MR Imaging of Autoimmune Pancreatitis

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KEYWORDS

• Autoimmune • Pancreatitis • IgG4 • MR imaging • Computed tomography

KEY POINTS

- AIP is a fibro-inflammatory disorder with 2 distinct subtypes that may be differentiated based on clinical, histologic, and radiologic features.
- Type 1 is a multi-organ IgG4-related disease with the pancreas being the most commonly involved organ.
- Type 2 AIP typically involves younger patients and possible concomitant inflammatory bowel disease with significant overlap with pancreatic findings of type 1 disease.
- Differentiation between the two entities may be based on clinical grounds, and histology and is important due to different treatment strategies and overall prognostication.

INTRODUCTION

Definition and Epidemiology

Autoimmune pancreatitis (AIP) is characterized by inflammatory destruction of the pancreatic tissue.[1] The autoimmune nature of pancreatic destruction was first proposed by Yoshida and colleagues[2] in 1995, though an association between pancreatitis and increased serum globulin levels was reported in the early 1960s.[3] Investigations by Kamisawa and colleagues[4] highlighted several extrapancreatic manifestations that were associated with AIP and had similar abundant infiltration of immunoglobulin G4 (IgG4)-positive plasma cells on histology. Further studies during the last decade explored and identified the spectrum of IgG4-related disease,[5,6] with the pancreas being the most commonly involved organ in IgG4-related disease.[7,8] However, not all AIPs fall under the category of IgG4-related disease and not all patients with the IgG4-related disease have pancreatic involvement or AIP.[9–11] The terms *type 1 AIP* and *lymphoplasmacytic sclerosing pancreatitis* (LPSP) are used interchangeably for this disease. Type 2 or idiopathic duct-centric chronic pancreatitis (IDCP) is a related disease that shares some histopathologic and clinical features with the type 1 disease with differences in the diagnostic criteria and treatment approach.

Limited studies have attempted to estimate the annual incidence of AIP in the general population. A landmark 2002 national survey of randomly selected hospitals in Japan revealed a point prevalence of 0.82 per 100,000.[12] The overall prevalence rate in 2007 and 2011 was estimated at 2.2 and 4.6 per 100,000, respectively.[13,14]

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Approximately 3% to 4% of cases with suspected chronic pancreatitis may be related to AIP.[15,16] Likewise, 4% of patients undergoing pancreaticoduodenectomy for pancreatic head mass may have AIP on histopathology.[17]

Histologic and Clinical Findings

AIP is subdivided into 2 distinct entities based on clinical manifestations and histology, type 1 and 2.[18,19] Most of the primary studies evaluating and proposing AIP type 1 as a distinct diagnosis were performed in Asian populations.[18] AIP type 1 is now recognized as a systemic disease with IgG4-positive plasma cell infiltration of virtually every organ system that can be associated with fibrosis.[20] Elevated serum IgG4 may be seen in about two-thirds of patients but has a low positive predictive value because of its elevation in patients with pancreatic adenocarcinoma, cholangiocarcinoma, and primary sclerosing cholangitis.[19] Endoscopic-guided or surgical core biopsy helps obtain a histologic diagnosis and is preferred over fine-needle aspiration (FNA), which has a variable yield.[21] Type 1 AIP or LPSP demonstrates infiltration of IgG4-positive plasma cells in the periductal and interlobular areas, leading to fibrosis, pancreatic duct narrowing, and acinar atrophy on histology.[22–24] Although nonspecific, the presence of IgG4 as greater than 40% of the total IgG-positive plasma cells and an IgG4/IgG ratio of greater than 0.4 on immunostaining of the pancreatic tissue favors a diagnosis of type 1 AIP.[25,26] The clinical presentation of AIP is highly variable, pertaining to the inflammation and fibrosis of the pancreas. In a study of 235 patients, the median age was 67 years (range 35–86) and the most common involved organ was the pancreas (60%) followed by the salivary glands (34%), kidneys, lacrimal glands (23%), and the retroperitoneum (20%).[27] In another study of 57 patients with type 1 AIP, epigastric pain or discomfort (58%), jaundice (54%), weight loss (51%), and new-onset diabetes (38%) were the most common disease presentations.[22,27] Other extrapancreatic manifestations of IgG4-related disease include but are not limited to thyroiditis, interstitial pneumonia, lymphadenopathy, cholangitis, and cholecystitis.[20]

In contrast, type 2 AIP or IDCP was introduced in studies on Western populations as chronic pancreatitis histologically recognized by neutrophil infiltration and epithelial destruction (granulocytic epithelial lesions).[28] Unlike type 1, there is no increased incidence of elevated serum IgG4 levels[29] and number of IgG4-positive cells in the pancreatic tissue (<10 per high power field [HPF], <40% of IgG-positive plasma cells[30]). It typically affects younger patients with a median age of 31 years (range 23–49), and the most common clinical presentation is of acute recurrent pancreatitis with concurrent inflammatory bowel disease seen in up to 44% of patients.[31] Patients may also present with obstructive jaundice secondary to the presence of a focal mass. One important reason for differentiating these two entities is the risk of relapse after induction corticosteroid therapy, which is 30% to 33% in type 1 and only 9% to 11% in type 2 AIP.[32]

Diagnostic Criteria

Given the diffuse and systemic nature of the IgG4-related disease that includes type 1 AIP and the distinct histopathology of type 2 AIP demonstrating granulocytic epithelial lesions, diagnostic criteria were proposed to facilitate the analysis of AIP. The International Association of Pancreatology published its consensus diagnostic criteria for AIP diagnosis in 2011.[33] Five cardinal components were considered: imaging features of the ducts and the pancreatic parenchyma, serology, histology, systemic involvement, and significant response to corticosteroid therapy.[33] Additional population-specific studies tried to validate and propose enhanced algorithms for AIP diagnosis.[34,35] Of note, the Unifying-Autoimmune-Pancreatitis-Criteria (U-AIP) was recently introduced to unify the AIP diagnosis, improve the diagnostic accuracy, and embrace the AIP diagnosis within the framework of the broader M-ANNHEIM classification scheme for chronic pancreatitis.[36] U-AIP criteria consist of negative pancreatic cancer workup in addition to disease features, including histology (typical histology; either LPSP or IDCP), imaging and serology (computed tomography [CT]/MR imaging/endoscopic retrograde cholangiopancreatography (ERCP) in addition to elevated serum IgG4 or autoimmune antibodies), and response to corticosteroid therapy.[36] U-AIP was developed in an effort to unify different criteria, including the Japanese, Korean, Mayo-HISORt (Histology, Imaging features, Serology, Other organ involvement, and Response to steroid treatment), and Italian criteria for the diagnosis of AIP[33,36] (**Table 1**).

Imaging Modalities

Imaging plays an essential role in the evaluation of AIP by characterizing the pancreatic parenchyma, main pancreatic duct (MPD), peripancreatic lymph nodes, and fatty tissue.[37] Imaging modalities, including CT and MR imaging; endoscopic techniques, including ERCP and endoscopic ultrasonography (EUS); and functional imaging, including PET, have all been investigated for the evaluation of AIP.[37] CT is often the first, and