J Hepatobiliary Pancreat Surg (2005) 12:76–83
DOI 10.1007/s00534-004-0937-0

Journal of HBP Surgery

Complete obstruction of the lower common bile duct caused by autoimmune pancreatitis: is biliary reconstruction really necessary?

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Abstract
Recent observations suggest that an immune response is involved in the development of chronic pancreatitis. We report a case of autoimmune pancreatitis in a patient who showed complete obstruction of the lower common bile duct. A 63-year-old man was admitted to a local hospital, complaining of appetite loss and back pain. The patient had obstructive jaundice, and percutaneous transhepatic gallbladder drainage was performed. Fluorography through the biliary drainage catheter showed complete obstruction of the lower common bile duct. The patient had no history of alcohol consumption and no family history of pancreatic disease. Physical examination revealed an elastic hard mass palpable in the upper abdomen. Abdominal ultrasound and abdominal computed tomography (CT) scans showed enlargement of the pancreas head. While autoimmune pancreatitis was highly likely, due to the patient's high serum immunoglobulin level, the possibility of carcinoma of the pancreas and/or lower common bile duct could not be ruled out. Laparotomy was performed, and wedge biopsy samples from the pancreas head and body revealed severe chronic pancreatitis with infiltration of reactive lymphocytes, a finding which was compatible with autoimmune pancreatitis. Cholecystectomy and biliary reconstruction, using choledochojejunostomy, were performed, because the complete bile duct obstruction was considered to be irreversible, due to severe fibrosis. After the operation, prednisolone (30 mg/day) was given orally for 1 month, and the entire pancreas regressed to a normal size. Complete obstruction of the common bile duct caused by autoimmune pancreatitis has not been reported previously; this phenomenon provides an insight into autoimmune pancreatitis and provokes a controversy regarding whether biliary reconstruction is needed for the treatment of complete biliary obstruction caused by autoimmune pancreatitis.

Key words Autoimmune chronic pancreatitis · Complete obstruction of the lower common bile duct

Introduction

Despite recent advances in imaging techniques for pancreatic tumors, the diagnosis of pancreatic tumors is occasionally difficult.[1] Particularly, the differential diagnosis of pancreatic carcinoma from chronic pancreatitis is clinically important for making a final decision on whether to perform resection, because pancreatic carcinoma is a fatal disease unless it is properly treated.[2] Chronic pancreatitis occasionally causes a severe form of biliary stenosis or obstruction, which mimics the biliary obstruction caused by pancreatic carcinoma. Although alcohol abuse is the main cause of chronic pancreatitis,[3] in 30% of patients with chronic pancreatitis, the disease has no obvious cause and is classified as idiopathic chronic pancreatitis.[4] Sarles et al.[5] first reported a primary inflammatory sclerosis of the pancreas that may have been caused by "phenomena of self-immunization".[5] Since their report, several authors have reported chronic pancreatitis with an autoimmune-mediated mechanism. Yoshida et al.[6] first proposed the concept of autoimmune pancreatitis (AIP) and criteria for the diagnosis of AIP[6] and cases of AIP have recently been reported with increasing frequency worldwide.[7] While biliary stenosis and/or obstruction are often associated with AIP, no criteria for surgical indication have yet been precisely determined and, therefore, whether the biliary obstruction is reversible has never been discussed.

We experienced a patient with complete obstruction of the lower common bile duct caused by AIP, which was surgically treated with choledochojejunostomy, followed by steroid therapy. The diagnosis of AIP, based on imaging analyses, is presented and appropriate treatment, particularly for patients with associated complete biliary obstruction, is discussed.

Offprint requests to: Y. Sakurai
Received: May 19, 2004 / Accepted: September 14, 2004

Table 1. Laboratory data on admission

Blood chemistry		Blood count	
Total protein	8.7 g/dl	WBC	9000/μl
Albumin	4.2 g/dl	HGB	12.3 g/dl
ZTT	18.1 U	RBC	3.99×10^6/μl
TTT	5.6 U	HCT	35.8%
BUN	19 mg/dl	PLT	51.0×10^4/μl
Creatinine	0.5 mg/dl		
Total bilirubin	2.2 mg/dl	FBS	129 mg/dl
Direct bilirubin	1.5 mg/dl	HbA1c	6.5%
AST	72 mU/ml	Amylase	107 U
ALT	179 mU/ml	Elastase I	2679 ng/dl
LDH	127 mU/ml	Trypsin	3700 ng/ml
ALP	195 mU/ml	Phospholipase A2	1060 ng/dl
Cholinesterase	3200 mU/ml	PFD test	104.4%
γ-GTP	144 mU/ml		
Na^+	135 mEq/l	Tumor markers	
K^+	4.7 mEq/l	CEA	1.5 ng/ml (5.0)
Cl^-	99 mEq/l	CA19-9	59.6 U/ml (37)
		RA factor	90 IU/ml
Protein analysis		Antinuclear Ab	1:40
A/G	1.02 (1.54–2.47)	C3c	102 mg/dl
Alb (%)	50.4 (60.7–71.3)	C4	30 mg/dl
α1-globulin (%)	3.6 (1.9–2.9)	CH50	38.7 U/ml
α2-globulin (%)	12.5 (6.1–9.6)	Anti-DNA Ab	3.1 U
β-globulin (%)	10.6 (7.0–10.5)	Anti-RNP Ab	Negative
γ-globulin (%)	22.9 (10.3–20.4)	Anti-SSB Ab	Negative
		Anti-SSA Ab	1:16
Globulin fraction			
IgG	2030 mg/dl		
IgA	236 mg/dl		
IgM	103 mg/dl		

Numbers in parenthesis indicate upper limits or ranges of normal values

Case report

A 63-year-old man was admitted to a local hospital in late February 2000, complaining of appetite loss and back pain. Because obstructive jaundice and dilatation of the biliary tree was found, percutaneous transhepatic gallbladder drainage (PTGBD) was performed at the local hospital. Pancreatic carcinoma was suspected on the basis of the radiographic findings (i.e., enlargement of the pancreatic head) and the patient was transferred to our hospital for further treatment.

The patient had no history of alcohol consumption and no family history of pancreatic disease. On physical examination, an elastic hard mass was palpable in the upper abdomen. No enlarged superficial lymph node was palpable. Neither liver nor spleen was palpable. The clinical data showed cholestatic liver dysfunction (Table 1). Determinations of pancreatic enzyme levels revealed elevation of elastase-1, serum trypsin, lipase, and phospholipase A2, but pancreatic amylase was in the normal range. Fasting blood sugar was 129 mg/dl. Hemoglobin A1c (Hb A1c) was 6.5%, which was slightly higher than the normal range. Serum carcinoembryonic antigen (CEA) level was within the normal range, but carbohydrate antigen (CA) 19-9 was 59.6 U/ml. Antinuclear antibody was positive at a titer of 1:40. Rheumatoid arthritis (RA) and anti-Ro [SS-A] antibodies were positive. Immunological findings showed marked elevation of immunoglobulin G (IgG). The pancreatic functional diagnostant (PFD) test (*P*-aminobenzoic acid [PABA] test) value was 101.4%.

Ultrasonography showed diffuse enlargement of the entire pancreas, with a so-called "sausage like" appearance. The entire pancreas was depicted as a diffuse hypoechoic area (Fig. 1), without dilatation of the main pancreatic duct. Abdominal computed tomography (CT) scan also demonstrated enlargement of the pancreas, and no peripancreatic lesion was identified. Irregular enhancement in the head and poor enhancement in the body and tail of the pancreas were noted in the early arterial phase of contrast-enhanced CT scans (Fig. 2). No calcification or tumor masses were detected in the other portions of the pancreas (Fig. 2).

Percutaneous transhepatic cholangiography was performed, and fluorography through the PTGBD catheter showed complete obstruction of the lower common bile duct. Magnetic resonance cholangiopancreatography disclosed obstruction of the common bile duct and segmental narrowing of the main pancreatic duct (Fig. 3). While enlargement of the entire pancreas was noted, well-circumscribed mass lesions were not detected. Superior mesenteric artery (SMA) arteriography demonstrated no encasement or tumor vessels around the pancreatic artery and pancreaticoduodenal arcades (photographs not shown). The venous phase of SMA revealed smooth narrowing of the portal vein (Fig. 4A,B). No irregularity was found in the walls of these venous structures. No further evidence that could be a clue to the differential diagnosis of pancreatic carcinoma from chronic pancreatitis was obtained. These findings indicated that the biliary obstruction was highly likely to have been caused by AIP.

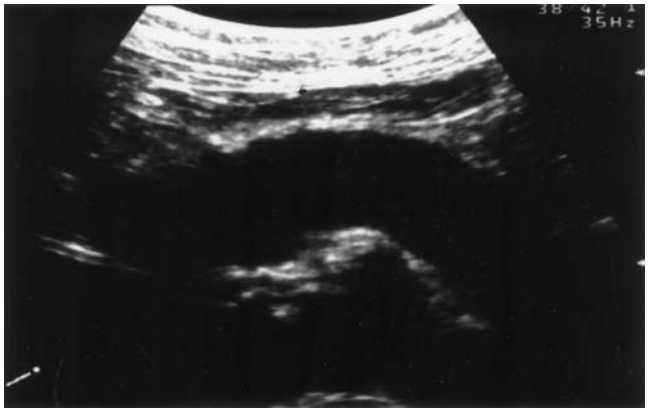


Fig. 1. Abdominal ultrasonography on admission, showing diffuse enlargement of the entire pancreas—a "so-called" sausage-like appearance. The whole pancreas is depicted as a diffuse hypoechoic area

Because the biliary obstruction was complete and was considered to be irreversible, and the possibility of carcinoma of the pancreas and/or lower common bile duct could not definitely be ruled out, laparotomy was performed, on April, 25, 2000. The operative findings indicated that the entire pancreas was enlarged and fibrotic. Operative ultrasound revealed enlargement of the en-

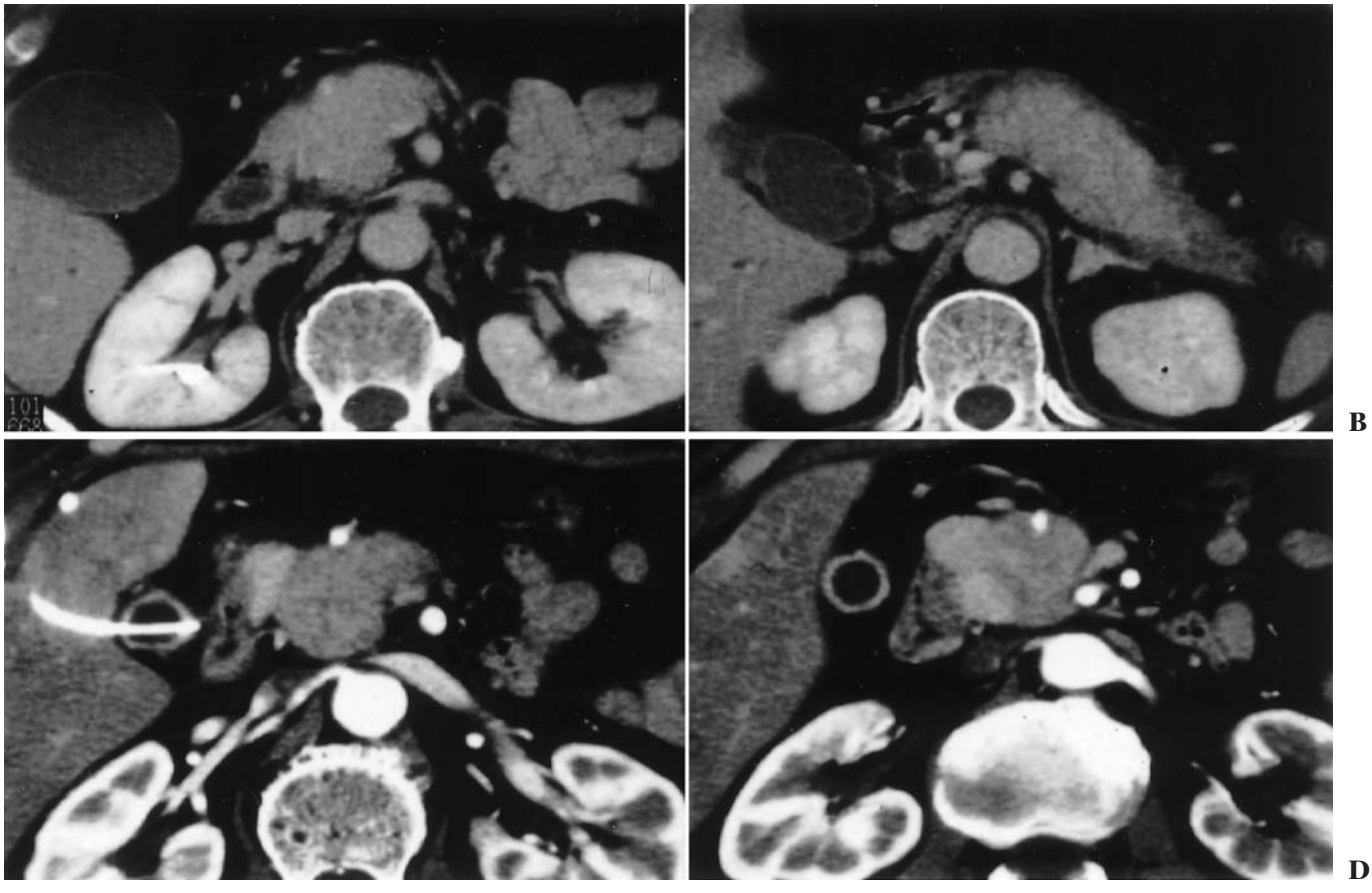


Fig. 2. A,B Enhanced abdominal computed tomography (CT) scans obtained at a local hospital, showing diffuse enlargement of the pancreas. **C,D** Early-phase images of contrastenhanced CT scan on admission, showing that a portion of the pancreas head was normally enhanced by the contrast media

tire pancreas, without any circumscribed tumors in the pancreas (Fig. 5) or dilatation of the pancreatic duct. Wedge biopsy samples were obtained from the head and body of the pancreas, and revealed a severe form of chronic pancreatitis, with infiltration of reactive lymphocytes. The pancreatic acinar cells were completely replaced by fibrotic tissues, and these histological findings were compatible with AIP (Fig. 6). Intraoperative cholangiography showed complete obstruction of the lower common bile duct (photograph not shown). Cholecystectomy, complete resection of the extrahepatic common bile duct (including the portion showing obstruction), and choledochojejunostomy were performed, based on the fact that the complete obstruction of the lower common bile duct appeared to be irreversible, due to severe fibrotic changes in the pancreas. Endoscopic retrograde pancreatography performed after surgery revealed diffuse irregular narrowing in the entire length of the main pancreatic duct (Fig. 7). After the operation, prednisolone, at an initial dose of 30 mg/day, was administered orally for 1 month, and the dose was then gradually reduced. The patient was discharged from the hospital 30 days after surgery. During follow up, the elevated serum pancreatic enzymes soon returned to within the normal ranges, and the enlarged pancreas also returned to the normal size (Fig. 8C,D). Steroid administration was stopped 3 years after the operation, and the patient has been in good health and has stayed asymptomatic to date.

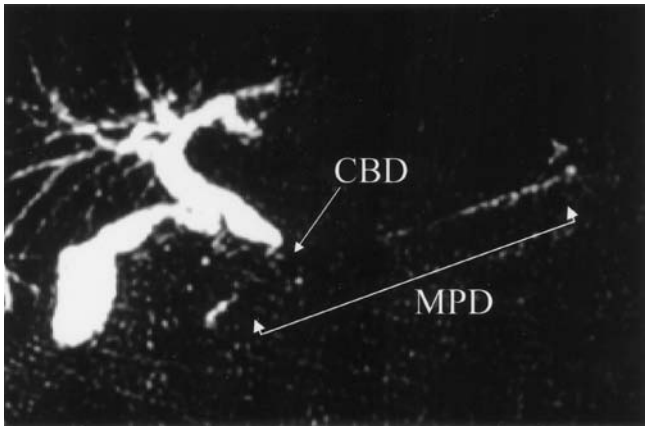


Fig. 3. Magnetic resonance cholangiopancreatography, revealing obstruction of the common bile duct (*CBD*) and narrowing of the main pancreatic duct (*MPD*)

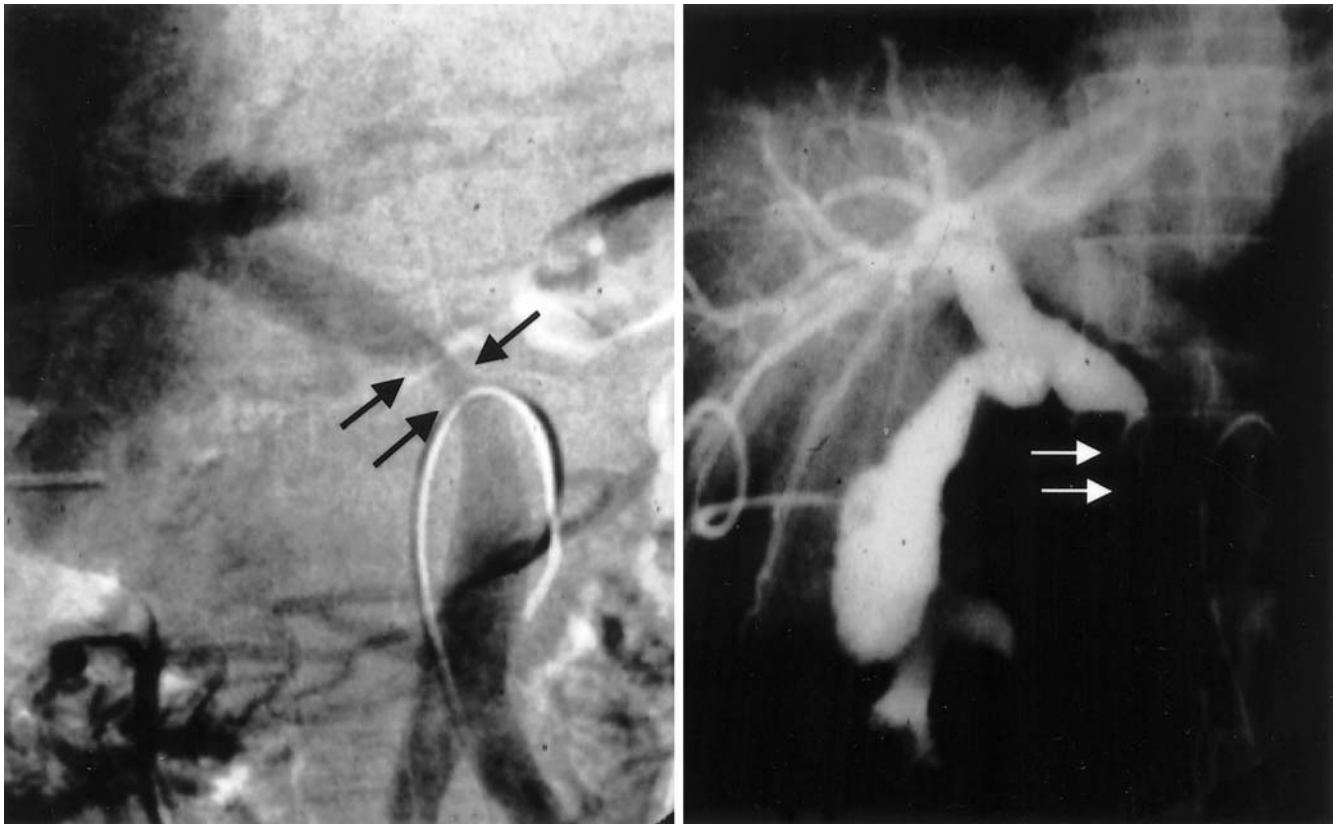


Fig. 4. **A** Venous phase of superior mesenteric arteriography and **B** that associated with cholangiogram, revealing smooth narrowing of the portal vein, which was probably due to enlargement and sclerotic changes in the pancreatic head. *Arrows* in **A** show smooth narrowing of the portal vein; *arrows* in **B** show complete obstruction of the common bile duct

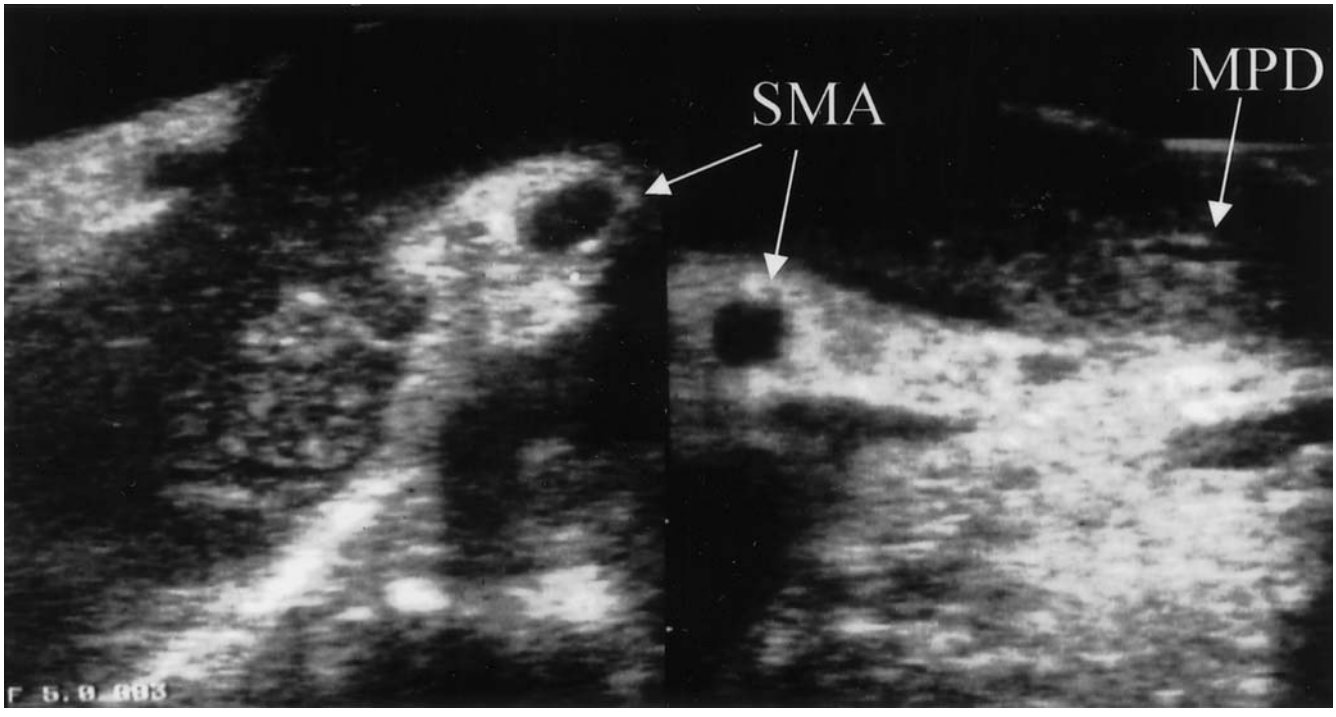
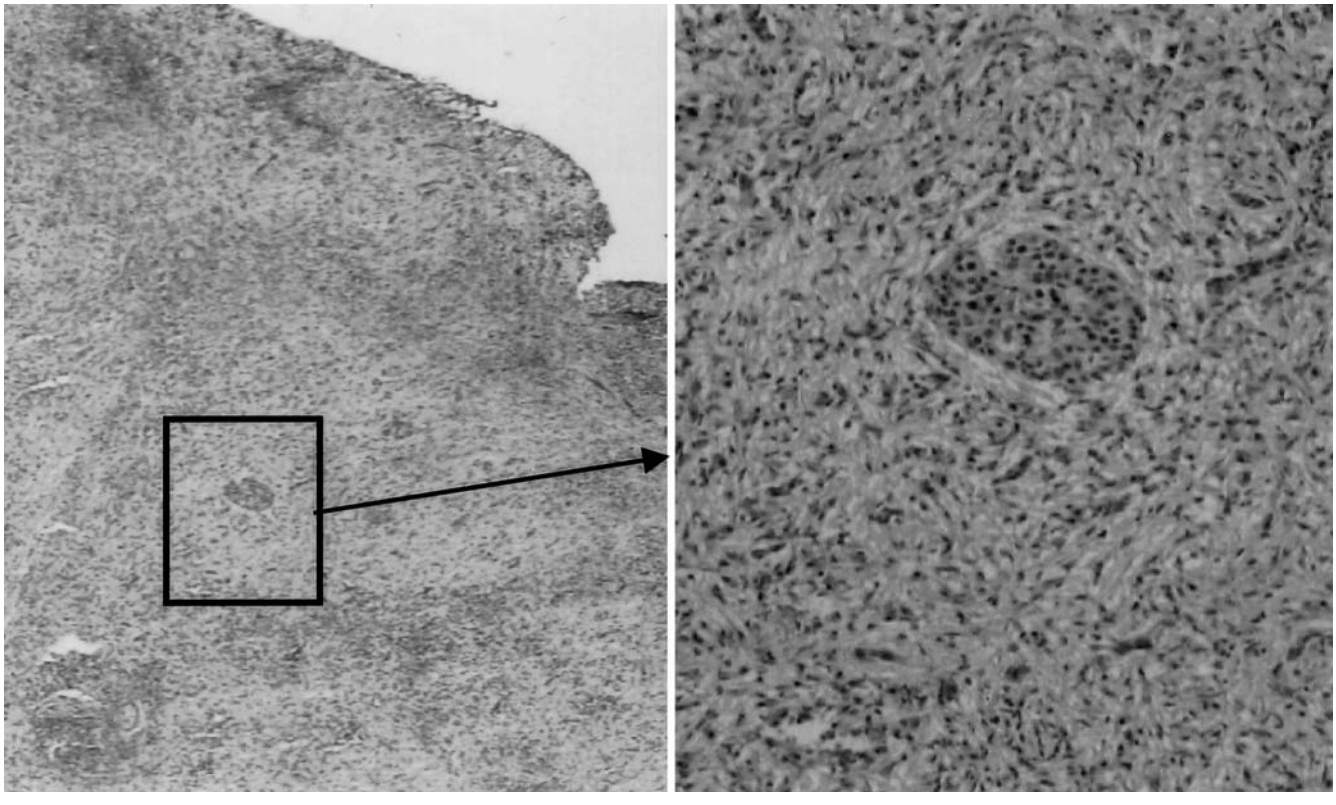


Fig. 5. Operative ultrasound examination, revealing enlarged entire pancreas without any circumscribed tumor in the pancreas. *SMA*, superior mesenteric artery



A **B**

Fig. 6 A, B. Wedge biopsy sample from the head and body of the pancreas revealed severe chronic pancreatitis, with infiltration of reactive lymphocytes, a finding compatible with autoimmune pancreatitis. **A** HE, × 40; **B** HE, × 160

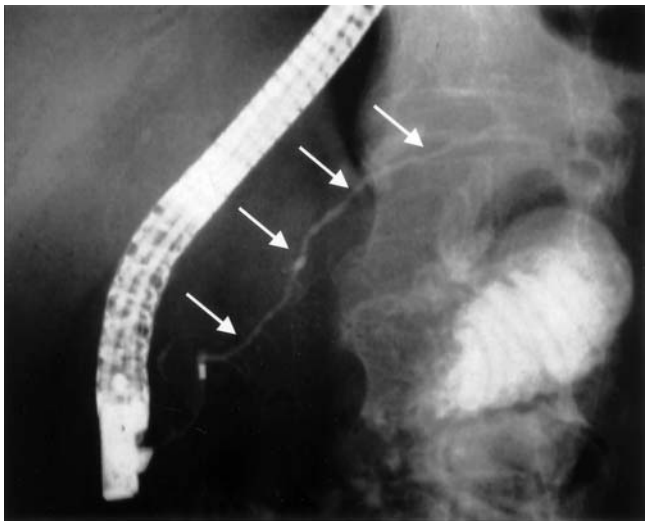


Fig. 7. Endoscopic retrograde pancreatography (ERP) examination performed after the operation, revealing diffuse irregular narrowing (*arrows*) in the entire length of the main pancreatic duct

Discussion

The reasons that the present case report warranted publication were twofold. First, although it has been reported that AIP causes biliary stenosis and/or obstructive jaundice,[6] the present patient represents the first case of complete obstruction of the common bile duct caused by AIP that has ever been presented in the literature. Second, the validity of the indication for biliary reconstruction for AIP patients with complete obstruction has yet to be discussed in detail, although, in the present patient, steroid therapy after the biliary bypass created by choledochojejunostomy was effective for the treatment of AIP. The question as to whether or not complete obstruction of the common bile duct is reversible with steroid therapy remains to be answered, and discussion concerning this issue has been limited in the previously published literature.

AIP is a recently described clinical entity causing chronic pancreatitis.[6] It often presents as diffuse enlargement of the pancreas and/or as a focal mass in the pancreas head, causing obstruction of the common bile

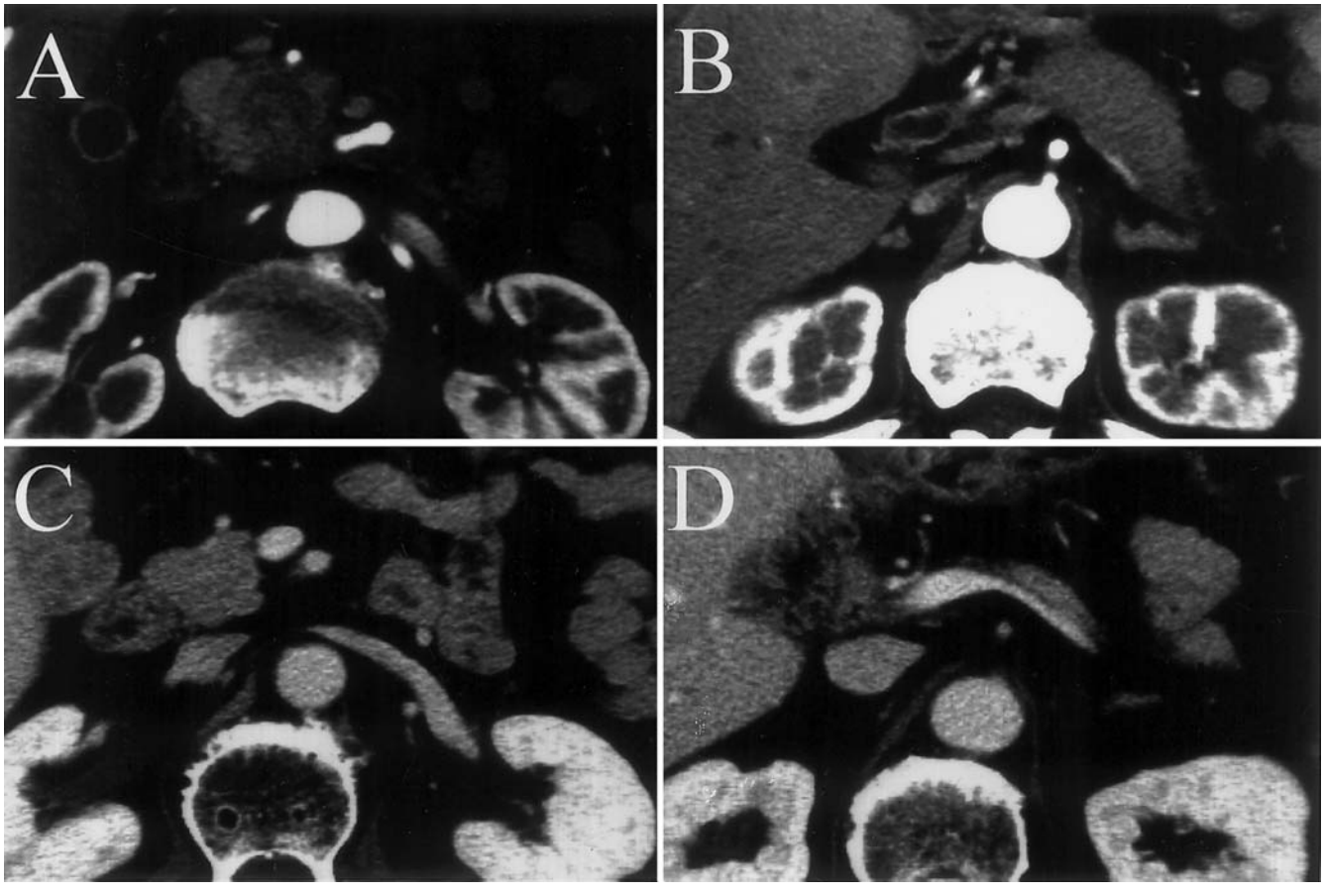


Fig. 8A–D. Enhanced abdominal CT scans before (**A**,**B**) and after steroid therapy (**C**,**D**). The pancreas showed marked regression of size

duct, resulting in obstructive jaundice,[6] AIP is therefore sometimes mistaken for pancreatic carcinoma. In fact, our patient was also diagnosed as having pancreatic carcinoma when he presented at the other hospital. Most patients with suspected AIP have been treated surgically. AIP is often associated with other autoimmune diseases, such as Sjögren's syndrome,[8] primary biliary cirrhosis,[9] primary sclerosing cholangitis,[9,10] and inflammatory bowel disease.[11–13] Although the precise mechanism underlying AIP is still controversial, the frequent association with autoimmune diseases supports the hypothesis that an autoimmune mechanism may be involved in the pathogenesis and pathophysiology of AIP.[14] A number of laboratory abnormalities, such as positivity for antinuclear antibody, hypergammaglobulinemia, and the presence of antibody to carbonic anhydrase have been shown to occasionally present in AIP patients.[15–17]

The present case fulfilled the characteristics listed in the criteria of AIP.[6] Nevertheless, although steroid therapy has been recognized as a primary treatment for AIP,[6,18] we performed an operation, because the possibility of carcinoma of the pancreas head and the lower common bile duct could not be completely ruled out. The wedge biopsy samples from the head and body of the pancreas revealed severe chronic pancreatitis with the infiltration of reactive lymphocytes, a finding which was compatible with AIP.

Steroid therapy was given in the majority of reported patients, soon after the diagnosis of AIP was made.[19] However, a limited amount of information has been available concerning the effectiveness of steroid for patients with complete obstruction of the common bile duct caused by AIP. Unfortunately, some of the reports on AIP patients with obstruction lack detailed information about the biliary tree, and therefore the extent of stenosis and/or obstruction of the biliary tree is unknown. This may be related to the face that the majority of AIP cases have been reported by gastroenterologists rather than by surgeons. Although no information concerning long-term follow up of patients with AIP with complete obstruction has been available, Kahl et al.[20] reported, in a series of patients with chronic pancreatitis associated with biliary stricture in whom endoscopic stenting was performed, that about half of the patients required surgery during a long-term follow up period. This evidence suggests the irreversibility of the biliary stricture occurring in chronic pancreatitis. These findings cannot be extrapolated to AIP, however, because steroid therapy has been shown to be effective for biliary stricture in AIP. Nonetheless, a relatively large series of AIP patients with associated biliary stenosis reported by Kamisawa et al.[1] indicated that, among 17 patients, 3 were treated with bypass, 6 with resection, and 6 with steroid therapy. Precise surgical indications and the determination of the operative procedure, however, were not documented in that report. It has been reported that some patients show no alleviation of biliary stenosis on steroid therapy, but there are also reported cases of remission of pancreatitis after the cessation or during the tapering of steroid therapy.[21] Angiography in these patients[21] indicated that none showed stenosis of the portal vein, but, rather, deviation was seen, in only four patients. While steroid therapy would have been attempted after biliary drainage in the present patient, the findings obtained by the imaging analyses could not ultimately rule out the possibility of pancreatic carcinoma, and this possibility could justify the surgical intervention. A similar case, of a patient with lymphoplasmacytic sclerosing pancreatocholangitis treated with pancreatoduodenectomy, has recently been reported.[22]

Although obstruction and/or stenosis of the lower common bile duct is frequently caused by carcinoma of the pancreas head, complete obstruction caused by chronic pancreatitis certainly occurs, although rarely. In fact, complete obstruction caused by AIP has not been reported in the previous literature, although associated biliary stenosis and/or obstructive jaundice have occasionally been reported.[1] Surgical interventions, such as biliary reconstruction and pancreatic resection, have been reported in some patients with AIP with bile duct stenosis.[1] In the present patient, because complete obstruction of the common bile duct and the resultant obstructive jaundice occurred initially, biliary drainage was performed, which was definitely an essential primary treatment. Although a severe form of pancreatic fibrosis sometimes occurs as a consequence of AIP and biliary obstruction and/or stenosis, whether biliary reconstruction is really necessary remains controversial. In the present patient, the lower common bile duct was completely obliterated by the fibrosis of the pancreas head. The final diagnosis was made by the wedge biopsy samples from the head and body of the pancreas, revealing severe chronic pancreatitis with the infiltration of lymphocytes. The normal pancreatic acinar cells were replaced by tissue showing severe fibrosis. At present, as long as the diagnosis of AIP with biliary stenosis is made, steroid therapy for the first 2 weeks may be the primary treatment, to check the effect on the biliary stenosis. If the effect on the biliary stenosis is insufficient, surgical intervention, including biliary reconstruction, should be considered, which could also be done to rule out the possibility of pancreatic carcinoma or carcinoma of the lower common bile ducts.

In summary, although it remains controversial whether biliary reconstruction is really necessary for AIP associated with complete biliary obstruction, the case reported here provides an insight into the pathogenesis and treatment of AIP associated with complete

biliary obstruction, in terms of different therapeutic strategies. The accumulation of further cases is required to determine the validity of surgical intervention.

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