

Autoimmune Pancreatitis: A Case Report

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ABSTRACT

Autoimmune pancreatitis is a fibro-inflammatory form of chronic pancreatitis. It is diagnosed by the combination of imaging studies such as a CT scan and pancreatography, laboratory analyses that include IgG4 and/or autoantibodies, histopathological evaluations and positive response to corticosteroid therapy. We report the case of a 41-year-old female with a history of jaundice and increasing abdominal pain for two weeks prior to her clinic visit. Laboratory results were significant for an increase in alkaline phosphatase (ALP) and erythrocyte sedimentation rate (ESR). Magnetic resonance cholangiopancreatography (MRCP) confirmed areas of stenosis and dilatation in the pancreatic duct and in the intra- and extra-hepatic bile ducts similar to primary sclerosant cholangitis. Laboratory analyses showed increased levels of IgG4 with the presence of antinuclear antibodies.

KEYWORDS

Autoimmune pancreatitis; Immunoglobulin G4; Sclerosant colangitis

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INTRODUCTION

Autoimmune pancreatitis is a fibro-inflammatory form of chronic pancreatitis that accounts for 5%-6% of chronic pancreatitis. It divided into two categories.¹ Type I involves both genders but is more prevalent among males and associated with hyperimmunoglobulin G4, anti-nuclear antibody, anti-smooth muscle antibody, anti-lactoferrin antibody, and anti-carbonic anhydrase antibody.^{2,3} Extra-pancreatic manifestations and association with other autoimmune diseases is also common in type I autoimmune pancreatitis. Type II is not associated with either specific autoantibodies or extra-pancreatic manifestations. Increased IgG4 to levels above 135 mg/dl in type I differentiates autoimmune pancreatitis from other pancreatic disorders although high IgG4 levels have been reported in pancreatic carcinoma and chronic pancreatitis.³ However in detecting autoimmune pancreatitis, pancreatic enlargement and narrowing of the pancreatic duct should be considered.

Histopathological evaluations show lymphocytic and plasmacytic infiltration around the pancreatic ducts accompanied with lymphoid follicles and an increase in the thickness of the intralobular septate and fibrosis as well as obliterans phlebitis. Although this condition can result in various extra-pan-

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creatic lesions similar to primary sclerosant cholangitis it can be differentiated by detection of IgG4⁺ plasma cell infiltration around the pancreatic ducts and appropriate response to corticosteroid therapy. The overall prognosis is not well-defined. An endoscopy may reveal focal infiltration of plasma cells in the stomach, duodenum, and colon.⁴ Autoimmune pancreatitis may be accompanied by other autoimmune diseases such as ulcerative colitis or autoimmune hepatitis. CT scan images may show various conditions including local or diffused enlargement of the pancreas, a pancreatic mass or a normal pancreas.⁵ Local mild lymphadenopathy is also a common finding. Focal involvement mostly occurs in the head of the pancreas. Autoimmune pancreatitis should be differentiated from pancreatic carcinoma by the absence of diffuse pancreatic duct stenosis in cases of pancreatic carcinoma.^{6,7} Cholangiopancreatography demonstrates the presence of local or diffused pancreatic duct stenosis that may be associated with biliary duct stenosis.⁸

The diagnostic criteria for autoimmune pancreatitis are a combination of radiologic, laboratory, and histopathologic findings.

Short course corticosteroid treatment should be considered for patients who refer with typical autoimmune pancreatitis presentations even if serological and histopathological findings are absent. The presence of radiological and laboratory findings in accordance with autoimmune pancreatitis is sufficient to administer corticosteroid therapy. Due to extra-pancreatic manifestations and association with other autoimmune diseases, autoimmune pancreatitis is sometimes introduced as a systemic disease. This case report introduces a patient with autoimmune pancreatitis who manifested with extra-pancreatic presentations similar to primary sclerosant cholangitis. It is important to consider autoimmune pancreatitis as a possible diagnosis for patients with jaundice and abdominal pain who do not have diagnostic results of routine laboratory tests and are unresponsive to conventional treatments.

CASE REPORT

A 41-year-old female referred with a history of increasing abdominal pain and jaundice since 2 weeks

prior. The patient did not have any history of alcohol consumption, drug abuse, previous liver and biliary or hematologic diseases, transfusion, high risk sexual behavior, and recent travel to high risk regions for infectious diseases. The patient had diffuse abdominal pain that increased with eating and the sclera was icteric. There was no evidence of fever, diarrhea, constipation, ascites, hematemesis, hematochezia, lymphadenopathy, hepatosplenomegaly, or weight loss. Routine laboratory analysis revealed increased liver function test results, especially alkaline phosphatase (ALP), total and direct bilirubin, and erythrocyte sedimentation rate (ESR). Pancreatic enzymes were normal (Table 1).

Abdominal ultrasound evaluations reported a normal-size liver with increased tissue echo and mild dilatation of the intra- and extra-hepatobiliary ducts. Common biliary duct, portal system, and liver veins were normal. MRI imaging of the abdomen showed mild dilatation of the intra- and extra-hepatobiliary ducts (Figure 1). By taking into consideration the observed biliary duct dilatation and absence of any intra-hepatic conditions, we requested laboratory markers for viral hepatitis, hemochromatosis, Wilson's disease, celiac, and primary biliary cirrhosis - all had negative results. Peripheral blood smear showed no evidence of hemolysis. Due to the high ALP, irregular dilatations and stenosis of the intra- and extra-hepatobiliary ducts and pancreatic duct results from MRCP, the presence of ANA and IgG4 were evaluated, both of which were both positive (Figure 2). Thus according to the association of clinical presentations that included abdominal pain and obstructive jaundice with the presence of specific autoimmune markers the patient underwent corticosteroid therapy, 30mg daily, with a diagnosis of autoimmune pancreatitis accompanied by autoimmune sclerosant cholangitis. At the one month follow up visit post-treatment, the control laboratory tests and MRCP revealed normal liver function results along with normal IgG4 and ANA, and normal intra- and extra-hepatobiliary ducts.

DISCUSSION

Autoimmune pancreatitis can be diagnosed ac-

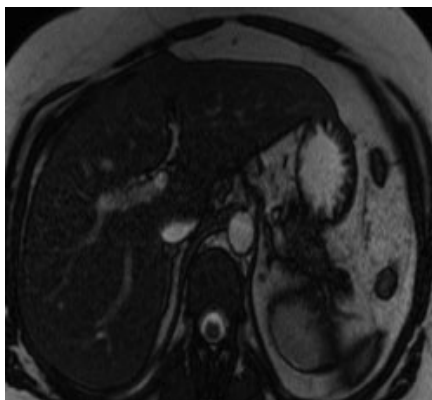


Fig. 1: MRI imaging study. Axial images from MRI of the abdomen showed irregular narrowing and dilatation of the intrahepatic bile ducts (arrow).

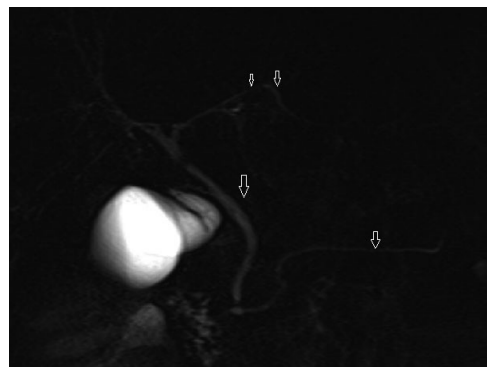


Fig. 2: Magnetic resonance cholangiopancreatography (MRCP) imaging study showed mild narrowing and dilatation of the intrahepatic bile ducts, mild dilatation of the CBD, and irregularity of the pancreatic duct (arrows).

Table 1: Laboratory data.

Blood index	Case	Normal range	Blood index	Case	Normal range	Blood index	Case	Normal range	Blood index	Case	Normal range
WBC (μ L)	16800	4-11x10 ³	LDL (mg/dl)	251	Up to 130	PTT (sec)	30	25-40	ESR (ml/h)	115	F<20
Neutrophils	82%		HDL (mg/dl)	32	30-80	INR	1	1	CRP	2+	
Lymphocytes	18%		TG (mg/dl)	345	40-200	Total Bil. (mg/dl)	2.5	<1.1	HbsAg	Neg	
Eosinophils	1%		Cr (mg/dl)	0.9	Up to 1.5	Direct Bil. (mg/dl)	1	<0.2	Anti-HCV	Neg	
Monocytes	2%		Urea (mg/dl)	20	25-50	Na (meq/L)	145	135-145	Anti-HAV	Neg	
RBC	3000000	3.9-5.1x10 ⁶	AST (mg/dl)	137	5-40	K (meq/L)	4	3.5-5.3	ANA (U/ml)	1.9	0-1.2
HCT	34%	36-47	ALT (mg/dl)	175	5-40	Ca (mg/dl)	9.7	8.5-10.5	Anti-LKM	Neg	
FBS (mg/dl)	136	103	ALP (mg/dl)	1276	64-306	Amylase (U/L)	67	Up to 90	IgG4 (mg/dl)	276	11-157
Cholesterol (mg/dl)	352	Up to 200	PT (sec)	12.5	11-14	Lipase (U/L)	103	Up to 60	AMA	Neg	
U/A	Ok	-		-	-		-	-		-	-

Abbreviations: WBC: White blood cells; RBC: Red blood cells; HCT: Hematocrit; FBS: Fasting blood sugar; LDL: Low density lipoprotein; HDL: High density lipoprotein; TG: Triglycerides; CR: Creatinine; BUN: Blood urea nitrogen; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; ALP: Alkaline phosphatase; PT: Prothrombin time; PTT: Partial thromboplastin time; INR: International normalized ratio for prothrombin time; Total Bil.: Total bilirubin; Direct Bil.: Direct bilirubin; Na: Sodium; K: Potassium; Ca: Calcium; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; HBsAg: Hepatitis B surface antigen; Anti-HCV: Antibody hepatitis C virus; Anti-HAV: Antibody hepatitis A virus; ANA: Antinuclear antibody; Anti-LKM: Antibodies to liver-kidney microsomes; IgG4: Immunoglobulin G4; AMA: Anti-mitochondrial antibody; U/A: Urine analysis

according to the following criteria: 1) narrowing of the pancreatic duct with segmental or diffused irregularity and localized or diffused pancreatic enlargement observed in imaging modalities; 2)

increase in serum IgG4 levels and the presence of autoantibodies such as antinuclear antibody and rheumatoid factor (RF); and 3) intralobular fibrosis, plasma cell and lymphocytic infiltration around

the pancreatic ducts and local lymph node enlargement.^{9,10} Autoimmune pancreatitis is defined as the presence of criterion 1 with either criterion 2 or 3.

However, the most recent criteria for diagnosis of autoimmune pancreatitis has changed as follows:³

A. Imaging: diffused pancreas enlargement, segmental or diffused irregular narrowing of the main pancreatic duct.

B. Laboratory findings: increased IgG4, presence of autoantibodies.

C. Histopathologic findings: lymphoplasmacytic infiltration and fibrosis.

D. Accompanied by other autoimmune diseases.

A definite diagnosis is defined by either criteria A+C, A+B, A+B+C, or A+B+C+D, whereas a probable diagnosis is the presence of criteria A+D and suspicion of disease is only criteria A.

Recent Mayo Clinic studies have introduced additional criteria for the histopathological diagnosis of autoimmune pancreatitis; predictive images in CT scan or pancreatography and increased IgG4 level, and response to corticosteroid therapy.¹¹ They have reported diffused enlargement of the pancreas in 27% of patients diagnosed with autoimmune pancreatitis. Increased IgG4 was present in 71% of patients with mean values of 134 mg/dl.

Autoimmune pancreatitis is more prevalent among males and commonly presents with mild abdominal pain without typical pancreatitis pain that sometimes is accompanied by obstructive jaundice.¹ Increased pancreatic and hepatobiliary enzymes may also be present.¹² Therefore the endocrine and exocrine functions of the pancreas may be impaired.

Histopathological evaluations show intralobular fibrosis, lymphocytic and IgG4⁺ plasma cell infiltration, and obliterans phlebitis observed in biopsies and autopsies. None of these findings are present in chronic pancreatitis in alcoholics and those with Sjögren's syndrome.¹³⁻¹⁶ Specific inflammatory changes in patients with autoimmune pancreatitis strongly suggest a close relation to mutational fibrosclerosis.

Extrapancreatic manifestations of these patients include sclerosant cholangitis,¹⁷ retroperitoneal fi-

brosis,¹⁸ interstitial nephritis,¹⁹ chronic thyroiditis, interstitial pneumonia, in addition to mediastinal and peritoneal lymphadenopathy.

Autoimmune pancreatitis associated sclerosant cholangitis can be differentiated from primary sclerosant cholangitis by the presence of IgG4⁺ plasma cell infiltration around the pancreatic duct and a response to corticosteroid therapy.

The current patient's pancreas imaging evaluations were normal however her IgG4 level increased to 276 mg/dl. The presence of ANA in conjunction with the above results and appropriate response to corticosteroid therapy fulfilled the diagnostic criteria for autoimmune pancreatitis.²⁰

Routine laboratory evaluations in this patient revealed a significant increase in ALP and direct bilirubin; the patient also had obstructive jaundice.

Sonography and MRI showed dilatation of ducts secondary to stenosis and obstruction confirmed by MRCP as secondary dilatation and stenosis in the pancreas and biliary ducts which was similar to sclerosant cholangitis.^{21,22} A control MRCP at one month after corticosteroid therapy showed no evidence of dilatations and stenosis.

This report introduced a case of autoimmune pancreatitis with pancreatic duct stenosis, increased IgG4, positive antinuclear antibody, and appropriate response to corticosteroid therapy as well as its association with sclerosant cholangitis, which resolved after therapy. We discussed the diagnostic criteria in this rare condition.²³⁻²⁶

CONFLICT OF INTEREST

The authors declare no conflict of interest related to this work.

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