

Autoimmune Pancreatitis with Effective Steroid Therapy

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Autoimmune pancreatitis has recently been described as a clinical entity that causes chronic pancreatitis. This unique form of chronic pancreatitis is characterized by minimal attacks of abdominal pain, irregular narrowing of the pancreatic duct, and a diffuse enlargement of the pancreas. Autoimmune pancreatitis is associated with hypergammaglobulinemia. In addition, there is histological evidence of lymphoplasmacytic inflammation, the occasional coexistence of other autoimmune diseases, and has a favorable response to glucocorticoid treatment. Recently autoimmune pancreatitis has been increasingly reported particularly in Japan. We report two patients with autoimmune pancreatitis who were treated successfully with corticosteroid therapy.

Key Words: Pancreatitis, autoimmunity, glucocorticoids

INTRODUCTION

Although alcohol remains the most commonly identified risk factor for chronic pancreatitis, idiopathic pancreatitis accounts for approximately 30-40% of chronic pancreatitis cases.¹ Since Sarles, et al.^{2,3} first reported a particular type of pancreatitis with hypergammaglobulinemia, many reports have suggested that an autoimmune mechanism may be involved in some patients with chronic pancreatitis.⁴⁻¹⁰ Recently, the diagnostic criteria for autoimmune pancreatitis was suggested, and both isolated autoimmune chronic pancreatitis and syndromic autoimmune chronic pancreatitis were included in recent etiology-risk-

based chronic pancreatitis classification systems.¹ This paper reports two cases of autoimmune chronic pancreatitis treated successfully with corticosteroids.

CASE REPORT

Case 1

A 49-year-old man was admitted complaining of abdominal pain. He had been treated for diabetes mellitus with an oral hypoglycemic agent for the previous 7 months. Over the next 4 days, he developed abdominal pain, and jaundice with pruritus. He denied any history of alcohol abuse. On admission, he was acutely ill and lost 5 kg of body weight over 1 year. A physical examination revealed no particular findings. A laboratory examination (normal values in parentheses) showed a total bilirubin level of 1.9 mg/dL (0.2 - 1.2), an alkaline phosphatase level of 279 IU/L (38 - 115), a gamma-glutamyl transferase level of 588 IU/L (12 - 54), an aspartate aminotransferase level of 174 IU/L (13 - 34), an alanine aminotransferase level of 328 IU/L (5 - 46), an amylase level of 91 IU/L (30-115), and a lipase level of 30 IU/L (5 - 60). The white blood cell count was 5520/ul and the proportion of eosinophils was 9.9%. The serum γ -globulin level was elevated to 2.14 g/dl, and the IgG level was elevated to 2380 mg/dL (700 - 1600), while both the IgM and IgA levels were normal. The anti-smooth muscle antibody test was positive. The antinuclear antibody, anti-SS-A antibody, anti-SS-B antibody, anti-DNA antibody, ANCA, and anti-mitochondrial antibody tests

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were all negative. The fasting plasma glucose level was 137 mg/dL, and the hemoglobin A1c level was 7.5% (4-6). Abdominal computed tomography (CT) revealed a diffuse enlargement of the pancreas (Fig. 1A). Endoscopic retrograde cholangiopancreatography (ERCP) showed a diffuse irregular narrowing at the main pancreatic duct and multiple stenoses of the bile duct with mild intrahepatic duct dilatation (Fig. 2B). Endoscopic naso-biliary drainage (ENBD) was performed to relieve the obstructive jaundice and was removed 7 days later. A percutaneous gun biopsy of the liver was performed under ultrasonography guidance in order to evaluate the coincidence of primary sclerosing cholangitis. The liver biopsy specimen showed no definite evidence of primary sclerosing cholangitis. Isolated autoimmune chronic pancreatitis was indicated and prednisolone (30 mg/day) was administered for one week with the dose being tapered to 5 mg per day over 7 weeks. The biochemical tests became normal after 20 days of steroid use, and after 50 days, the prednisolone was withdrawn. The patient has been well for 8 months without recurrence, and the diabetes mellitus is currently well controlled with oral hypoglycemic agents after steroid therapy.

Case 2

A 54-year-old man was admitted for evaluation

of abdominal pain over 7 days. He denied any history of alcohol abuse. On admission, he was acutely ill with general weakness, and lost 2 kg of body weight over the previous 3 months. A physical examination revealed no particular findings. The laboratory examination showed a total bilirubin level of 0.3 mg/dL (0.2-1.2), an alkaline phosphatase level of 132 IU/L (38-115), a gamma-glutamyl transferase level of 18 IU/L (12-54), an aspartate aminotransferase level of 13 IU/L (13-34), an alanine aminotransferase level of 16 IU/L (5-46), an amylase level of 284 IU/L (30-115), and a lipase level of 320 IU/L (5-60). The white blood cell count was 5510/ul and the proportion of eosinophils was 3.1%. The CA19-9 level was within the normal range. The abdominal CT revealed a diffuse enlargement of the body and tail of the pancreas relative to the normal pancreatic head. Magnetic resonance imaging (MRI) of the pancreatobiliary system demonstrated a diffuse enlargement of the pancreas with a spared head portion and a normal contour of the common bile duct. On ERCP, a diffuse irregular narrowing was noted at the main pancreatic duct of the body and tail, and the common bile duct was not dilated (Fig. 2A). In order to rule out pancreatic cancer, a percutaneous gun biopsy of the pancreas was performed under ultrasonography guidance. The biopsy specimen from the pancreas revealed an atrophy of acinar cells and fibrosis with an infiltration of inflammatory cells

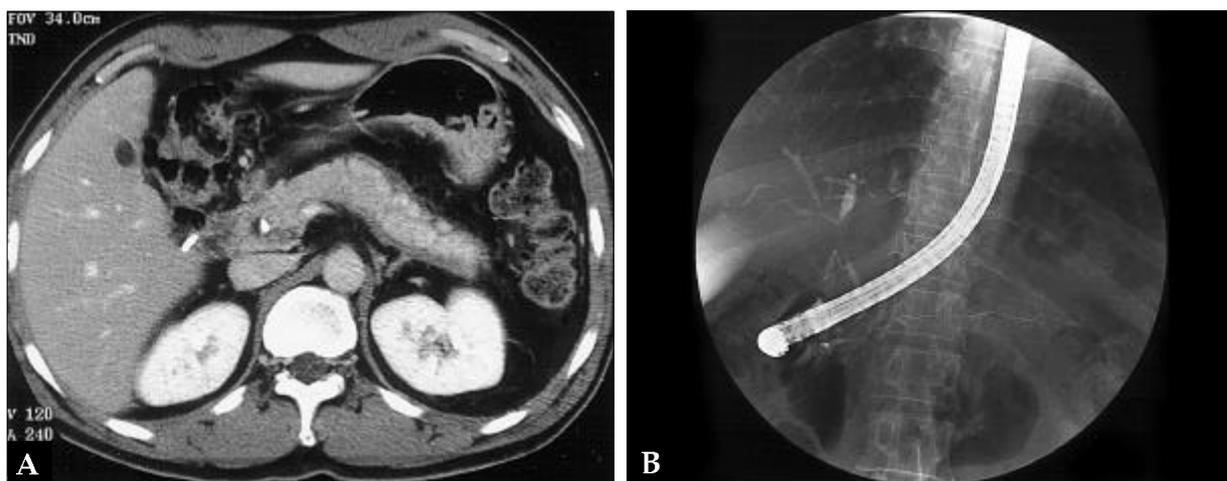


Fig. 1. Case 1. (A) abdominal computed tomography showing a diffuse enlargement of the pancreas. (B) Endoscopic retrograde cholangiopancreatography showing a diffuse irregular narrowing of the main pancreatic duct and a marked stenosis of the bile duct with mild intrahepatic duct dilatation.

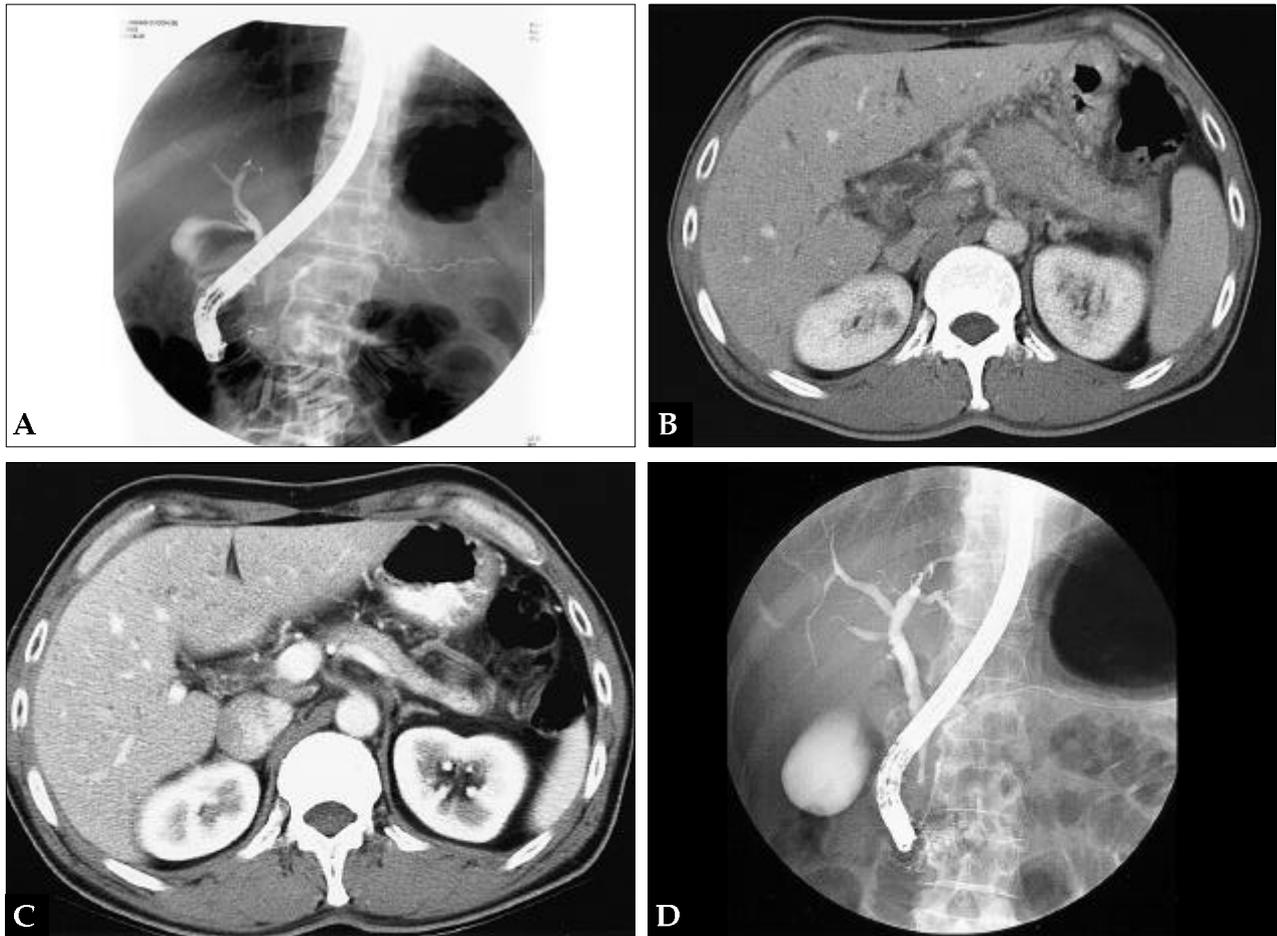


Fig. 2. Case 2. (A) Initial endoscopic retrograde cholangiopancreatography (ERCP) showing a diffuse irregular narrowing at the main pancreatic duct of the body and tail. The main pancreatic duct at the head portion and the common bile duct were spared. (B) Abdominal CT taken one month later showing a diffuse enlargement of the pancreas and an abrupt narrowing of the distal common bile duct with a proximal ductal dilatation. (C) Abdominal CT taken 4 months after steroid therapy showing that the pancreatic swelling is resolved. (D) ERCP taken 7 months after steroid therapy showing a normalization of the main pancreatic duct and the relief of the stenosis of the common bile duct.

(Fig. 3). One month later, he was readmitted for abdominal pain and jaundice. The laboratory examination (normal values in parentheses) showed a total bilirubin level of 7.2 mg/dL (0.2 - 1.2), an alkaline phosphatase level of 654 IU/L (38 - 115), a gamma-glutamyl transferase level of 221 IU/L (12 - 54), an aspartate aminotransferase level of 79 IU/L (13 - 34), an alanine aminotransferase level of 157 IU/L (5 - 46), an amylase level of 96 IU/L (30 - 115), a lipase level of 103 IU/L (5 - 60), and a fasting glucose level of 144 mg/dL (70 - 110). The serum rheumatic factor level was 15 IU/L (0 - 20). The serum γ -globulin level was elevated to 2.71 g/dL, and the IgG level was elevated to 2450

mg/dL (700 - 1600), while both the IgM and IgA levels were normal. The anti-smooth muscle antibody test was positive. However, the antinuclear antibody, anti-SS-A antibody, anti-SS-B antibody, anti-DNA antibody, ANCA, and anti-mitochondrial antibody tests were all negative. Abdominal CT revealed a diffuse enlargement of the pancreas and an abrupt narrowing of the distal common bile duct with a dilatation of the both intrahepatic ducts (Fig. 2B). ERCP showed a diffuse irregular narrowing of the entire pancreatic duct and a segmental stenosis of the common bile duct at the pancreatic head portion with a proximal dilatation. Endoscopic retrograde biliary drainage

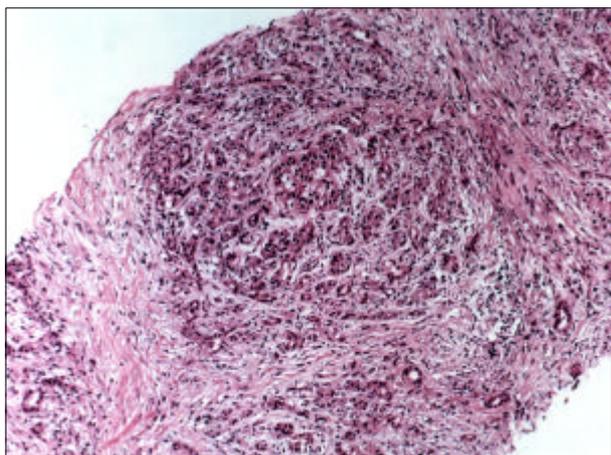


Fig. 3. Case 2. biopsy specimens from the pancreas showing massive fibrosis with an infiltration of lymphocytes and destroyed acinar cells.

(ERBD) with a plastic stent was performed to relieve the obstructive jaundice. Autoimmune pancreatitis was strongly suggested, and prednisolone (30 mg/day) was administered for one week with the dose being tapered to 5 mg per day over 7 weeks. The biochemical tests became normal after 20 days of steroid use, and the prednisolone was administered for 2 months and subsequently withdrawn. Four months later, the abdominal CT revealed a resolution of the pancreatic swelling (Fig. 2C). On an ERCP done, 7 months later, the main pancreatic and common bile ducts were normalized and the ERBD was removed (Fig. 2D). The patient has been well for 8 months without recurrence.

DISCUSSION

Autoimmune chronic pancreatitis is a distinct entity with characteristic histological, morphological, and clinical features. Features of autoimmune pancreatitis such as hypergammaglobulinemia have been recognized for more than 35 years.² Autoimmune chronic pancreatitis may be isolated or is occasionally observed in association with the Sjögren syndrome, primary biliary cirrhosis, primary sclerosing cholangitis, Crohn's disease, ulcerative colitis, or other immune-mediated disorders.¹¹⁻¹⁷

The clinical findings of autoimmune chronic

pancreatitis encompass those of typical pancreatitis but often involve milder symptoms and usually without acute attacks. Obstructive jaundice appears to be a common feature of autoimmune chronic pancreatitis.⁴⁻¹⁰ In the first admission, case 2 did not suffer from jaundice, due to the localized inflammation of the pancreatic body and tail with a spared pancreatic head. In the second admission, the inflammation spread to the pancreatic head and obstructive jaundice had developed. It was suggested that the obstructive jaundice of autoimmune pancreatitis was caused by the narrowing of distal common bile duct due to the inflammation at the pancreatic head. In case 1, ERCP showed multiple stenoses of the bile duct with mild intrahepatic duct dilatation, which were consistent findings with primary sclerosing cholangitis. The clinical presentation and biopsy specimen from the liver suggested isolated autoimmune chronic pancreatitis, but the coincidence of the primary sclerosing cholangitis could not be ruled out.

On abdominal ultrasound or CT, the autoimmune chronic pancreatitis was shown as a diffuse enlargement of the pancreas without calcification which is an essential criterion for diagnosis.¹⁸⁻²⁰ However, if the inflammation was localized to any part of the pancreas, it is difficult to distinguish it from pancreatic cancer. Therefore a biopsy of the pancreas is essential in order to make a correct diagnosis, as was done in case 2.

In autoimmune chronic pancreatitis, it has been reported that the clinical symptoms and radiological findings are dramatically improved by steroid therapy.^{9,19-22} However, the dose and treatment duration of the steroids have not been reported. In our case, a dose of 30 mg of prednisolone per day was administered, which was tapered over 7 weeks. In case 2, the CT showed a marked reduction of the diffuse pancreatic swelling and ERCP revealed a normalized pancreatic duct after the steroid treatment. The patients have had no recurrence after withdrawing the steroid. This suggests that the steroids may be withdrawn after the symptoms are relieved and the abnormal laboratory findings are normalized without a maintenance dosage. In our case, ENBD and ERBD were performed to relieve the obstructive jaundice. However, it was not yet determined

how long biliary drainage was necessary to manage of the obstructive jaundice in autoimmune pancreatitis.

In conclusion, because it is a curable disease, autoimmune pancreatitis should be considered if a patient complains of milder abdominal pain with a diffuse enlargement of the pancreas and hypergammaglobulinemia. Steroids are treatment of choice for managing autoimmune pancreatitis and can be withdrawn after the symptoms are relived and abnormal laboratory findings are normalized.

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