

CASE REPORT

A Case of Autoimmune Pancreatitis Associated with Retroperitoneal Fibrosis

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ABSTRACT

Context Autoimmune pancreatitis is characterized by diffuse enlargement of the pancreas, diffuse irregular narrowing of the main pancreatic duct, severe lymphoplasmacytic infiltration and fibrosis of the pancreas. Retroperitoneal fibrosis may occasionally be associated with autoimmune pancreatitis.

Case report We report a 77-year-old man with autoimmune pancreatitis associated with retroperitoneal fibrosis. Abdominal ultrasonography and computed tomography demonstrated diffuse enlargement of the pancreas and a capsule-like rim. Furthermore, a retroperitoneal mass was recognized anterior to the abdominal aorta. Antinuclear antibody, IgG and IgG4 values were elevated. Therefore, this patient was diagnosed as having autoimmune pancreatitis associated with retroperitoneal fibrosis. We performed steroid therapy using prednisolone. After 4 weeks, both IgG and IgG4 values decreased and both the swelling of the pancreas and also the retroperitoneal mass were obviously diminished.

Conclusion This is a rare case of autoimmune pancreatitis associated with retroperitoneal fibrosis.

INTRODUCTION

Autoimmune pancreatitis is a new entity characterized by diffuse enlargement of the pancreas, diffuse irregular narrowing of the main pancreatic duct, increased levels of serum gammaglobulin or immunoglobulin G, the presence of antibodies, and severe lymphoplasmacytic infiltration and fibrosis of the pancreas [1, 2, 3, 4, 5, 6, 7]. Retroperitoneal fibrosis is an uncommon entity which usually originates in the retroperitoneal space [8, 9]. It is documented that retroperitoneal fibrosis is rarely associated with autoimmune pancreatitis [10, 11, 12, 13, 14, 15], but there have been a few cases reported of retroperitoneal fibrosis treated by steroid therapy [12, 13, 14]. We report a rare case of autoimmune pancreatitis associated with retroperitoneal fibrosis in which both lesions improved in response to steroid therapy.

CASE REPORT

A 77-year-old man consulted a local hospital because of abdominal discomfort and appetite loss in June 2003. Abdominal computed tomography (CT) showed pancreatic swelling, suggesting pancreatic cancer. Therefore, he was referred to our hospital for closer examination and treatment.

There was no jaundice or abdominal tenderness. He was a heavy drinker (ethanol

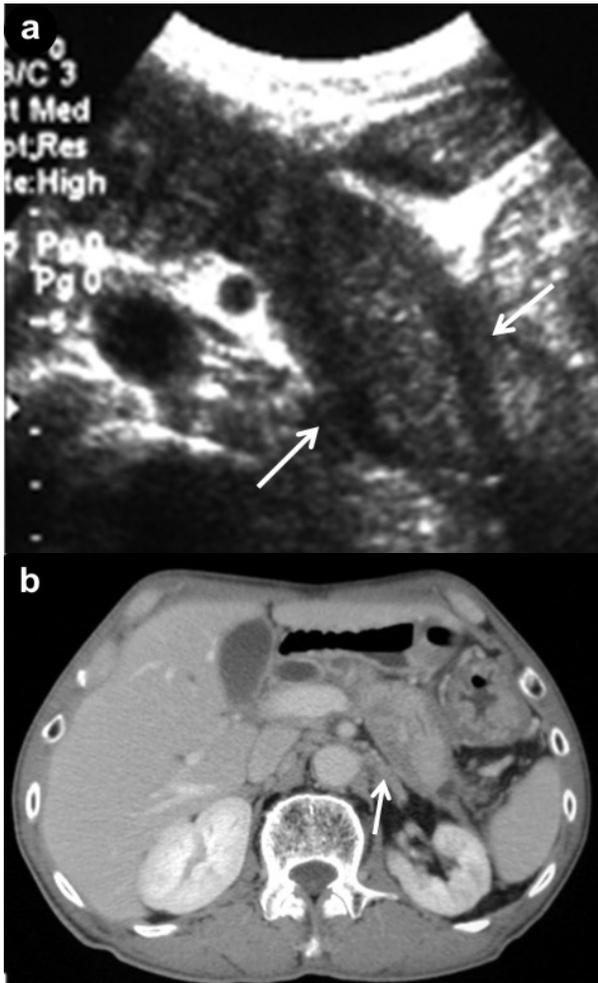


Figure 1. Abdominal ultrasonography (a.) and computed tomography (b.) showing diffuse enlargement of the pancreas and capsule-like rim, with a low echo on US (a. arrows) and a low density on CT images (b. arrow).

135 g/day for 20 years). Biochemical tests showed the following: alkaline phosphatase (ALP) and gamma-glutamyl transpeptidase (GGT) elevated to 1,322 IU/L (reference range: 115-359 IU/L) and 354 IU/L (reference range: 11-48 IU/L), respectively, although aspartate aminotransferase (AST 25 IU/L, reference range: 10-48 IU/L), alanine aminotransferase (ALT 36 IU/L, reference range: 3-50 IU/L) and lactate dehydrogenase (LDH 213 IU/L, reference range: 120-214 IU/L) were normal. Pancreatic enzymes were elevated: amylase 183 IU/L (reference range: 40-113 IU/L), lipase 140 IU/L (reference range: 11-53 IU/L), and elastase 1 1,100 ng/dL (reference range: 0-400 ng/dL). Immunological tests were elevated: antinuclear antibody x80, IgG 2,160 mg/dL

(reference range: 870-1,700 mg/dL), IgG4 348 mg/dL (reference range: 0-135 mg/dL) and rheumatoid factor 157 IU/mL (reference range: 0-20 IU/mL), although other autoantibodies including antimitochondrial antibody (AMA), anti SS-A antibody, anti SS-B antibody, perinuclear-antineutrophil cytoplasmic antibody (P-ANCA) and cytoplasmic-antineutrophil cytoplasmic antibody (C-ANCA) were negative. As far as serum tumor markers were concerned, carcinoembryonic antigen (CEA) was elevated to 10.6 ng/mL (reference range: 0-5 ng/mL) while carbohydrate antigen 19-9 (CA 19-9) was normal. The HLA haplotype was DRB1*0405-DQB1*0401.

Abdominal ultrasonography (US) and CT demonstrated diffuse enlargement of the pancreas (Figure 1). A capsule-like rim was also recognized around the pancreas, showing a low echo on US and low density with delayed enhancement on CT images (Figures 1 and 2). The rim was hypointense on both T1 and T2-weighted magnetic resonance imaging (MRI). Furthermore, a retroperitoneal low density mass 20x5 mm in diameter was recognized anterior to the abdominal aorta with delayed enhancement on CT image (Figure 2). Although we examined the ureteral system on ureterography, hydronephrosis was not demonstrated. Endoscopic retrograde cholangiopancreatography (ERCP) demonstrated diffuse narrowing of the main pancreatic duct. Furthermore, marked stenosis of the

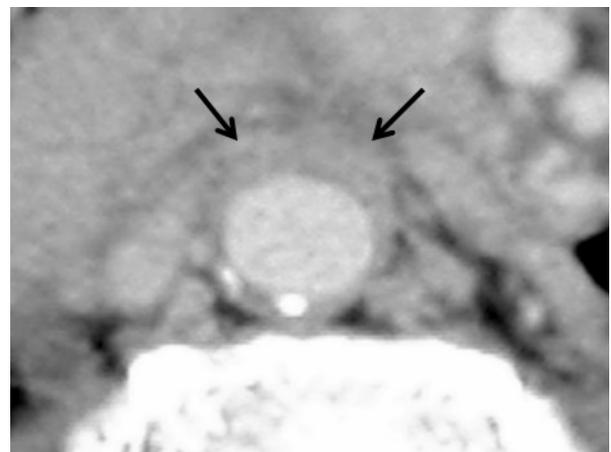


Figure 2. A retroperitoneal mass (arrows) was recognized anterior to the abdominal aorta on computed tomography.

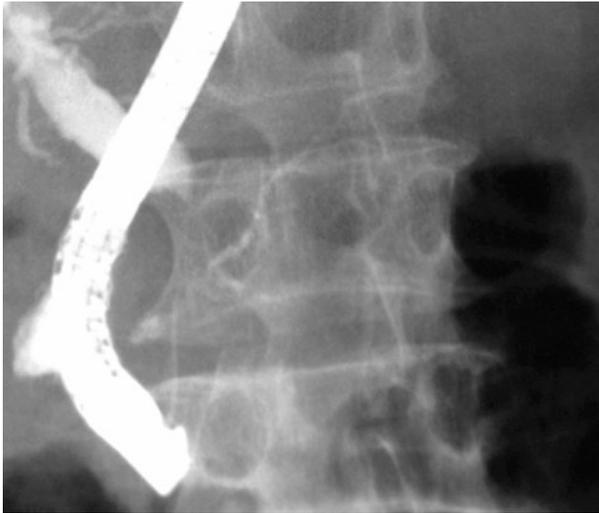


Figure 3. Endoscopic retrograde cholangiopancreatography demonstrated diffuse narrowing of the main pancreatic duct and marked stenosis of the lower common bile duct.

lower common bile duct and dilatation of the upper common bile duct (12 mm in diameter) and intrahepatic bile duct were recognized at ERCP (Figure 3).

We diagnosed this case as autoimmune pancreatitis associated with retroperitoneal fibrosis. In this case, there were no other extrapancreatic lesions, such as sclerosing cholangitis, orbital pseudotumor, and Riedel's thyroiditis. We performed steroid therapy using prednisolone 30 mg daily for 4 weeks after which we reduced the dose by 5 mg every 2 weeks until the daily dose reached 5 mg. After 4 weeks, the pancreatic and biliary ductal enzymes, such as amylase, lipase, elastase 1, ALP, and GGT had gradually decreased. Furthermore, both serum IgG and IgG4 levels decreased (IgG 1,020 mg/dL; IgG4 170 mg/dL). In addition, the swelling of the pancreas decreased and the retroperitoneal mass diminished to 15x2 mm in diameter in abdominal US and CT (Figure 4ab). Furthermore, the diffuse narrowing of the main pancreatic duct and the stenosis of the lower common bile duct improved, and the dilatation of the upper common bile duct was reduced to 10 mm in diameter at ERCP (Figure 4c). At present, the patient is taking prednisolone 5 mg daily. The pancreas is atrophic and the retroperitoneal mass is almost not visible at CT. The diameter of the

main pancreatic duct and the common bile duct improved to within the normal range in magnetic resonance cholangiopancreatography (MRCP). There has been no recurrence or worsening for 3 years since the onset of the autoimmune pancreatitis.

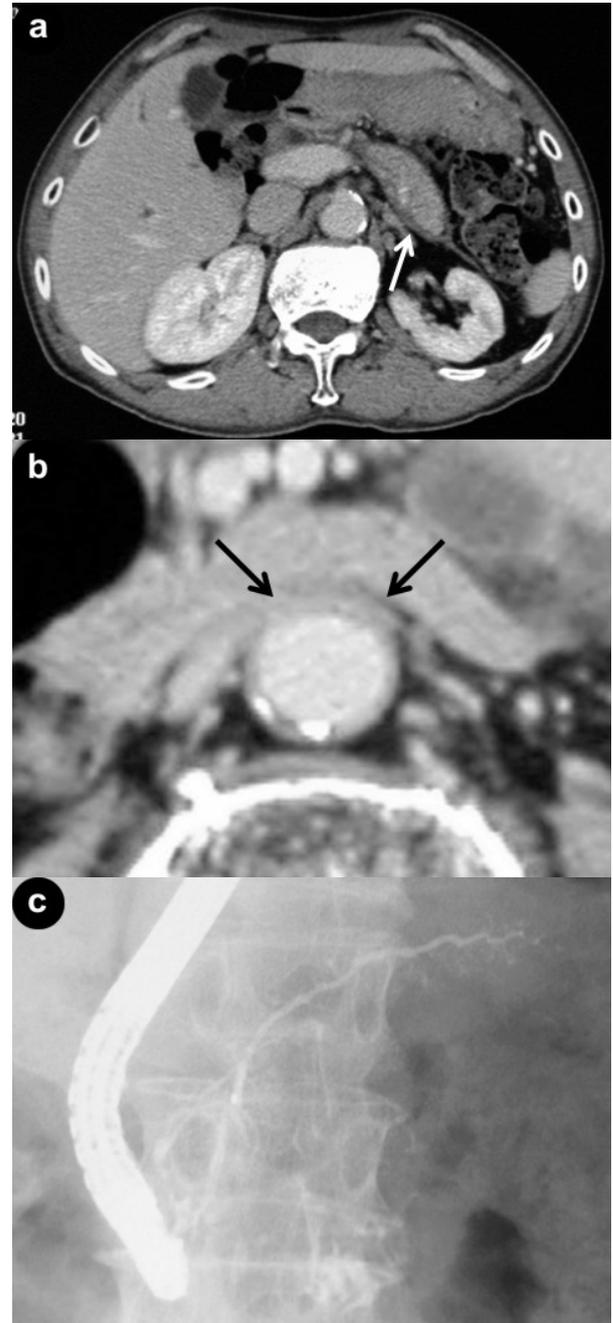


Figure 4. Both the swelling of the pancreas with capsule-like rim (a.) and also the retroperitoneal mass were obviously improved on abdominal computed tomography (b. arrow). Furthermore, stenosis of the main pancreatic duct showed improvement on endoscopic retrograde cholangiopancreatography (c.).

DISCUSSION

In 1961, Sarles *et al.* described a type of chronic pancreatitis, which might be caused by an autoimmune mechanism and which has been termed chronic inflammatory sclerosis [1]. Toki *et al.* reported chronic pancreatitis showing diffuse irregular narrowing of the main pancreatic duct [2]. Yoshida *et al.* proposed the concept of autoimmune pancreatitis in 1995 [3]. Autoimmune pancreatitis is a new entity characterized by diffuse enlargement of the pancreas, diffuse irregular narrowing of the main pancreatic duct, increased levels of serum gamma-globulin or immunoglobulin G, the presence of antibodies, and severe lymphoplasmacytic infiltration and fibrosis of the pancreas [4, 5, 6, 7].

It has been reported that the serum IgG4 level in patients with sclerosing pancreatitis is significantly higher than that in patients with pancreatic cancer, and IgG and IgG4 levels are both significantly higher before steroid therapy than after four weeks of such therapy [16]. IgG4 is a useful marker for distinguishing autoimmune pancreatitis from other diseases of the pancreas, such as pancreatic cancer. In the present case, both serum IgG and IgG4 levels were elevated on admission and decreased after steroid therapy.

The HLA DRB1*0405-DQB1*0401 haplotype is often observed in autoimmune pancreatitis as compared to healthy subjects [17]. In this case, the same HLA pattern was observed. Therefore, when we encounter pancreatic disease where autoimmune pancreatitis is suspected, this HLA pattern could aid in the diagnosis of autoimmune pancreatitis in combination with IgG4.

Abdominal US and CT demonstrated diffuse enlargement of the pancreas and a capsule-like rim. Irie *et al.* reported that the capsule-like rim, which is thought to correspond to an inflammatory process involving peripancreatic tissues, appears to be a characteristic finding of autoimmune pancreatitis, and diffuse pancreatic enlargement along with hypointensity on T1-weighted MR images and delayed

enhancement on dynamic CT and MR studies are other features of this disorder [18]. Therefore, this sign may be useful for differentiating this disease from pancreatic cancer.

Retroperitoneal fibrosis was firstly reported by Ormond in 1948 [8]. Retroperitoneal fibrosis is an uncommon entity that usually originates in the retroperitoneal space. Trauma, inflammation, extravasation, malignant disease, chemical or drug-induced factors, Weber-Christian disease, retractile mesenteries or idiopathic causes all play a role in the etiology of retroperitoneal fibrosis [9]. It is supposed that about 70% of retroperitoneal fibrosis cases are idiopathic [19, 20]. In some cases of idiopathic retroperitoneal fibrosis, antinuclear antibodies have been detected [21, 22] and steroid therapy has been effective [23, 24], suggesting that an autoimmune mechanism may be involved. Although retroperitoneal fibrosis was localized in the periaortic space in this case, retroperitoneal fibrosis often involves the urinary tract and is accompanied by hydronephrosis. In previous reports, surgery and stenting were performed for retroperitoneal fibrosis with hydronephrosis [10, 11].

It has been reported that some cases of autoimmune pancreatitis are accompanied by retroperitoneal fibrosis [10, 11, 12, 13, 14, 15], and both autoimmune pancreatitis and retroperitoneal fibrosis were resolved by steroid therapy [12, 13, 14]. In the present case, steroid therapy was effective, because both the swelling of the pancreas and also the retroperitoneal mass obviously diminished after steroid therapy. Recently, a case of retroperitoneal fibrosis was reported to exhibit elevated levels of IgG4 in the absence of autoimmune pancreatitis, and steroid therapy was effective [25]. Therefore, if we encounter retroperitoneal fibrosis, the measurement of the IgG4 value and steroid therapy is recommended regardless of whether autoimmune pancreatitis is present.

Multifocal fibrosclerosis was first reported by Comings *et al.* [26], and is characterized by a rare fibroproliferative systemic disorder with

multiple manifestations, including retroperitoneal fibrosis, sclerosing cholangitis, orbital pseudotumor, and Riedel's thyroiditis [27]. Recently, a new entity of IgG4-related autoimmune disease was proposed [28]. In autoimmune pancreatitis patients, infiltration of IgG4-positive plasma cells associated with CD4 or CD8-positive T lymphocytes were detected in the peripancreatic tissues, bile duct, gallbladder, and salivary gland, as well as in the pancreas [28]. Furthermore, it has been reported that IgG4-positive plasma cells were observed in retroperitoneal tumors as well as in the pancreas [10, 13]. In this case, both the pancreatic swelling and also the retroperitoneal mass were reduced simultaneously after steroid therapy. Therefore, although IgG4-positive plasma cells were not observed, it is hypothesized that both the pancreas and the periaortic space were infiltrated by IgG4-positive plasma cells.

In conclusion, this is a rare case of autoimmune pancreatitis associated with retroperitoneal fibrosis, resulting in the improvement of both lesions in response to steroid therapy.

Received January 26th, 2007 - Accepted March 5th, 2007

Keywords Autoimmune Diseases; Immunoglobulin G; Pancreatitis; Retroperitoneal Fibrosis; Steroids

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Document URL: <http://www.joplink.net/prev/200705/05.html>

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