Autoimmune Pancreatitis

An Update on Diagnosis and Management

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KEYWORDS

- Autoimmune pancreatitis • Lymphoplasmacytic sclerosing pancreatitis
- Idiopathic duct-centric pancreatitis • IgG4
- International Consensus Diagnostic Criteria • Corticosteroids

KEY POINTS

- Autoimmune pancreatitis (AIP) can affect the pancreas primarily; however, it can also present as part of a systemic disease related to immunoglobulin G4.
- AIP is primarily a histologic diagnosis, but AIP is currently diagnosed using clinical characteristics.
- The mainstay of therapy for AIP is corticosteroids. Other therapies that have been explored include immunomodulator drugs.
- Relapse rates following corticosteroid therapy are high.

INTRODUCTION

Cases of autoimmune pancreatitis (AIP) were described as early as the 1960s by Sarles and colleagues.[1] However, the term autoimmune pancreatitis was first introduced by Yoshida and colleagues[2] in 1995 after these investigators studied a Japanese cohort with causes suggestive of autoimmune origin. Although AIP is recognized as a distinct disease process, the incidence remains unknown. A 2009 survey in Japan estimated that the incidence of AIP in the Ishikawa district (population 1.16 million) was approximately 1 per 100,000.[3] The rate of undiagnosed AIP in large cohorts of patients undergoing pancreatic surgical resection of presumed pancreatic cancer is approximately 2%.[4,5]

AIP was initially recognized as a disease associated with characteristic clinical, radiologic, and serologic features affecting primarily the pancreas, with the ability to

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involve other organs. However, more recently AIP has been associated with other immune-mediated diseases, including immunoglobulin (Ig) G4–associated cholangitis (IAC), salivary gland disorders, mediastinal fibrosis, retroperitoneal fibrosis, tubulointerstitial disease and inflammatory bowel disease, and increased levels of IgG4, both in tissue plasma cells and in the serum,[6] thus terming this collection of disease processes IgG4-related systemic disease.

With improved understanding of AIP and its distinct clinical profiles and variable association with a systemic IgG4 disease process, AIP has been classified into type 1 and type 2 AIP. In type 1 AIP, the pancreas is affected as part of a systemic IgG4-positive disease, also known as lymphoplasmacytic sclerosing pancreatitis (LPSP). Type 2 AIP is characterized by histologically confirmed idiopathic duct-centric pancreatitis, often with granulocytic epithelial lesions (GELs) with or without granulocytic acinar inflammation along with absent (0–10 cells per high-power field [HPF]) IgG4-positive cells, and without systemic involvement. Classic clinical characteristics include obstructive jaundice, abdominal pain, and acute pancreatitis, which make exclusion of pancreatic cancer necessary before the diagnosis of AIP. However, unlike pancreatic malignancies, AIP may respond to therapy with corticosteroids.

Although AIP is primarily a pathologic diagnosis, attempts have been made to clinically diagnose AIP using various clinical criteria. In 2011 an international symposium on AIP yielded the International Consensus Diagnostic Criteria (ICDC),[7] which can be used to classify AIP as type 1, type 2, or AIP–Not Otherwise Specified. This article discusses clinical, pathologic, and serologic features of AIP with mention of the various diagnostic guidelines that have been used to diagnose AIP, with a special focus on ICDC. Management options are also discussed.

Clinical Characteristics

Patients with type I AIP typically present at an older age (on average 16 years older) than patients presenting with type 2 AIP.[8] Patients with either type of AIP commonly present with obstructive jaundice, abdominal pain, and/or biochemical evidence of pancreatitis. The study of a large cohort of 731 patients found that obstructive jaundice was the presenting symptom in 75% of patients with type 1 AIP compared with abdominal pain being the most common presentation in 68% of patients with type 2 AIP.[8] The obstructive jaundice may be related to pancreatic swelling and compression of the biliary tree, or be caused by proximal extrahepatic and intrahepatic duct stricture, which can be part of an associated IAC.[9] The abdominal pain is typically mild and may or may not be associated with documented attacks of acute pancreatitis. AIP is not a common cause for idiopathic recurrent pancreatitis. Increases in IgG4 levels are typically seen more often with type 1 AIP, with the degree of increase in IgG4 level necessary to satisfy level 1 evidence for the diagnosis of type 1 AIP greater than twice the upper limit of normal. A level less than twice the upper limit of normal is consistent with level 2 evidence per ICDC guidelines.[7] Imaging findings range from either diffuse or focal pancreatic involvement, often with evidence of other organ involvement (OOI), including hilar lymphadenopathy, extrapancreatic biliary duct involvement, or renal masses. Type 1 AIP is more likely to have biliary tract disease and a higher rate of relapse compared with type 2 AIP.[10]

Diagnostic Guidelines

Because therapy and prognosis differ greatly between the two diseases, exclusion of pancreatic adenocarcinoma must be confirmed before pursuing AIP as a diagnosis. It is also important to diagnose AIP because treatment may avert the long-term consequences of the disease, in addition to avoiding unnecessary surgery.