Background: Autoimmune pancreatitis (AIP) is a unique form of chronic pancreatitis that is characterized by swelling of the pancreas, narrowing of the main pancreatic duct (MPD), elevation of serum gamma globulin, or immunoglobulin G or presence of autoantibody, lymphoplasmacytic infiltration and dense fibrosis on histopathology. It is responsive to steroid therapy. The incidence of AIP can reach 5–6% of chronic pancreatitis. It can present as obstructive jaundice, body weight loss, and pancreas head mass mimicking pancreatic cancer. The recognition of AIP can avoid major surgery such as pancreatic resection.

Methods: From May 2003 to July 2007, a total of 5 cases of AIP were reviewed retrospectively. The diagnosis was made on imaging study, serology, steroid response and/or histology if surgery was carried out.

Results: There were 2 male and 3 female patients, with a mean age of 61 (39–75) years. Atypical AIP was found in the first case and typical AIP in the remaining 4. The presenting clinical pictures were mild epigastric pain, obstructive jaundice, and loss of body weight in 4 cases, with associated autoimmune disease in 1. Diffuse or long segmental enlargement of the pancreas without peripancreatic fat infiltration was found in all patients except 1 who only had focal pancreatic head enlargement. Distal common bile duct (CBD) stricture was seen in 4 cases and the median CBD stricture length was 1.2 (0.5–2.5) cm. Multiple narrowing of the whole MPD was seen in 2 cases, focal narrowing of the MPD in 2 and long segmental narrowing of the MPD in 1. Serum immunoglobulin G tests were done in 4 cases and were elevated in all. Antinuclear antibody was positive in 3. The first case was operated on after a preoperative diagnosis of suspicious pancreatic head tumor. The subsequent 3 cases were diagnosed correctly as AIP. The last case presented with distal CBD stricture and hypoechoic lesion in the pancreas head on endoscopic ultrasound, with only borderline pancreatic enlargement on computed tomography, and he was operated on. Retrospective endoscopic retrograde pancreatogram review revealed MPD narrowing in the pancreatic body. Endoscopic retrograde brush cytology was performed and was negative for malignancy in 3 cases. Steroid therapy was given in 3 and was responsive, but there were 2 recurrences.

Conclusion: AIP should be a differential diagnosis in distal CBD stricture and pancreatic head mass when the patient has: (1) diffuse or long segmental enlargement of the pancreas without peripancreatic fat infiltration, with multiple narrowing of the MPD without much upstream dilatation, or narrowing of the MPD not corresponding to the region of CBD stricture; and (2) abnormal immunoserologic tests. [J Chin Med Assoc 2008;71(1):14–22]

Key Words: antinuclear antibody, autoimmune chronic pancreatitis, common bile duct stricture, immunoglobulin G
Autoimmune chronic pancreatitis

pancreas-related symptoms such as mild epigastric pain, loss of body weight, obstructive jaundice, and extra-pancreatic symptoms such as associated autoimmune diseases like Sjögren’s syndrome, rheumatoid arthritis, inflammatory bowel disease, and retroperitoneal fibrosis. It can present as an atypical form of AIP with focal pancreatic mass mistaken as pancreatic cancer. One quarter of Whipple resection (benign cases) was due to AIP in North America, so by recognizing the disease, major surgery can be avoided. Herein, we report our experience with 5 cases of AIP.

Methods

From May 2003 to July 2007, a total of 5 cases of AIP (with no alcohol history) were reviewed retrospectively. The diagnosis was made on imaging study and one of the following criteria: serology, steroid response and histology if surgery was carried out. Computed tomography (CT), endoscopic retrograde cholangiopancreatography (ERCP), and serology for antinuclear antibody (ANA) were performed in all 5 cases. Serum immunoglobulin (Ig) G was measured in 4 cases, endoscopic retrograde brush cytology (ERBC) in 3, and endoscopic transpapillary biopsy (ETPB) from distal common bile duct (CBD) in 2. Enlarged pancreas was considered if the anteroposterior diameter of the pancreas was greater than 2 cm on CT.

Results

There were 2 male and 3 female patients, with a mean age of 61 (39–75) years. The clinical pictures, associated autoimmune disease, image pattern of the pancreas, main pancreatic duct (MPD), length of distal CBD stricture, serology results, steroid outcome, and follow-up duration are shown in Table 1.

In the first case (Figure 1), total bilirubin was 6.6 mg/dL, carcinoembryonic antigen (CEA) was 2.8 ng/L (upper limit, 5 ng/L), CA19-9 was 109 U/mL (upper limit, 33 U/mL), and ANA was positive at 1:320. She was operated on after a preoperative diagnosis of suspicious pancreatic uncinate process tumor, distal CBD stricture, obstructive jaundice and with a biliary stent in situ. She was operated on after a preoperative diagnosis of suspicious pancreatic uncinate process tumor, distal CBD stricture, obstructive jaundice and with a biliary stent in situ. Intraoperative biopsy showed fibrosis, lymphocyte infiltration, small pancreatic duct destruction and obliterative phlebitis (Figure 2), and pancreas resection was not performed. She was given steroid therapy (prednisolone 40 mg/day for 1 week, followed by 5 mg reduction/week). The MPD and
CBD stricture resolved after 8 weeks (by ERCP), and she then maintained good response for 4 years.

The subsequent 3 cases were diagnosed as AIP without operation. The second case (with distal CBD stricture and obstructive jaundice; Figure 3) had total bilirubin of 2.9 mg/dL, CEA of 2.9 ng/L, CA19-9 of 83.8 U/mL, and negative ANA. He was given steroid therapy (same dose as Case 1) but the clinical

![Figure 1](image1.jpg)

**Figure 1.** (A) Computed tomography shows a focal mass in the pancreas head region (arrow). (B) ERC shows distal stricture (arrow). (C) ERP reveals multiple narrowing of the main pancreatic duct (arrows). (D) Resolved main pancreatic duct narrowing after steroid therapy.

![Figure 2](image2.jpg)

**Figure 2.** (A) Histology shows fibrosis (arrow). (B) Obliterative phlebitis (arrow).
The course was complicated by *Candida* esophagitis in the 3rd week of steroid therapy, resulting in reduced steroid dosage (20 mg/day from the 4th week, with a reduction of 7.5 mg/week). The distal CBD stricture resolved after 8 weeks of steroid therapy but recurred 5 months later. Given his associated comorbid diseases (ischemic heart disease, diabetes mellitus), risk of fluid retention with higher dose of steroid, and reluctance to undergo repeated endoscopic procedure, he underwent biliary metallic stent insertion. He was stable for 2 years until he died of intracranial hemorrhage due to head injury.

The third case (Figure 4) had narrowing of the MPD in the body and tail regions, without CBD stricture. ANA was positive with a titer of 1:160, and Sjögren’s syndrome was diagnosed in our rheumatology department. Her CEA was 1 ng/L and CA19-9 was 4.2 U/mL. No steroid was given, and the process remained stable for 3.5 years.

The fourth case, with typical imaging pictures (swelling of pancreas without peripancreatic fat infiltration and narrowing of the MPD), presented with ANA positive at 1:160, CEA of 4.2 ng/L, and CA19-9 of 2.5 U/mL. She had steroid therapy (prednisolone...
30 mg/day due to small body weight, with a reduction of 5 mg/week) with improved CBD obstruction, but recurrence of CBD stricture (by abdominal ultrasound) and elevation of liver function test were seen after 3 months.

The last case (Figure 5) presented with distal CBD stricture for 2 months with borderline pancreas enlargement on CT. Endoscopic ultrasound (EUS) demonstrated a hypoechoic lesion in the pancreatic head region, endoscopic retrograde pancreatogram
(ERP) revealed normal MPD in the head region. The patient was operated on under the impression of suspicious intrapancreatic CBD tumor. The CEA level was 1.6 ng/L, CA19-9 was 42.3 U/mL, and ANA was negative. Histology showed lymphoplasmacytic infiltration, fibrosis without fat necrosis, ductal dilatation, and stone (Figure 6). Retrospective review of ERP of the last case showed that he had focal narrowing of the MPD at the body region.

ERBC was performed in 3 cases; all were negative for malignancy. The median follow-up duration was 24 (2–48) months. Cases 2, 4 and 5 had diabetes mellitus, but no other symptoms such as steatorrhea.

Discussion

There are 4 types of diagnostic criteria for AIP: the revised Japanese and Kim et al’s criteria9,21 emphasize imaging study, whereas the Mayo Clinic’s HISORt criteria (histology, imaging, serology, other organ involvement, and its response to steroid therapy) and Italian criteria23,24 focus on histology. In HISORt and the revised Japanese criteria,21,23 atypical form or focal type of AIP or tumefactive pancreatitis are included.25–28 The diagnoses of our cases fit with the revised Japanese and Kim et al’s criteria9,21 in imaging study of pancreatic enlargement (either diffuse or focal), MPD narrowing (focal or multiple) and any one of the following such as serology or pathology or response to steroid. There is no international consensus with regard to the diagnostic criteria for AIP. For practical purposes, the revised Japanese and Kim et al’s criteria would be more useful as they focus on imaging studies. The revised Japanese criteria added focal enlargement of the pancreas, and steroid response was included in Kim et al’s criteria.

We had 2 male and 3 female patients with a mean age of 61 years. In the literature, males are twice as common as females, and they are usually more than 50 years old.9 Our female predominance may be due to the small number of cases. Obstructive jaundice and mild abdominal pain were found in 4 of 5 cases in our series, while jaundice was seen in 63% and abdominal pain in 35% from Kim et al’s cases.9 We had 1 case associated with Sjögren’s syndrome. The incidence
and types of associated autoimmune disease vary with different studies, ranging from 20% in Kim’s group up to 50% in an Italian study.6,24 In the Italian study, about half of the associated autoimmune disease was diagnosed before the onset of AIP, while the remaining half was diagnosed during the follow-up period.1 The most common associated autoimmune diseases were inflammatory bowel disease in Western literature,24 rheumatoid arthritis and sialoadenitis in the Japanese study, and retroperitoneal fibrosis in Kim et al’s series.29

The CT images in AIP include diffuse or focal enlargement of the pancreas with delayed homogeneous enhancement of focal mass or capsule like low-density ring. The pancreatogram pictures were of diffuse or focal narrowing of the MPD without much upstream dilatation.30,31 We had diffuse pancreatic enlargement in 2 cases, long segment enlargement in 2 and focal pancreatic enlargement in 1; we did not have the delayed homogeneous enhanced parenchyma or ring picture as mentioned in the literature.30,31 We had diffuse narrowing of the MPD in 2 cases, long segment narrowing of the MPD in 1 and focal narrowing of the MPD in 2 without much upstream dilatation. In the fifth case, EUS detected a hypoechoic mass in the pancreatic head region but with no MPD stricture in that region; the patient was diagnosed with intrapancreatic CBD tumor and was operated on. Retrospectively, he did have MPD narrowing in the body region and elevated IgG, and together with the pathology results, he was finally diagnosed with AIP.

With EUS, hypoechoic mass could be found in 6 of 14 cases.17 Serum IgG4 was included in Kim et al’s, HISTORt’s, and the revised Japanese criteria for the diagnosis of AIP. IgG4 is more sensitive than IgG in AIP patients (73.3% vs. 54.3%), and was elevated in 20% of AIP patients without IgG elevation in Kim et al’s experience.9 Kawa and Hamano reported that the sensitivity of IgG was 70.5% and that of IgG4 was 90.9% in AIP.32 In the literature, the sensitivity of IgG4 can range from 67% to 71%,33,34 Elevated IgG4 is associated with more extrapancreatic organ involvement.34 Autoantibody test was positive in 2 of 31 AIP patients who had no elevation of IgG or IgG4,29 and was included in Kim et al’s and the Japanese criteria.

On histology, our first and fifth cases had lymphoplasmacytic infiltrations and fibrosis which were included in the Japanese and Kim et al’s criteria. Such histologic findings were not specific to AIP and could also be found in 88% of alcoholic chronic pancreatitis.35 The severity of lymphoplasmacytic infiltration was dependent on the activity and stage of the disease and could be minimal in 1 third of AIP patients.36 Lymphoplasmacytic sclerosing pancreatitis (LPSP) and more than 10 positive IgG4 cells per high power field can be the sole diagnostic criterion for AIP in the HISTORt (Mayo Clinic) criteria.23 LPSP is characterized by dense periductal infiltration of lymphocytes, plasma cells, perilobular, intralobular fibrosis, obliterative phlebitis and a lack of the changes seen in other chronic pancreatitis such as ductal dilatation, stones, and fat necrosis. But these findings need a larger tissue specimen, at least more than a wedge biopsy,37 and therefore has less clinical practicality. Only 8 of 14 AIP patients who underwent EUS-guided trucut biopsy had the pictures of dense lymphoplasmacytic infiltration and positive IgG4 stained cells of more than 10 cells per high power field.38 Also, the diagnosis of LPSP required a skilled pathologist, and only 6 of 31 cases of LPSP were correctly diagnosed the first time round,37 and obliterative phlebitis could be easily missed unless elastic special stain is used. Regarding positive IgG4 cells on histology, only 37% of AIP patients had such findings, and they could also be found in 25% of alcoholic chronic pancreatitis.39

In cases without preoperative suspicion of AIP, the diagnosis of AIP can still be possible by solely depending on histology using the HISTORt (Mayo Clinic) criteria.

Steroid was given in 3 cases with 2 recurrences in our series. Our third case had only narrowing of the MPD in body and tail with no CBD stricture, and the fifth case underwent Whipple’s operation; therefore, no steroid was given in these 2 cases. Pancreatic enlargement and biliary strictures can improve spontaneously in some AIP.8 Pancreatic enlargement and narrowing of the MPD can improve with steroid therapy in almost all patients, though some irregularity of the MPD and side branches can remain.40 CBD stricture can improve with varying degrees and biliary drainage tube can be removed in almost all patients.40 Extrapancreatic lesions such as salivary gland and lymph node enlargement, and retroperitoneal fibrosis can improve with steroid therapy.41

Recurrence after steroid therapy ranged from 6% to 31%.9,42 The reason for recurrence in our second case was probably due to lower steroid dose owing to the complication of esophageal Candidiasis. Zambonni et al also reported a recurrence rate of 67% (2 of 3 cases) with steroid therapy.43 For those with recurrence, high-dose steroid should be re-administered.40 Steroid is effective and indicative, particularly in those with CBD stricture or positive immunoserologic results.8

The following points can be used to differentiate AIP from alcoholic chronic pancreatitis. AIP usually
does not cause severe pain, the enlarged pancreas usually has no or only mild peripancreatic fat infiltration, and phlegmonous changes, peripancreatic fluid and pseudocysts are rare, whereas alcoholic chronic pancreatitis may have calcification and calcificoliths. ERP in AIP usually shows diffuse or segmental MPD narrowing without much upstream dilatation of the MPD or side branches. With steroid therapy, the narrowing of the MPD will show a response in 2 weeks.

In conclusion, AIP should be considered in the differential diagnosis in distal CBD stricture and pancreatic head mass when the patient has: (1) diffuse or long segmental enlargement of the pancreas without peripancreatic fat infiltration, with multiple narrowing of the MPD without much upstream dilatation, or narrowing of the MPD not corresponding to the region of CBD stricture; and (2) abnormal immunoserologic tests.

References


