

CASE REPORT

IgG₄ Negative Sclerosing Cholangitis Associated with Autoimmune Pancreatitis

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ABSTRACT

Background Sclerosing pancreatitis is an autoimmune condition characterized by periductal lymphocytic infiltration on histology, and elevated serum auto-antibodies and IgG₄. Bile duct involvement is often associated with sclerosing pancreatitis but it is rarely the dominant feature.

Case report We report a patient with dominant biliary stricture and obstructive jaundice associated with IgG₄ negative autoimmune pancreatitis. Due to uncertainties regarding the preoperative diagnosis, the patient underwent bilio-enteric bypass with an intraoperative pancreatic and bile duct biopsy. Post operatively, due to disease recurrence, the patient was started on steroids with consequent remission of the disease.

Conclusion Sclerosing pancreatitis may sometimes present with biliary stricture due to bile duct involvement due to the inflammatory process. The condition is often recognized after surgical exploration for a suspected malignancy. Preoperative diagnosis permits treatment with steroids and endoscopic biliary decompression, and avoids unnecessary surgery.

INTRODUCTION

The first description of autoimmune pancreatitis was given by Sarles *et al.* in 1961

[1]. Sclerosing pancreatitis is an autoimmune condition characterized by minimal to no pancreatic atrophy, the presence of ductal changes and association with other autoimmune diseases such as Sjögren's syndrome [2], primary sclerosing cholangitis [3, 4], or primary biliary cirrhosis. Various autoantibodies and elevated serum IgG₄ have been associated with sclerosing pancreatitis. Bile duct involvement may coexist with sclerosing pancreatitis (sclerosing pancreatocholangitis) or it may occasionally be the presenting feature when it is called sclerosing cholangitis associated with sclerosing pancreatitis. Biliary involvement may occur in the intrahepatic or the extrahepatic portion of the bile duct. We report the case of a young male with IgG₄ negative sclerosing pancreatitis who presented with surgical obstructive jaundice which was successfully managed with hepaticojejunostomy and steroids.

CASE REPORT

A 30-year-old male presented with a 6 month history of peri-umbilical pain radiating to the back. One month previously, he had developed obstructive jaundice associated with recurrent episodes of cholangitis. His serum bilirubin was 11.3 mg/dL (reference range: 0-1 mg/dL), with a direct fraction of 8.35 mg/dL (reference range: 0.1-0.8 mg/dL), and his serum alkaline phosphatase was 532 IU/L (reference range: 0-240 IU/L). His serum transaminase levels were mildly

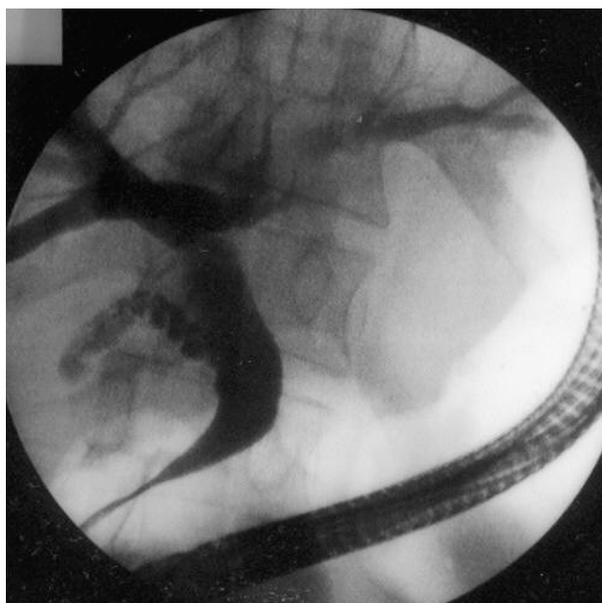


Figure 1. ERCP showed a dilated proximal common bile duct with a stricture in the lower common bile duct.



Figure 2. ERCP showing a mildly dilated main pancreatic duct.

elevated (AST: 64 IU/L, ALT: 50 IU/L; reference range: 0-40 IU/L) and his serum amylase was 640 IU/L (reference range: 0-90 IU/L). Ultrasonography (US) of the abdomen showed a dilated proximal common bile duct (CBD) and intrahepatic biliary radicals, and a thick walled intrapancreatic CBD; the head of the pancreas was bulky. There were no gallstones, CBD stones or any mass lesions in the CBD. A computed tomography (CT) scan of the abdomen showed the head of the pancreas to be bulky with a thick walled CBD and proximal biliary dilatation. The main pancreatic duct (MPD) was mildly dilated but there were no pancreatic stones, calcifications or peripancreatic fluid collection. Endoscopic retrograde cholangiopancreatography (ERCP) showed a 3 cm long tight stricture in the lower CBD with a dilated proximal system (Figure 1). The MPD was mildly dilated (Figure 2). Brush cytology from the CBD was obtained and stenting was performed. Cytology was negative for malignancy. The patient serum CA 19-9 level was measured and found to be elevated (56.6 ng/mL, reference range: 0-37 ng/mL). With a provisional diagnosis of distal CBD cholangiocarcinoma, the patient was scheduled for surgical exploration.

At surgery, the proximal CBD was dilated with a thick walled distal CBD. The pancreas was diffusely enlarged and quite hard without any sign of acute pancreatitis. Intra-operative US showed a dilated MPD without any pancreatic stones or parenchymal calcification. Multiple needle biopsies from the pancreas and the thick walled distal CBD were negative for malignancy on frozen section. With the diagnosis of an inflammatory head mass associated with chronic pancreatitis and biliary obstruction, a Roux-en-Y hepaticojejunostomy was performed. The patient improved postoperatively and his jaundice resolved within 5 weeks. Histopathological examination showed chronic inflammatory pancreatitis with fibrosis, destruction of acinar cells and periductal lymphocytic infiltration. Similar periductal fibrosis and lymphocytic infiltration were reported in the bile duct biopsy (Figure 3).

After the histopathological report, serum markers for autoimmune pancreatitis such as anti-nuclear antibody (ANA), anti-carbonic anhydrase (ACA) antibody, anti-lactoferrin (ALF) antibody and rheumatoid factor (RF) were measured and were negative. The serum IgG₄ level using the competitive ELISA

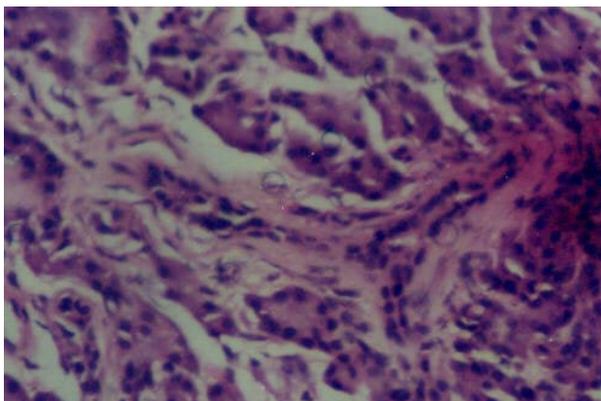


Figure 3. Photomicrograph of a pancreatic biopsy showing periductal sclerosis and lymphocytic infiltration. (H&E x200).

technique was 0.23 mg/mL (reference range: 0-0.46 mg/mL). Three months post-operatively, the patient presented with recurrent episodes of central abdominal pain. On evaluation, he had elevated serum amylase and his peripheral smear showed lymphocytosis. Repeat serum IgG₄ was again within reference limits (0.24 mg/mL) while the serum CA 19-9 level had normalized (33 ng/mL, reference range: 0-37 ng/mL). An abdominal US showed a normal liver with patent bilioenteric anastomosis and an enlarged bulky pancreas with peri-pancreatic inflammation. The patient was started on oral steroids (30 mg prednisolone/day) with resolution of his symptoms within a week. Thirteen months later, the patient is on a low dose maintenance steroid (10 mg prednisolone/day) without any recurrence.

DISCUSSION

Autoimmune pancreatitis was first described in 1961 by Sarles *et al.* in a patient with pancreatitis and hypergammaglobulinemia [1].

This entity is characterized by:

- a) increased levels of serum gammaglobulin or IgG;
- b) diffuse enlargement of pancreas;
- c) fibrotic changes around the MPD with lymphocytic infiltration;
- d) rare pancreatic calcification or pancreatic cysts;
- e) occasional association with other autoimmune diseases;

f) effective oral steroid therapy.

The disease has also been called chronic inflammatory sclerosis of the pancreas, sclerosing pancreatitis, and sclerosing pancreatocholangitis. Bile duct involvement in the form of intrahepatic pseudotumors or extrahepatic sclerosing cholangitis may occur along with sclerosing pancreatitis. It is rare that sclerosing cholangitis changes are predominant and associated with minimal or no pancreatitis.

The pathogenesis and pathophysiology of autoimmune pancreatitis is unclear. The occasional coexistence of pancreatitis with other autoimmune diseases suggests that there may be a common target antigen in the pancreas and other exocrine organs, such as the salivary glands, biliary tract and renal tubules [2, 3, 4].

The presence of autoantibodies such as ANA, anti-neutrophil cytoplasmic antibody cytoplasmic (ANCA-C), anti-neutrophil cytoplasmic antibody perinuclear (ANCA-P), RF, etc. may be seen in 50-75% of patients with sclerosing pancreatitis. Serum levels of IgG₄ are often elevated (10-15%) but the clinical significance of raised IgG₄ is unclear [5, 6]. Characteristic features on pancreatography, if associated with elevated levels of these antibodies, are virtually diagnostic for autoimmune pancreatitis.

The clinical presentation is variable. Sclerosing pancreatitis may present with a feature of chronic pancreatitis or may present as a mass in the head of the pancreas (pseudotumor) [7, 8]. Careful evaluation of the pancreatic head mass is needed if it is associated with the typical features of sclerosing pancreatitis on pancreatography and elevated levels of auto-antibodies. In this situation steroids are therapeutic and an unnecessary pancreaticoduodenectomy may be avoided [9]. However, many cases are diagnosed after the resection of a suspicious pancreatic head mass [10, 11].

Presentation with biliary obstruction, as seen in our patient, occurs more often in sclerosing pancreatitis in contrast to alcoholic chronic pancreatitis. Biliary involvement also responds to steroid therapy. However, in the

presence of jaundice with cholangitis, endoscopic biliary decompression is required. In the case of an uncertain diagnosis, as in the present case, surgical exploration and biopsy/resection is often resorted to in order to obtain a diagnosis. Bile duct involvement can recur at a different site after excision or bypass; hence, steroids are indicated even after successful biliary drainage.

Many studies have established the role of steroids in sclerosing cholangitis associated with autoimmune pancreatitis [12, 13, 14, 15]. However, the exact duration of steroid therapy is not clear because of the variable presentation and the uncommon nature of the disease.

CONCLUSION

Sclerosing cholangitis with sclerosing pancreatitis may present as a dominant biliary stricture or as a pancreatic head mass (pseudotumor). The diagnosis is often made on biopsy after surgical resection of a pancreatic head mass. If the diagnosis is made preoperatively, biliary obstruction can be managed by endoscopic stenting and surgery can be avoided. Steroids are necessary for inducing remission of the disease and resolution of the symptoms after stenting. Steroids are also required after surgery for preventing recurrence.

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Keywords Cholangitis, Sclerosing; Pancreatic Diseases; Pancreatitis

Abbreviations ACA: anti-carbonic anhydrase; ANCA-C: anti neutrophil cytoplasmic antibody cytoplasmic; ANCA-P: anti-neutrophil cytoplasmic antibody perinuclear; ALF: anti-lactoferrin; ANA: anti-nuclear antibody; CBD: common bile duct; MPD: main pancreatic duct; RF: rheumatoid factor

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