Management of Autoimmune Pancreatitis

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KEYWORDS

• Autoimmune pancreatitis • Lymphoplasmacytic sclerosing pancreatitis
• Idiopathic duct centric pancreatitis • IgG-4 • Corticosteroids • Immunomodulator
• Azathioprine • Rituximab

KEY POINTS

- Autoimmune pancreatitis (AIP) can affect the pancreas primarily; however, it can also present as part of a systemic disease related to IgG-4.
- AIP is primarily a histologic diagnosis; however, currently AIP is diagnosed using clinical characteristics.
- The mainstay of therapy for AIP is corticosteroids.
- Relapse rates following corticosteroid therapy are high.
- Treatment of steroid-refractory AIP includes immunomodulators in conjunction with steroids, or rituximab.

INTRODUCTION

Autoimmune pancreatitis (AIP) is a disease with characteristic clinical (eg, obstructive jaundice, acute pancreatitis, and abdominal pain), radiological (eg, diffusely enlarged pancreas or pancreatic mass), and serologic features (elevated serum immunoglobulin-4 [IgG-4]) affecting primarily the pancreas with the ability to involve other organs. Given these clinical presentations, the exclusion of pancreatic cancer is necessary before considering the diagnosis of AIP.

The international consensus diagnostic criteria (ICDC) classified AIP as type 1, type 2, and AIP not otherwise specified (NOS).[1] In type 1 AIP, the pancreas is affected as part of a systemic IgG-4–positive disease, also known as lymphoplasmacytic sclerosing pancreatitis (LPSP). Type 2 AIP is characterized by histologically confirmed

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idiopathic duct centric pancreatitis (IDCP) often with granulocytic epithelial lesions (GELs) with or without granulocytic acinar inflammation along with absent (0–10 cells/high-power field [HPF]) IgG-4–positive cells, and without systemic involvement. There is a strong association between AIP and other immune-mediated diseases, including IgG-4–associated cholangitis (IAC), salivary gland disorders, mediastinal fibrosis, retroperitoneal fibrosis, tubulointerstitial disease, and inflammatory bowel disease (IBD).

Multiple pathophysiological mechanisms for AIP have been proposed, including it being an autoimmune disorder demonstrated by the predominance of immune cells, including B-lymphocyte antigen CD 20, into various tissues, including the pancreas, and the characteristic response to corticosteroids.[2] Other associated disease mechanisms associated with AIP include disease susceptibility–related factors, such as human leukocyte antigen serotypes, molecular mimicry, and specific regulatory immune pathways involving regulatory T cells.[3] Recently a drug-induced immune-based pancreatitis has been reported in association with other systemic immune adverse effects, including colitis, in patients being treated with immune check-point inhibitors (ICI), such as cytotoxic T-lymphocyte–associated protein 4 (CTLA-4) and programmed death-ligand 1 (PD-L1) inhibitors.[4,5] Initial experience suggests that discontinuation of the ICI medication with or without steroid therapy may be effective.

Accurate assessments of incidence and prevalence of AIP remain largely unknown, although one study in Japan estimates that the incidence of AIP was approximately 1 per 100,000.[6] The rate of undiagnosed AIP in large cohorts of patients undergoing pancreatic surgical resection of presumed pancreatic cancer is approximately 2%.[7,8] Although most cohorts have described adult patients, there is a growing, although limited, recognition of children who present with AIP, the largest of which reported the average age at diagnosis of 13 years, with presentations similar to type 2 AIP.[9]

Most patients with either type of AIP can be successfully managed with corticosteroid therapy rather than immune modulation or surgical intervention.[10] However, in patients who do not tolerate or whose disease is refractory to steroid therapy, there is an evolving understanding for the role of immune modulation, rituximab, and more invasive interventions.

Although this review article includes discussion of the clinical, radiologic, serologic, and pathologic features useful in making the diagnosis of AIP, this has been discussed in greater detail in another recent review.[11] We will therefore aim to emphasize management strategies for this complex disease.

CLINICAL CHARACTERISTICS

Clinical Presentation

Patients with either type of AIP commonly present with obstructive jaundice, abdominal pain, and/or biochemical evidence of pancreatitis, although those with type I AIP typically present at an older age (on average 16 years older).[12] 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.[12] The obstructive jaundice may be related to pancreatic swelling and compression of the biliary tree, or due to proximal extrahepatic and intrahepatic duct stricture, which can be part of an associated IAC.[13] 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.