

CASE REPORT

Autoimmune Pancreatitis Presenting as Simultaneous Masses in the Pancreatic Head and Gallbladder

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ABSTRACT

Context Autoimmune pancreatitis is a rare variant of chronic pancreatitis characterized by pancreatic ductal narrowing and pancreatic parenchymal edema on computed tomography and rarely with intermittent attacks of abdominal pain. Recently, it has been found to be a systemic disease with lymphoplasmacytic infiltration that has been associated with several autoimmune diseases and described in multiple organs including the extrahepatic bile duct, liver and gallbladder.

Case report We describe the clinical, radiographic and histopathologic aspects of a patient who presented with synchronous masses in the pancreatic head and gallbladder. Postoperatively, the patient's jaundice subsided and IgG4 levels, which were drawn one week postoperatively, were all within normal limits. Nonetheless, immunohistochemical staining for IgG4 was positive.

Conclusion Autoimmune pancreatitis is the most common benign entity identified in patients that underwent pancreaticoduodenectomy for presumed pancreatic adenocarcinoma. Our patient with autoimmune pancreatitis presented with simultaneous inflammatory masses in the gallbladder and pancreatic head, an association not previously reported. Preoperative evaluation of IgG4 or autoantibody levels may have obviated the need for an operation. Therefore, we have

begun screening for elevated serum IgG4 concentrations to identify patients with possible autoimmune pancreatitis who present without definitive pathological or radiographic evidence for malignancy. If preoperative diagnosis is not made, immunohistochemical staining of pathology specimens can confirm the diagnosis.

INTRODUCTION

Recently it has been recognized that autoimmune pancreatitis (AIP) or lymphoplasmacytic sclerosing pancreatitis is not merely a focal disease of the pancreas, but rather a systemic disease. Lymphoplasmacytic infiltration is often present in peripancreatic retroperitoneal tissue, extrahepatic bile duct, gallbladder, liver, gastric mucosa, salivary gland and lymph nodes. It may also be associated with autoimmune diseases including sclerosing cholangitis, rheumatoid arthritis, sarcoidosis, Sjogren's syndrome and type 1 diabetes mellitus [1, 2, 3]. Herein we describe the clinical, radiographic and histopathologic aspects of a patient who presented with synchronous masses in the pancreatic head and gallbladder.

CASE REPORT

A 68-year-old woman presented with postprandial epigastric pain that was relieved with emesis. The patient had fevers, chills,

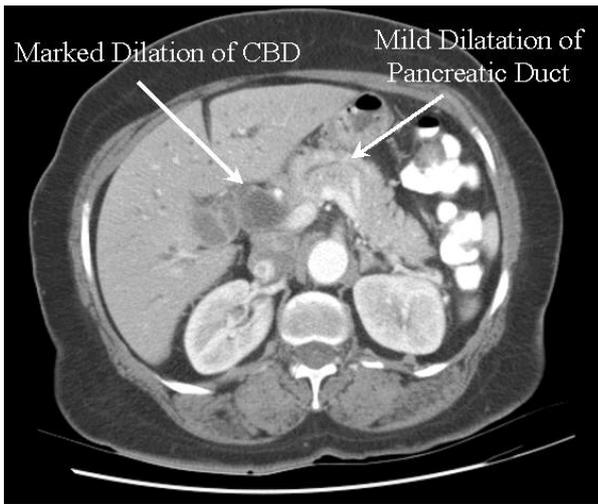


Figure 1. Mildly dilated pancreatic duct and markedly dilated common bile duct and cystic duct on CT scan.

jaundice, pruritus, dark urine, and decreased oral intake. The patient denied a family history of pancreatitis or pancreatic cancer. On physical exam she was icteric and had increased serum concentrations of total and direct bilirubin of 9.9 mg/dL (reference range: 0-1.2 mg/dL) and 7.5 mg/dL (reference range: 0-0.2 mg/dL), respectively. Her other liver function tests were elevated with an ALT of 154 U/L (reference range: 0-35 U/L), AST of 136 U/L (reference range: 0-35 U/L) and an alkaline phosphatase of 688 U/L (reference range: 30-130x U/L). A pancreatic protocol CT scan showed intrahepatic ductal dilation that extended to the ampulla (Figure 1). An ill-defined 3.0x4.0 cm region of low attenuation was identified in the pancreatic head (Figure 2), and a thickened gallbladder fundus with contrast-enhancement was

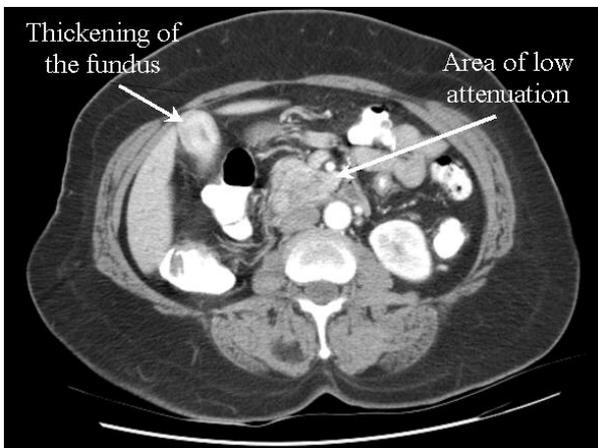


Figure 2. CT scan showing low attenuation, ill-defined lesion in the pancreatic head with enhancing mural thickening at the gallbladder fundus.

identified.

Endoscopic retrograde cholangiopancreatography with endoscopic ultrasound demonstrated a tortuous, mildly dilated pancreatic duct, obstructed by a hypoechoic and heterogeneous mass in the pancreatic head. The ampulla bulged into the duodenum and prevented cannulation of the common bile duct. Fine needle aspiration of the pancreatic head revealed no evidence of malignancy and was comprised predominantly of bland surface epithelium and mixed inflammatory cells.

She was scheduled for resection of a presumed pancreatic malignancy and/or gallbladder cancer. Intraoperatively, discrete masses were palpated in the head of the pancreas and in the gallbladder fundus. The gallbladder was not diffusely thickened and there was no other evidence of cholecystitis. The patient underwent a pylorus-preserving pancreaticoduodenectomy with a partial hepatectomy encompassing the gallbladder fossa. No intraoperative frozen sections were obtained, but permanent histological sections revealed a marked, chronic lymphoplasmacytic infiltrate and sclerosing fibrosis centered around the common bile duct and pancreatic duct with prominent lymphoid follicles within the lamina propria and submucosa. The gallbladder wall was also infiltrated with a diffuse lymphoplastic process (Figure 3). Thirty-nine lymph nodes showed lymphoid

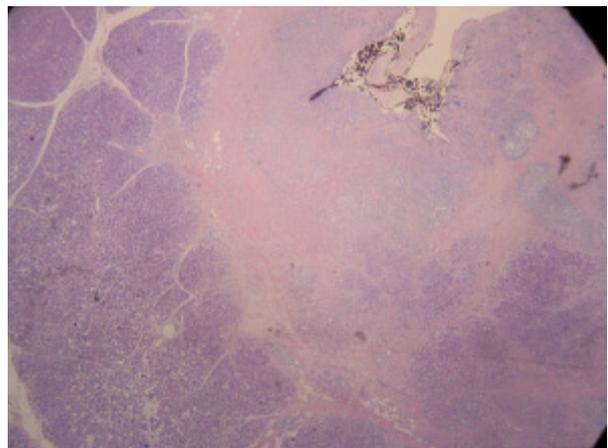


Figure 3. Histopathological features of autoimmune pancreatitis (AIP). A sclerotic lesion with a dense chronic inflammatory infiltrate composed of plasma cells, lymphocytes, and scattered eosinophils is observed around the pancreatic and bile ducts (hematoxylin and eosin, original magnification x10).

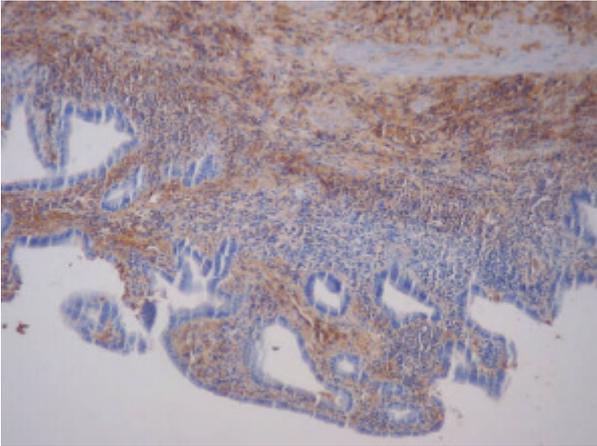


Figure 4. The gallbladder is involved by a chronic cholecystitis with prominent follicles that contain numerous IgG4 positive plasma cells (immunostaining of IgG4, x 40).

hyperplasia. Postoperatively, the patient's jaundice resolved and IgG4 levels that were drawn one week postoperatively were all within normal limits. Nonetheless, immunohistochemical staining for IgG4 was positive (Figure 4).

DISCUSSION

AIP is a rare type of chronic pancreatitis characterized by intermittent attacks of abdominal pain associated with pancreatic ductal narrowing and pancreatic parenchymal edema on computed tomography. AIP is, however, the most common benign etiology identified in patients that underwent pancreaticoduodenectomy for presumed pancreatic adenocarcinoma [4]. The pancreatic lesions consist of poorly circumscribed fibrotic lesions with lymphoplasmacytic infiltration [1, 3, 5]. Laboratory evaluation may reveal a hypergammaglobulinemia of IgG4 and the presence of autoantibodies [2, 6, 7]. IgG4 is the most rare IgG subclass, accounting for 3-6% of all IgG [2, 6, 7]. Its half-life is approximately 3 weeks, and it is associated with atopic dermatitis, asthma and certain parasitic infections. Patients with AIP may have increased serum concentrations of IgG4-containing immune complexes that deposit in exocrine tissues [8, 9].

The Japanese Pancreatic Society has proposed diagnostic criteria that include: main pancreatic ductal narrowing, with irregularity of its wall involving at least 1/3 of its entire length and diffuse enlargement of the pancreatic gland [10, 11, 12]. These criteria must be associated with either an elevation in serum IgG4 or presence of autoantibodies and/or histological demonstration of fibrotic changes with lymphocytic and plasma cell infiltration of the pancreas [10, 11, 12]. Using a cutoff of 135 mg/dL for serum IgG4, Hamano *et al.* found that levels above this were sensitive (95%) and specific (97%) for differentiating AIP from pancreatic cancer [6]. Although it was initially believed that the entire pancreatic duct must be involved for the diagnosis of AIP, it is now believed that pancreatic ductal narrowing may be segmental, focal or diffuse [9]. The pancreas in our patient histologically demonstrated focal narrowing in the head of the pancreas and as a result had mild dilatation proximal to this obstruction (Figure 3).

The diagnostic algorithm of all patients with diffuse pancreatic swelling on CT should include the concentration of serum IgG4. If present, an ERCP should be obtained to assess for the presence of a sclerosing pattern on ERCP and lymphoplasmacytic infiltration with benign pancreatic ductal epithelium on FNA [9]. Patients that are diagnosed prior to surgery may be treated with 4 weeks of glucocorticoid therapy, often resulting in complete symptomatic and radiographic resolution [8, 9].

Unfortunately, AIP is rarely diagnosed preoperatively, and 2.5-5% of all pancreaticoduodenectomies are performed in the setting of AIP instead of suspected pancreatic adenocarcinoma [9, 13]. Half of all AIP patients have associated autoimmune diseases, such as, diabetes mellitus, sclerosing cholangitis, rheumatoid arthritis, Sjogren's syndrome, nephropathy and retroperitoneal fibrosis which should prompt work-up for AIP in patients with known autoimmune diseases and pancreatic findings on CT scans [3, 4, 5, 9, 14]. The IgG4 serum concentrat

ions in an average of 40 patients with suspected pancreatic cancer must be measured for one patient with AIP to be identified preoperatively. The projected cost to identify one patient would be further lowered by excluding patients with a definitive diagnosis of malignancy [4, 13].

Our patient with AIP is the first reported case to present with simultaneous inflammatory masses in the gallbladder and pancreatic head. Although diffuse gallbladder thickening occurs in a large number of patients with AIP, our patient had an isolated mass in the fundus [15]. Preoperative evaluation of IgG4 or autoantibody levels may have obviated the need for an operation. Therefore, we have begun screening for elevated serum IgG4 concentrations to identify patients with possible AIP who present without definitive pathological or radiographic evidence for malignancy. If the diagnosis is suspected, but serum levels of IgG4 are not elevated, immunohistochemical staining of pathology specimens can confirm the diagnosis [16, 17].

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Keywords Autoimmunity; Immunoglobulin G; Pancreatitis

Abbreviations AIP: autoimmune pancreatitis

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