

CASE REPORT

Autoimmune Pancreatitis Diagnosed on the Basis of Immunohistology Alone. A Case Report

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ABSTRACT

Context The differential diagnosis between autoimmune pancreatitis and pancreatic cancer is sometimes difficult, especially for those patients in whom laboratory and radiological criteria are lacking.

Case report A 72-year-old woman was found to have a tumor in the head of the pancreas. Laboratory data showed no abnormal values, including gammaglobulins or autoantibodies. Endoscopic retrograde cholangiopancreatography showed extrinsic stenosis of the main pancreatic and lower common bile ducts. Computed tomography showed a lesion in the head of the pancreas. With a tentative diagnosis of head of the pancreas cancer, the patient underwent pancreaticoduodenectomy. Macroscopically, a tumor 2 cm in diameter not having clear margins was evident in the head of the pancreas. Histological examination showed the infiltration of lymphocytes, plasma cells, and eosinophils with lymphoid follicles around the main pancreatic duct. Immunohistological examination demonstrated that the main pancreatic duct was surrounded by abundant IgG4-positive plasma cells.

Conclusions The patient was diagnosed as having autoimmune pancreatitis on the basis of the immunohistological findings alone,

without any well-defined criteria such as high serum level of IgG4 and presence of autoantibodies before or after surgery.

INTRODUCTION

Recently, Japanese authors have developed the concept of autoimmune pancreatitis (AIP). The characteristics of this new disease entity are: 1) diffuse swelling of the pancreas evident on abdominal ultrasonography (US) and computed tomography (CT), and irregular narrowing or stenosis of the main pancreatic duct by more than one-third on endoscopic retrograde cholangiopancreatography (ERCP) or magnetic resonance cholangiopancreatography (MRCP); 2) increased level of serum gammaglobulins or the presence of autoantibodies; and 3) the presence of fibrotic changes with lymphoplasmacytic cell infiltration around the main pancreatic duct. Either the first and second criteria or the first and third criteria are necessary for a diagnosis of AIP [1, 2, 3, 4, 5]. Clinically, however, if a patient has a tumor of the head of the pancreas with stenosis of the main pancreatic duct or lower common bile duct and no evidence of AIP in terms of preoperative imaging or laboratory parameters, then cancer of the pancreatic head or lower bile duct is suspected.

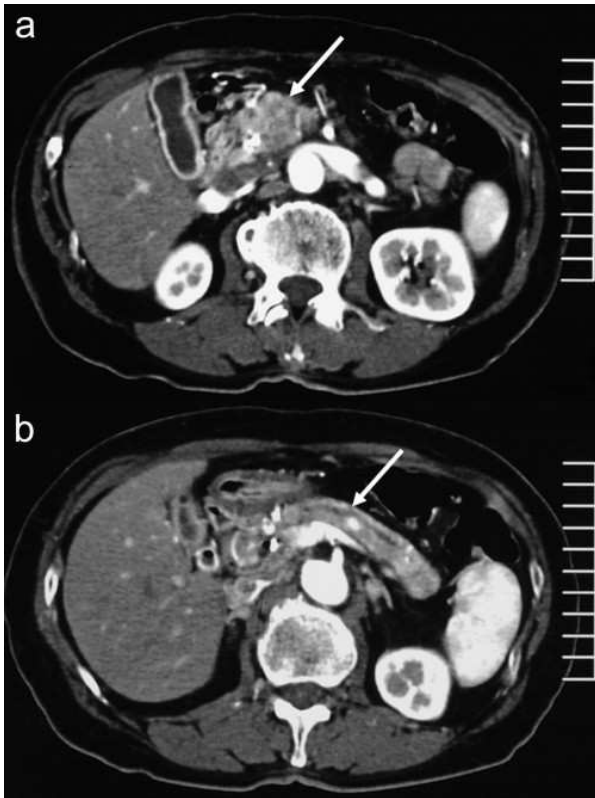


Figure 1. Computed tomography demonstrates the heterogeneous tumor (**a.** arrow) in the head of the pancreas and mild dilatation of the main pancreatic duct (**b.** arrow).

Here, we present the first report of a case of AIP which was diagnosed on the basis of immunohistological findings alone after pancreaticoduodenectomy without any clinically characteristic findings, including the presence of hypergammaglobulinemia and autoantibodies before or after surgery.

CASE REPORT

A 72-year-old woman was admitted to a local hospital in early July 2004 complaining of abdominal discomfort and liver dysfunction. She had never consumed alcohol or smoked cigarettes. Her laboratory data were as follows: aspartate aminotransferase (AST) 45 U/L (reference range: 10-37 U/L); alanine aminotransferase (ALT) 104 U/L (reference range: 3-34 U/L); gamma-glutamyl-transpeptidase (gamma-GT) 1,224 U/L (reference range: 10-55 U/L); lactate dehydrogenase (LDH) 245 U/L (reference range: 105-220 U/L); alkaline phosphatase

(ALP) 1,380 U/L (reference range: 104-338 U/L); leucine aminopeptidase (LAP) 355 U/L (reference range: 33-58 U/L); total bilirubin 0.9 (reference range: 0-1.0 g/dL). Dupan-II was 650 U/mL (reference range: 0-150 U/mL). However, levels of other tumor markers such as CA 19-9, CEA, elastase-I and SPAN-I were within the normal ranges. Furthermore, the preoperative serum total protein and gammaglobulin levels were 7.2 g/dL (reference range: 6.5-8.1 g/dL) and 13% (reference range: 10.4-20.1%), respectively.

A CT scan demonstrated a heterogeneous tumor in the head of the pancreas with mild dilatation of the main pancreatic duct (Figure 1). Endoscopic retrograde cholangiopancreatography (ERCP) revealed extrinsic stenosis of the main pancreatic and lower common bile ducts (Figure 2). Endoscopic nasobiliary drainage was performed to improve the patient's liver function, and she was then transferred to our department with a diagnosis of cancer of the head of the pancreas or lower bile duct.

A pancreaticoduodenectomy was performed in September, 2004. Macroscopically, a tumor about 2 cm in diameter lacking clear margins was evident in the head of the pancreas. Histological examination revealed extensive fibrosis and the infiltration of lymphocytes, plasma cells, and eosinophils with lymphoid follicles around the main pancreatic duct and pancreatic parenchyma without any characteristic features of pancreatic duct cancer (Figure 3a). An immunohistological study also showed significant infiltration of CD4- and CD8-positive lymphocytes around the pancreatic duct. IgG4-positive plasma cells were also present around the main pancreatic duct and pancreatic parenchyma (Figure 3b). On the basis of these findings, the tumor was diagnosed as AIP in the pancreas.

Postoperatively, the levels of serum IgG4, anti-nuclear antibody, rheumatoid factor, and anti-smooth muscle antibody remained within normal limits. The patient's postoperative course was uneventful, and she is currently doing well without any signs of recurrence 15 months after surgery.

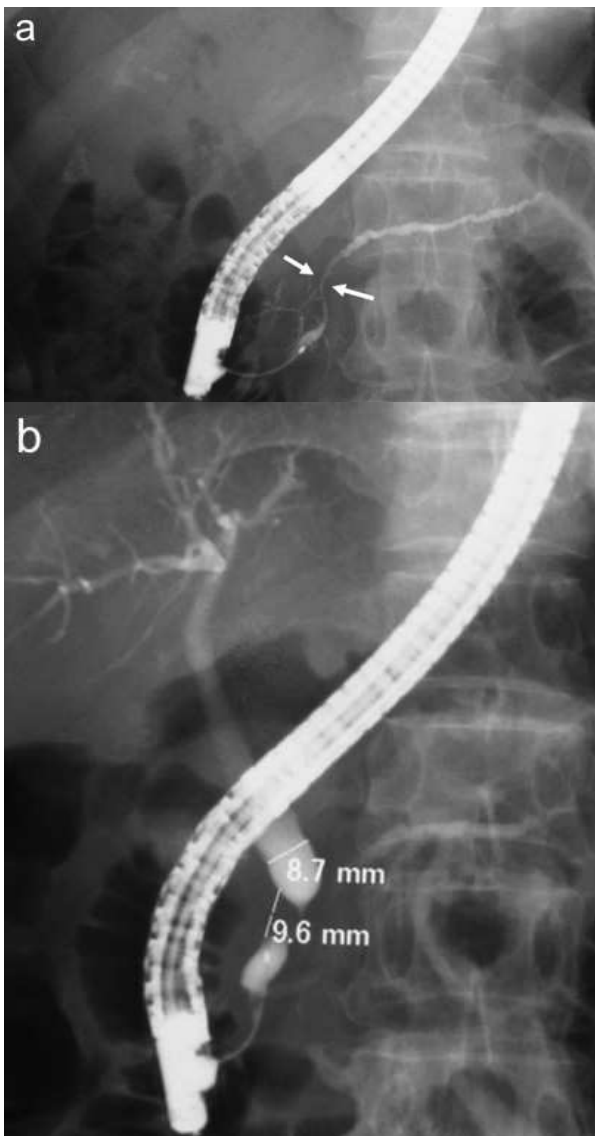


Figure 2. Endoscopic retrograde cholangiopancreatography (ERCP) reveals extrinsic stenosis of the proximal main pancreatic (a. arrow) and lower common bile duct (b.).

DISCUSSION

Clinically, AIP is difficult to differentiate from pancreatic cancer. There have been several cases of AIP for which resection was performed because of a high suspicion of pancreatic cancer. Kamisawa *et al.* reported 17 cases of AIP, including 6 cases which were resected [1]. Three of the latter patients had enlargement of the head of the pancreas and the other three had diffuse enlargement of the pancreas (diameter unknown). All 6 patients had biliary stenosis with jaundice before surgery, three patients had hypergam-

maglobulinemia, three patients had a high serum IgG level, one patient had a high serum IgG4 level, and all 6 patients were positive for autoantibodies. Surgical resection was performed because of a strong suspicion of malignant disease [1]. Servais *et al.* described two patients in whom pancreatic cancer was suspected because of a severe narrowing of the lower bile duct and the presence of a heterogeneous mass (4.5 cm and 3 cm in diameter, respectively) in the head of the pancreas; both subsequently underwent surgery. One of the two patients had only hypergammaglobulinemia and the other had hypergammaglobulinemia with positivity for ANA after surgery [6]. Furthermore, Taniguchi *et al.* reported a patient without hypergammaglobulinemia who showed a marked elevation of tumor markers, such as CA 19-9, DUPAN-II and SPAN-1, at the time of admission. Ultrasonography showed a low-echoic lesion, 3 cm in diameter, at the head of the pancreas and ERCP showed focal irregular narrowing of the main pancreatic duct in the head of the pancreas, and mild dilatation of the pancreatic duct in the body and tail. With a diagnosis of head of the pancreas cancer, a pancreaticoduodenectomy was performed. Histological examination revealed fibrosis, and infiltration of lymphocytes and plasma cell in the head of the pancreas, which are typical features of

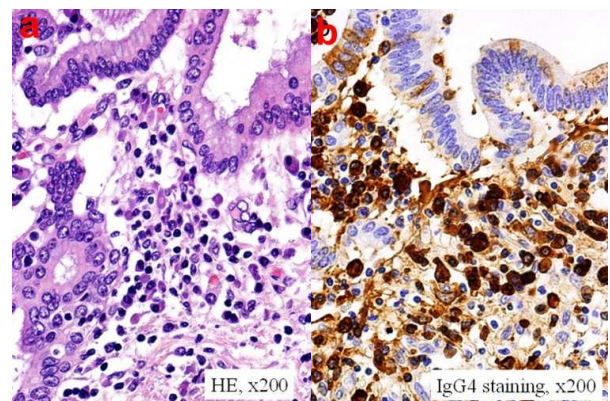


Figure 3. a. Histological findings, showing extensive fibrosis and infiltration of lymphocytes, plasma cells, and eosinophils with lymphoid follicles surrounding the main pancreatic duct and pancreatic parenchyma (H&E, x200). **b.** Main pancreatic duct and parenchyma are revealed by abundant IgG4-positive plasma cells (IgG4 staining, x200).

AIP [7]. However, this patient was found to have an elevated IgG4 level after surgery. The 9 patients described above were diagnosed as having AIP on the basis not only of histology, but also elevated serum levels of gammaglobulins, IgG, IgG4 or autoantibodies before or after surgery [1, 6, 7].

Our patient had already been admitted to a local hospital because of abdominal discomfort with liver dysfunction. Stenosis of the main pancreatic duct and lower common bile duct was localized in the head of the pancreas, and CT showed a focal lesion, 2 cm in diameter, in the same location. Therefore, this case did not fulfill the diagnostic criteria for AIP before surgery. Pancreatic head cancer was strongly suspected, and a pancreaticoduodenectomy was performed. Histological analysis of the resected specimen showed fibrosis and infiltration of lymphocytes and abundant plasma cells around the pancreatic duct with severe stenosis. IgG4-positive plasma cells, which are helpful for differentiating AIP from mass-forming pancreatitis, were present in the inflammatory pancreatic tumor. These findings were consistent with AIP. Although no characteristic findings were demonstrated by diagnostic imaging and laboratory tests, the diagnosis of AIP was supported by histological findings alone. Thus, the small lesion in our present patient may be considered to have been early-stage AIP. Clinically, this type of AIP is difficult to diagnose or to differentiate from pancreatic cancer.

In summary, we have reported a case of AIP in which the lesion was small and no characteristic findings were obtained by imaging or blood tests. Additional case studies are necessary for clarifying the characteristics of AIP at such an early stage.

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Keywords Autoimmune Diseases; Histology;

Pancreaticoduodenectomy; Pancreatitis, Chronic

Abbreviations AIP: autoimmune pancreatitis

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