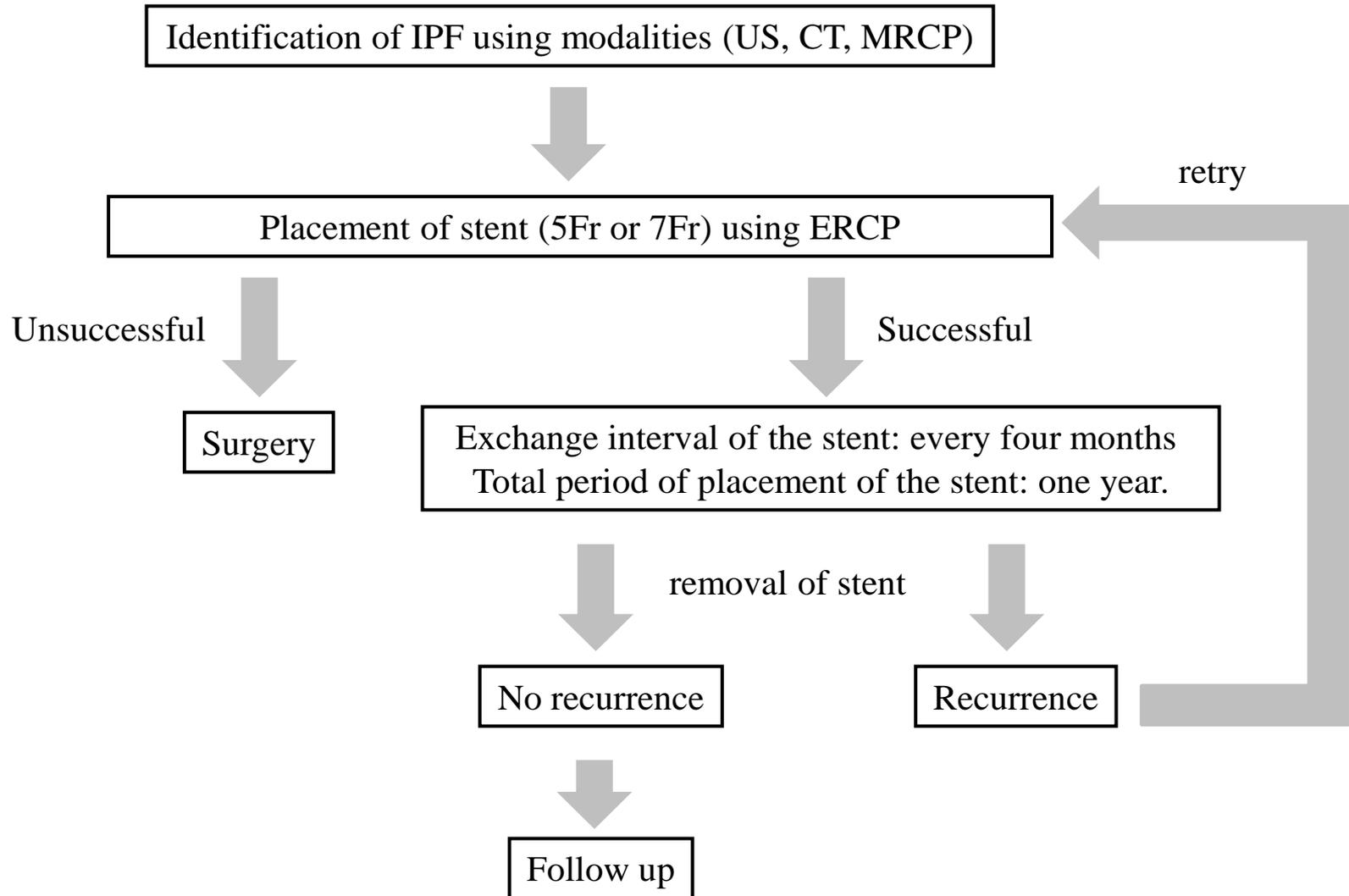


Figure 2. Schema of endoscopic transpapillary pancreatic stenting

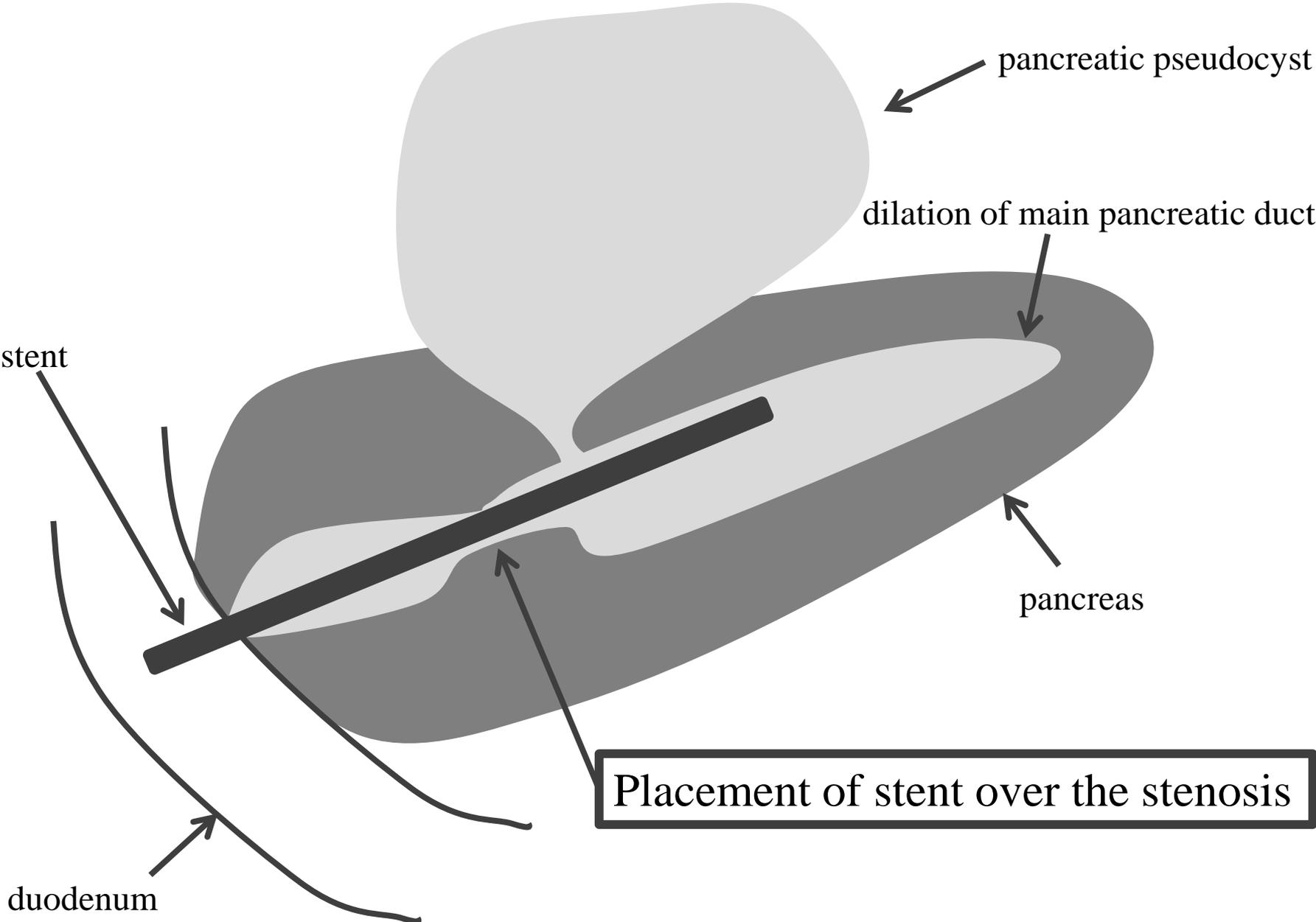


Figure 3. A case of endoscopic transpapillary pancreatic stenting



Table 1. Clinical feature of six patients with IPF

features	age (yr)	gender	type of IPF	previous pancreatic disease	etiology	symptom	Serum Amylase (IU/l)	WBC (X 10 <sup>3</sup> mm <sup>3</sup> )	CRP (mg/dl)	fluid amylase (IU/l)
case 1	58	Male	PA	CP	Alcohol	Back pain	257	7.8	1.2	17,684
case 2	61	Male	PA	CP	Alcohol	Abdominal pain	219	12.8	26.3	64,090
case 3	70	Male	PA	CP	Alcohol	Back pain	1,143	12.6	11.7	82,980
case 4	64	Male	PA	CP	Alcohol	Abdominal pain	21	16.0	20.4	-
case 5	71	Male	MP	CP	Alcohol	Epigastralgia Back pain	689	9.2	4.1	32,890
case 6	62	Male	PA	CP	Alcohol	Abdominal distension	35	5.6	0.1	46,890

PA: pancreatic ascites, MP: mediastinal pseudocyst, CP: chronic pancreatitis, WBC: white blood cell count, CRP: C-reactive protein

Table 2. Imaging feature of six patients with IPF

features	US	CT	MRCP	ERCP	Site of pancreatic ductal disruption	Pancreatic ductal stenosis	Pancreatic calculi	Pancreatic pseudocyst	Abscess formation
case1	○	○	○	○	Body	+ (Head)	-	+	-
case 2	○	○	○	○	Tail	+ (Body)	+ (Head-Tail)	+	+ Retoroperitoneal abscess
case 3	○	○	○	○	Body	+ (Head)	-	+	+ Retoroperitoneal abscess
case 4	○	○	○	○	Body	+ (Body)	+ (Head-Tail)	+	-
case 5	○	○	○	○	Body	+ (Body)	+ (Head-Body)	+	-
case 6	○	○	○	○	Body	+ (Body)	+ (Head)	-	-

Table 3. Results of endoscopic treatment of six patients with IPF

features	Peritoneal drainage	Size of stent	Interval for stenting	*Response for treatment	Surgery	Removal of stent	Observation period	Recurrence
case 1	+	5Fr	1 year	Well	-	+	2.3 year	-
case 2	+	7 Fr	1 year	Well	-	+	2.2 year	-
case 3	+	7Fr	1year	Well	-	+	5.4 year	-
case 4	-	5Fr	2 months	Continuous pain	Partington's procedure	+	1.6 year	-
case 5	+	5Fr	1.5 months	Intracystic bleeding	Distal pancreatectomy	+	1.1 year	-
case 6	+	5Fr	1 year	Well	-	+	3.4 year	+ [ Continuous pain recurred at 13 months after the removal of the stent. In spite of the replacement of the stent, symptoms did not improve. ] →Frey' procedure

\*Response for treatment means that symptoms, pancreatic stenosis, or amount of effusion disappear.