J Gastroenterol 2002; 37:133–137

Journal of Gastroenterology

Case report

Autoimmune pancreatitis starting as a localized form

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Autoimmune pancreatitis is a rare type of pancreatitis that is characterized by diffuse swelling of the pancreas and irregular stenosis of the pancreatic ductal system ("sclerosing" pancreatitis), caused by autoimmune processes. Previous reports have shown the complete form of the disease, but very few have presented follow-up imagings from the beginning to the complete form. We, herein, report a case of autoimmune pancreatitis starting as a localized form. A-56-year-old Japanese man developed obstructive jaundice.

Ultrasonography showed a hypoechoic mass in the head of the pancreas, and endoscopic retrograde pancreatography (ERP) showed localized stenosis of the pancreatic duct in the head of the pancreas. Computed tomography (CT) showed enlargement, with a capsule-like rim, in the head of the pancreas. Internal biliary tube drainage was performed to relieve the obstructive jaundice. The patient was followed-up under the tentative diagnosis of localized "mass-forming" pancreatitis. Four months after the drainage, CT showed diffuse swelling of the pancreas, with a capsule-like rim, and ERP demonstrated diffuse irregular narrowing of the pancreatic duct. Glucose intolerance was noted for the first time. Steroid was given as a diagnostic treatment for autoimmune pancreatitis. Two months after initiation of the steroid treatment, the ERP findings were normal, and CT showed a normal pancreas. The biliary tube was removed, and the glucose intolerance was subsequently alleviated. To summarize, we report a case of autoimmune pancreatitis starting as localized "mass-forming" pancreatitis with a peripheral rim on imagings. It is very important to be well aware of the presence of the localized form of autoimmune pancreatitis.

Received: July 4, 2000 / Accepted: February 2, 2001
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Key words: "sclerosing" pancreatitis, autoimmune pancreatitis, "mass-forming" pancreatitis, steroid therapy

Introduction

Chronic pancreatitis usually shows irregular dilatation of the pancreatic ducts and atrophy of the pancreatic parenchyma. An atypical variant of chronic pancreatitis, characterized by swelling of the pancreatic parenchyma and diffuse irregular stenosis of the pancreatic ductal system, has been called "sclerosing" pancreatitis. This condition has often been reported to be related to an autoimmune process (autoimmune pancreatitis), and the efficacy of steroid therapy has been reported.[1–3] This condition is sometimes associated with Sjögren's syndrome. However, in some patients with autoimmune pancreatitis, typical imagings are shown but evidence of an autoimmune process is lacking. Most previous reports of autoimmune pancreatitis have described the completed state of the disease,[1–5] and few have reported its natural course. We report a case of autoimmune pancreatitis, starting as localized "mass-forming" pancreatitis, with a capsule-like rim shown on computed tomography. We briefly discuss the clinical implications of the disease.

Case report

Swelling of the pancreas was incidentally noted on ultrasonography (US) performed at the time of a medical check-up in a 56-year-old Japanese man. After 1 month, he had developed obstructive jaundice, and was admitted to the Department of Surgery and Oncology, Kyushu University Hospital, for further diagnosis and treatment. He had no history of habitual alcohol consumption, abdominal trauma, or autoimmune diseases

such as Sjögren's syndrome. A physical examination on admission revealed jaundice, but no other abnormal findings. Complete blood cell counts were within normal limits. Serum chemistry showed elevation of total bilirubin to 7.8 mg/dl (direct bilirubin, 5.3 mg/dl) and liver dysfunction, with alanine aminotransferase (ALT), 126 IU/l (normal range [NR], 13–33 IU/l), aspartate aminotransferase (AST), 190 IU/l (NR, 6–30 IU/l), gamma glutamyl transpeptidase (gamma-GTP), 549 IU/l (NR, 10–47 IU/l), and alkaline phosphatase (ALP), 1484 IU/l (NR, 115–359 IU/l). Serum amylase level was 121 IU/l (NR, 50–159 IU/l), and serum elastase 1 level was 1150 ng/dl (NR, 100–400 ng/dl). A serological examination showed mild elevation of IgG, to 2200 mg/dl (NR, 872–1815 mg/dl) and IgE, to 1008 IU/ml (NR, 0–240 IU/ml), with normal levels of IgA and IgM. The patient's fasting level of blood glucose was 97 mg/dl, and the 75-g oral glucose tolerance test (OGTT) result was normal. Serum levels of carcinoembryonic antigen and carbohydrate antigen 19-9 were not elevated. The N-benzol-L-*p*-aminobenzoic acid (BT-PABA) excretion value (pancreatic exocrine function test) was within normal limits, the value being 72.3% (normal value, >70%).

Abdominal US revealed a hypoechoic solid mass, measuring 5 × 4 × 3 cm, in the head of the pancreas, and dilatation of the suprapancreatic bile duct. Computed tomography (CT) revealed swelling of the pancreas, with this being shown more prominently in the head portion. A low-density capsule-like rim was shown in parts of the enlarged head of pancreas, near the duodenum and renal vein (Fig. 1). Calcification was absent. The main pancreatic duct in the body and tail was dilated. Magnetic resonance imaging (MRI) showed enlargement of the head of the pancreas, with low intensity shown on T1-weighted images and delayed enhancement shown on the dynamic study. Percutaneous transhepatic cholangiography (PTC) showed smooth tapering stenosis of the common bile duct in the intrapancreatic portion, and dilatation of the proximal part (Fig. 2). Percutaneous transhepatic biliary drainage (PTBD) was instituted. A cytologic examination of the bile drained was negative for malignant cells. Endoscopic retrograde pancreatography (ERP) showed a localized irregular stenosis of the main pancreatic duct in the head and tail of the pancreas (Fig. 3). Cytology of

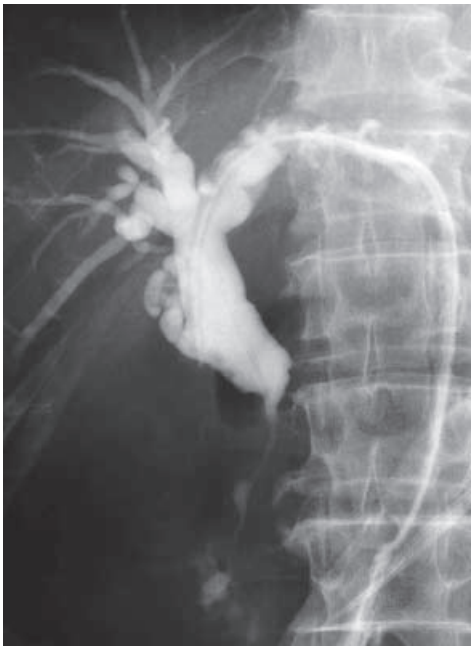

Fig. 2. Percutaneous transhepatic cholangiography (PTC) shows smooth tapering stenosis of the common bile duct in the intrapancreatic portion, with proximal dilatation

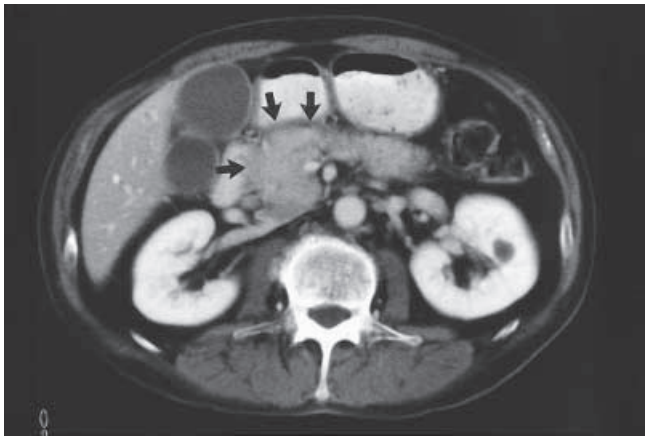

Fig. 1. Computed tomography (CT) reveals swelling of the pancreas, shown more prominently in the head. A low-density capsule-like rim (*arrows*) is shown in parts the enlarged head of the pancreas, near the duodenum and the renal vein

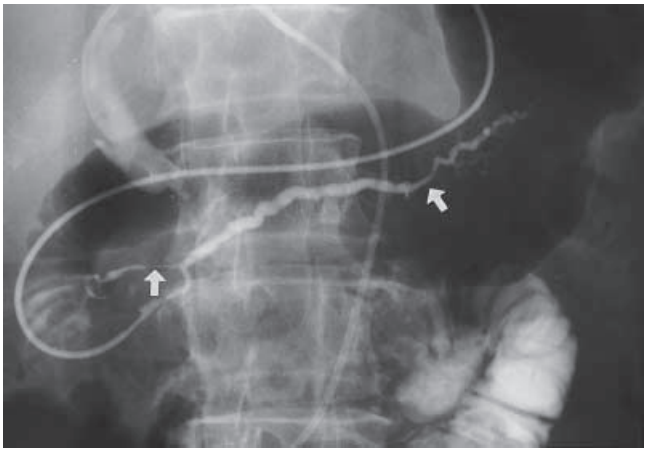

Fig. 3. Endoscopic retrograde pancreatography (ERP) shows localized irregular stenosis (*arrows*) of the main pancreatic duct in the head and tail of the pancreas

pancreatic juice obtained under secretin stimulation was also negative for malignant cells. Angiography showed hypervascularity in the head of the pancreas, with smooth encasement of the superior mesenteric, splenic, and portal veins. These US, MRI, and ERP findings suggested a diagnosis of "mass-forming" chronic pancreatitis, while CT indicated the presence of autoimmune chronic pancreatitis in the head of the pancreas. Immunological examination failed to reveal the presence of any autoimmune process. Autoantibodies were all negative, including anti-nuclear antibody, rheumatoid arthritis (RA) factor, anti-double-stranded DNA antibody, anti-mitochondrial antibody, anti-smooth muscle antibody, anti-ribonucleoprotein antibody, anti Sm antibody, anti-microsome antibody, anti-parietal cell antibody, and the lupus erythematosus (LE) test. Serum antibody to carbonic anhydrase II, which has been reported to be elevated in autoimmune pancreatitis, Sjögren's syndrome,[6] and autoimmune cholangitis,[7] was also negative. Therefore, a tentative diagnosis of localized "mass-forming" pancreatitis was made.

After PTBD, the patient's obstructive jaundice subsided, and the PTBD tube was buried in the skin for internal biliary drainage. The patient was followed-up at the outpatient clinic.

Follow-up imagings were obtained 4 and 12 months after he had been discharged. There were no marked changes in the imaging findings of the pancreas between the two follow-ups. ERP showed diffuse irregular narrowing of the main pancreatic duct (Fig. 4). CT showed diffuse swelling of the entire pancreas, with a peripheral rim (Fig. 5). US showed diffuse sausage-like swelling of the pancreas. Percutaneous needle biopsy of the pancreas showed marked fibrosis and mild chronic inflammatory cell infiltration, with scattered eosinophils (Fig. 6). All these findings strongly suggested a diagnosis of autoimmune pancreatitis. At the 12-month follow-up, the 75-g OGTT result showed a diabetic pattern for the first time. Thus, we decided to give oral prednisolone, at a dose of 30 mg/day. ERP 2 months after the initiation of the steroid treatment showed that the diffuse stenosis of the pancreatic duct was alleviated (Fig. 7), and CT showed that the swelling of the pancreas was reduced (Fig. 8). Serum levels of immunoglobulin (IgG and IgE) had declined to normal levels (Table 1). Liver function (AST, ALT, and ALP levels) was normalized, the results of the 75-g OGTT had improved, and the PTBD tube was removed. The patient is now well, with continuing steroid therapy (prednisolone, 10 mg/day).

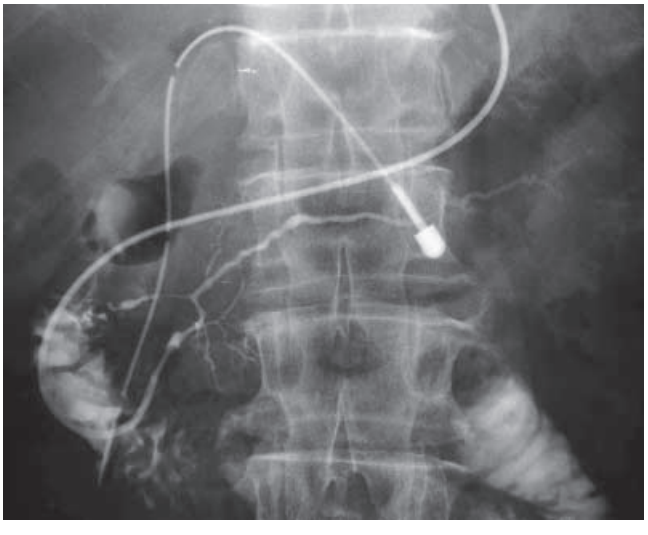

Fig. 4. Follow-up ERP shows diffuse irregular narrowing of the main pancreatic duct throughout the pancreas

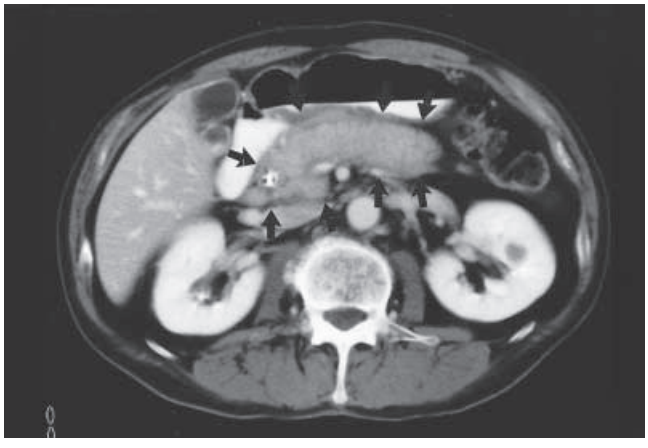

Fig. 5. Follow-up CT shows diffuse swelling of the entire pancreas, with a capsule-like rim (*arrows*)

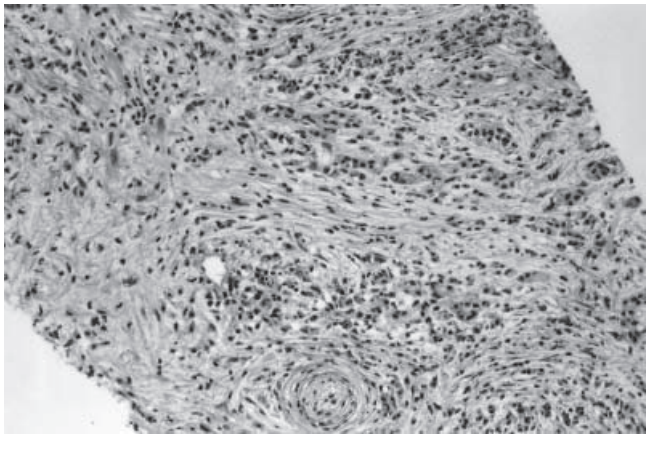

Fig. 6. A biopsy specimen shows fibrosis of the pancreatic parenchyma, with chronic inflammatory cell infiltrates. Original magnification ×100

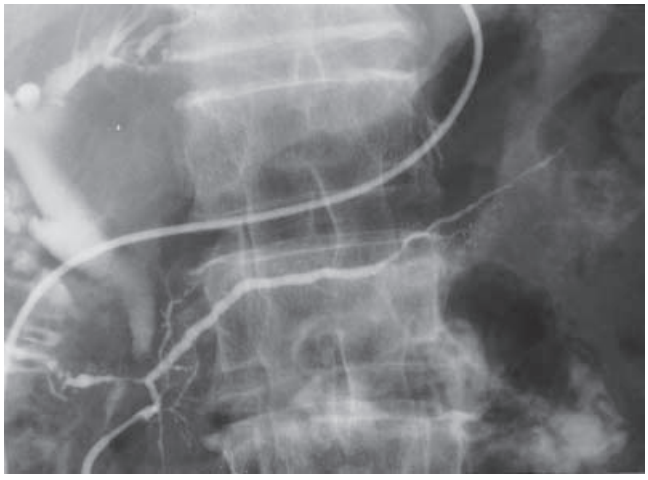

Fig. 7. ERP 2 months after the initiation of steroid therapy shows that the diffuse stenosis of the pancreatic duct has been alleviated

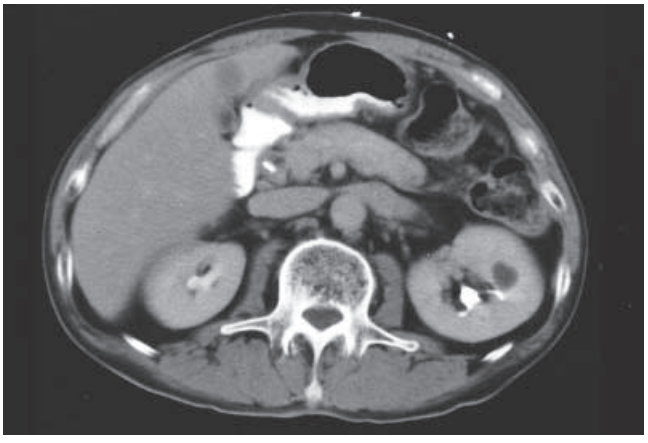

Fig. 8. CT 2 months after the initiation of the steroid therapy shows that the swelling of the pancreas is reduced

Table 1. Serial laboratory findings (normal ranges)

Date	1998/6/24	1998/7/29	1998/12/4	1999/6/18	1999/7/6	1999/8/2	1999/9/1
IgG (872–1815 mg/dl)			2200	2058	2192	1275	1021
IgE (0–240 IU/ml)					1008	887	311
Tbil (0.3–1.2 mg/dl)	7.8	1.3	0.6	0.5	0.5	0.3	0.8
AST (13–33 U/l)	126	56	34	21	20	35	22
ALT (6–30 U/l)	190	76	35	13	22	41	28
ALP (115–359 U/l)	1484	768	497	386	324	375	247
γ-GTP (10–47 U/l)	549	109	89	21	35	68	
		↑ PTBD			← PSL 30 mg	25	20	15	10 →

Tbil, Total bilirubin; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; γ-GTP, gamma glutamyl transpeptidase; PTBD, percutaneous transhepatic biliary drainage; PSL, prednisolone

Discussion

Autoimmune pancreatitis, a special variant of chronic pancreatitis, is characterized by swelling of the pancreatic parenchyma and diffuse irregular stenosis of the pancreatic ductal system, based on autoimmune processes. Sarles et al.[8] reported this special form of chronic pancreatitis as primary inflammatory sclerosis of the pancreas, possibly caused by autoimmune phenomena. When the autoimmune process is evident, the disease is called autoimmune pancreatitis. "Sclerosing" pancreatitis is a morphological diagnosis, while autoimmune pancreatitis is a diagnosis based on pathogenesis.

Yoshida et al.[1] proposed that chronic pancreatitis with the following characteristics should be referred to as autoimmune pancreatitis; (1) increased serum gammaglobulin or IgG levels; (2) presence of autoantibodies; (3) diffuse enlargement of the pancreas; (4) diffuse irregular narrowing of the main pancreatic duct on endoscopic retrograde cholangiopancreatography (ERCP); (5) fibrotic change with lymphocyte infiltration by histopathology; (6) no symptoms, or only mild symptoms, usually with an absence of acute attacks of pancreatitis; (7) common bile duct in the pancreas constricted, with dilation of the bile duct upstream, often with cholestatic liver dysfunction and hyperbilirubinemia; (8) no pancreatic calcification; (9) no pancreatic cysts; (10) occasional association with other autoimmune diseases; and (11) effectiveness of steroid therapy. In the present patient, the serum concentrations of IgG and IgE were elevated, and the morphological features were compatible with those of autoimmune pancreatitis, but no autoantibodies were positive. Thus, the patient was conclusively diagnosed as having autoimmune pancreatitis.

Irie et al.[9] reviewed the imaging findings of five patients with autoimmune pancreatitis and reported that a "capsule-like rim" on CT was diagnostic of au-

toimmune pancreatitis. This capsule-like rim corresponds to peripancreatic inflammation. In the present patient, initially, a capsule-like rim was clearly evident in the head of the pancreas, in which there was swelling and irregular stenosis of the pancreatic duct. On follow-up imagings, the morphological changes progressed from the head of the pancreas to the entire pancreas. Okazaki et al.[5] reported seven patients with localized stenosis of the pancreatic duct, and they suggested that this could be part of the manifestation of autoimmune pancreatitis, or a temporary process proceeding to diffuse stenosis of the pancreatic duct. However, they did not demonstrate the morphologic progression of the disease. Some autoimmune pancreatitis may start as a localized disease. Autoimmune pancreatitis should be differentiated from diffuse pancreatic carcinoma, while the localized type of autoimmune pancreatitis should be distinguished from "mass-forming" pancreatitis and pancreatic carcinoma. The capsule-like rim around the enlarged pancreas may be diagnostic of autoimmune pancreatitis in the early phase.

From the clinical point of view, steroid treatment is indicated for autoimmune pancreatitis. However, there is still controversy about the effectiveness of the steroid treatment, as well as controversy about the timing of its discontinuance when it has been proved effective. Some authors have reported that, after the steroid was discontinued, the pancreatitis deteriorated again,[3,10] and others have reported that, after the discontinuance, pancreatitis did not recur.[2] In the present patient, the morphologic changes in the pancreas, the liver dysfunction, the glucose intolerance, and the biliary stenosis were alleviated by the steroid treatment, and serum levels of IgG and IgE and pancreatic endocrine function were improved. The steroid treatment was initially 30 mg/day, for 3 weeks, and followed by 25 mg/day for 1 week, 20 mg/day for 2 weeks, 15 mg/day for 2 weeks, and then, finally, 10 mg/day. The steroid treatment will be discontinued 6 months after its start, and careful follow-up will be carried out thereafter.

Other concomitant autoimmune diseases have been reported in patients with autoimmune pancreatitis. Kawaguchi et al.[11] reported possible autoimmune pancreatitis in two patients with primary sclerosing cholangitis. In both patients, ERP showed diffuse narrowing of the main pancreatic duct, and histological findings of the pancreas revealed lymphoplasmacytic infiltration, interstitial fibrosis with acinar atrophy, and periductal inflammation with obliteration or stenosis of the pancreatic ducts. Montefusco et al.[12] also reported a combination of primary sclerosing cholangitis, autoimmune pancreatitis, and Sjögren's syndrome. In the present patient, the smooth narrowing of the common bile duct was probably caused by inflammatory enlargement of the head of the pancreas, and not by primary sclerosing cholangitis, because the stenosis was limited to the distal common bile duct in the head of the pancreas.

In the present communication, we have reported a case of autoimmune pancreatitis in a patient in whom progression of the disease was traced on imagings. It is very important to be well aware of the possibility of the localized form of autoimmune pancreatitis in order to avoid unnecessary surgery.

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