What Is the Latest in Autoimmune Pancreatitis

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KEYWORDS

• Autoimmune pancreatitis • Immunoglobulin G4-related disease
• Lymphoplasmacytic sclerosing pancreatitis • Granulocytic epithelial lesion
• Chronic pancreatitis • Immune-related adverse event

KEY POINTS

- Autoimmune pancreatitis (AIP) is composed of 2 subtypes, lymphoplasmacytic sclerosing pancreatitis and idiopathic duct centric pancreatitis, with distinct features in regard to pathology, immunology, epidemiology, clinical profile, and clinical course.
- Steroid-responsiveness is characteristic of AIP; therefore, a lack of response to steroid therapy should raise clinical concern for alternative diagnoses.
- Medical management of AIP involves induction of remission, management of relapse, and maintenance of remission.
- Corticosteroids are the mainstay of medical management of AIP, and other options include rituximab and immunomodulators, with emerging novel therapies targeting both B-cell and T-cell lineages.
- Timely diagnosis and treatment of AIP can decrease long-term consequences that include, but are not limited to, exocrine insufficiency or endocrine insufficiency.

INTRODUCTION

Autoimmune pancreatitis (AIP) is a chronic, steroid-responsive, fibroinflammatory disease of the pancreas.[1] AIP is composed of 2 distinct subtypes: type 1 AIP or lymphoplasmacytic sclerosing pancreatitis (LPSP) and type 2 AIP or idiopathic duct centric pancreatitis (IDCP).[1,2] Clinically, type 1 AIP commonly presents as obstructive jaundice with a pancreatic mass mimicking pancreatic cancer (PaC) and is histologically characterized by a lymphoplasmacytic infiltrate, storiform fibrosis, obliterative phlebitis, and positive tissue IgG4 staining.[2] In comparison, type 2 AIP usually presents with inflammatory pancreatitis, often in the context of underlying inflammatory bowel disease. While the pancreatic tissue fibroinflammatory appearance in type 2 AIP is similar to type 1 AIP, immunoglobulin G4 (IgG4) staining is either weak or absent,

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and the presence of granulocytic epithelial lesion (GEL) is considered the histologic hallmark. Level 1 and level 2 diagnostic criteria have been identified for both subtypes of AIP, depending on diagnostic reliability.[2] These combine imaging features of the pancreatic parenchyma and duct on computed tomography (CT) or MRI, serology (serum IgG4), other organ involvement, and histopathology.[1] The phases of medical management for AIP include induction of remission, maintenance of remission, and treatment of relapse.[1,2] "Remission" in AIP refers to the complete resolution of the inflammatory component of the disease with or without normal structure and function of the organs involved. "Recrudescence" in AIP refers to worsening of the disease before remission is achieved. "Relapse" in AIP refers to recurrent clinical, radiologic, or biochemical evidence of disease activity that occurs any time after achieving complete remission, often months to years after the index presentation. Corticosteroids remain the established first-line treatment of both AIP subtypes. Type 1 AIP is the pancreaticobiliary manifestation of IgG4-related disease (IgG4-RD). Options for medical treatment of type 1 AIP have evolved over the years with the inclusion of immunomodulators such as azathioprine, 6 mercaptopurine (6-MP), and mycophenolate and more recently rituximab (RTX). There are ongoing studies on newer alternatives such as biologic therapies for the treatment of patients with type 1 AIP summarized subsequently in this review.

History of Autoimmune Pancreatitis

Autoimmunity was suggested as an etiology of pancreatitis as early as 1961.[3] This was further explored by Kawaguchi,[4] who described this disease as LPSP in 1991. Shortly thereafter, it was observed that the natural history of chronic pancreatitis (CP) arising in the context of autoimmune diseases was distinct from other forms of CP warranting the consideration of this clinical entity as a subcategory of CP. The term "AIP" was first proposed by Yoshida in 1995.[5] By 2002, the Japan Pancreas Society (JPS) proposed the first diagnostic criteria for AIP, which comprised typical imaging findings with supportive serology and histopathology findings.[6,7] Around this time, a team of Mayo Clinic investigators led by Chari[8] had collectively initiated a detailed assessment of histology, imaging serology, other organ involvement and steroid-responsiveness of this emerging entity that was becoming easier to recognize in clinical practice based on published reports from around the world. A new diagnostic criteria that included these components were published from the United States in 2006 and would later go on to be known as the HISORt criteria. The JPS criteria were also revised in 2006.[9] Further study of AIP led to several groups around the world summarizing their experience for diagnosis and management of this clinical entity.[10–16] However, a lack of consensus led experts to converge on a universal criteria in 2010, The International Consensus Diagnostic Criteria (ICDC), which remain the standard of diagnosis for AIP.[2]

Initially, the Asian experience had indicated this entity to be primarily IgG4-mediated, which was in contrast with the European reports that seemed to indicate that IgG4 and autoantibodies do not play a major role in AIP. Further study of the clinicopathologic features of AIP cases in the United States led to the identification of 2 histologic groups designated as LPSP and IDCP in 2003.[15,17] It gradually came to light that these histologic entities appeared to characterize 2 distinct clinical phenotypes and while LPSP was characterized by an abundance of tissue IgG4+ cells, IDCP was not. Kamisawa[18] performed immunohistochemical investigations on cases of AIP which revealed infiltration of IgG4-positive cells not only in the pancreas but also in extrapancreatic organs, leading to AIP being identified as a pancreatic manifestation of systemic IgG4-related autoimmune disease. It was also recognized that type

1 AIP was the more common subtype around the world,[19–22] with a profile distinct from type 2 AIP in regard to pathology, immunology, epidemiology, clinical profile and clinical course.[23–25]

CLINICAL PRESENTATION, IMAGING FEATURES, AND HISTOLOGY

Lymphoplasmacytic Sclerosing Pancreatitis

Type 1 AIP or LPSP is the pancreatic manifestation of IgG4-RD.[1,2,24–26] It is typically diagnosed in individuals aged older than 60 years[1,25–27] (**Table 1**). There is a 3:1 male preponderance.[1,25,27] It commonly presents as painless obstructive jaundice. Other presentations include focal pancreatic mass, diffuse pancreatic enlargement or pancreatic duct stricture and rarely as acute pancreatitis.[1,25,26] Pancreaticobiliary disease is the most common clinical subtype of IgG4-RD. Other organ involvement in IgG4-RD include retroperitoneum and aorta phenotype (includes retroperitoneal fibrosis and sclerosing mesenteritis), head and neck-limited phenotype (includes orbital pseudotumor and hypophysitis), or Mikulicz and systemic phenotype (includes interstitial lung disease and interstitial nephritis).[1,2,24–28] Other organ involvement, when present alongside pancreaticobiliary manifestations, is a valuable diagnostic clue for type 1 AIP (**Fig. 1**A–C).

On CT or MRI, diffuse enlargement of the pancreas with delayed enhancement is a level 1 diagnostic criterion for LPSP.[1,2,26,29] The terms "sausage-shaped" or "featureless" may be used to describe an associated effacement of the lobular contour of the pancreas.[1,25,29] A capsule-like low attenuating rim around the enlarged pancreas is fairly characteristic and seen in 30% to 40% of patients.[25,29] There can also be segmental or focal enlargement of the pancreas.[1,2,26] Magentic resonnance cholangiopancreatography (MRCP) can delineate duct changes such as diffuse narrowing, segmental, or multifocal strictures without upstream dilation of the pancreatic duct.[25,30]

Histologically, LPSP is characterized by the presence of dense infiltration of plasma cells and lymphocytes, storiform fibrosis, and obliterative phlebitis and abundant IgG4-positive plasma cells (usually more than 10 IgG4-positive plasma cells per high-power field).[1,2,24–26,31] There are no GELs on histology. It is serologically characterized by elevated IgG4 serum levels.[1,2,24–27] While LPSP can be diagnosed using the ICDC criteria and does not always mandate histologic confirmation, it is critical to definitively exclude underlying malignancy prior to initiation of treatment.[27]

Idiopathic Ductal Centric Pancreatitis

Type 2 AIP or IDCP only involves the pancreas and is not a component of systemic disease. Compared to type 1 AIP, it occurs more often in younger patients, without a sex preponderance[1,2,25,26] (see **Table 1**). It most commonly presents as an episode of otherwise unexplained acute pancreatitis.[1,2,25,26] Other less common presentations of IDCP include painless obstructive jaundice, a focal pancreatic mass or symptomatic duct stricture.[1,2,25] It is associated with inflammatory bowel disease, frequently ulcerative colitis, in 15% to 30% of cases.[1,2,24–26]

On CT or MRI, IDCP closely mimics LPSP.[1,2,26,29] Imaging findings include diffuse enlargement of the pancreas, a low-density segment without a mass, interstitial pancreatitis, and pancreatic atrophy.[1,2,26]

Intraluminal and intraepithelial neutrophils in the medium and small ducts, leading to the destruction obliteration of pancreatic duct lumen, called GELs are pathognomonic for IDCP.[1,2,24–26,31] Tissue IgG4 staining is either scant or absent. Histologic confirmation is required for a definitive diagnosis of IDCP.[27] There is no association with serum

Table 1
Comparing features of type 1 autoimmune pancreatitis/lymphoplasmacytic sclerosing pancreatitis and type 2 autoimmune pancreatitis/idiopathic duct centric pancreatitis

	Type 1 AIP (LPSP)	Type 2 AIP (IDCP)
Average age at diagnosis	60–70 y	40–50 y
Sex	Male predominance	Equal
Most common clinical presentations	• Obstructive jaundice • Acute pancreatitis	• Acute pancreatitis • Obstructive jaundice
Histologic features	• Lymphoplasmacytic infiltration • Absent GELs • Storiform fibrosis • Obliterative phlebitis • >10 cells/HPF IgG4-positive cells	• Lymphoplasmacytic infiltration • GELs • Less prominent storiform fibrosis • Rare obliterative phlebitis rare or absent IgG4-positive cells
Imaging	Similar radiological findings for both subtypes	
Association with IBD	Not associated	Associated
Other organ involvement	• Retroperitoneal fibrosis • Biliary strictures • Sclerosing mesenteritis • Orbital pseudotumor • Hypophysitis • Interstitial nephritis • Mikulicz syndrome • Others	Not associated
Serum IgG4	Elevated	Not elevated
Risk of relapse	High	Low

Abbreviations: IBD, inflammatory bowel disease; HPF, high power field; IgG4-SC, Immunoglobulin G4 sclerosing cholangitis.

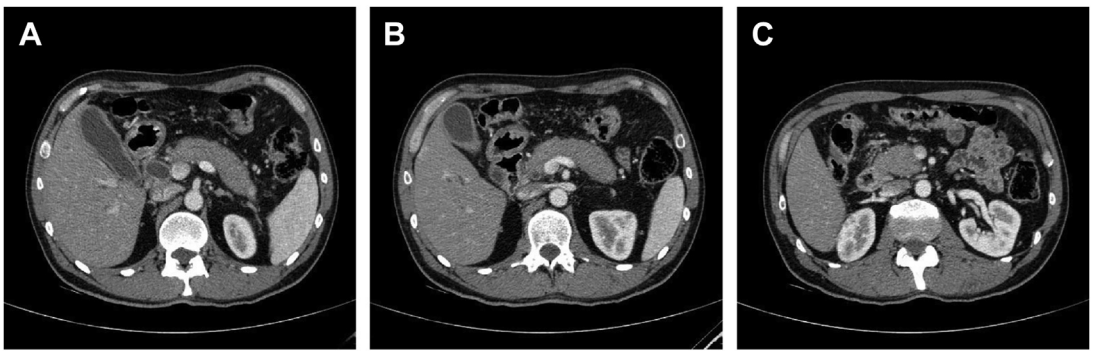

Fig. 1. Computed tomographic (CT) images showing (*A*) pancreatic, (*B*) biliary, and (*C*) renal involvement in type 1 AIP.

IgG4 and no other identified serologic marker for IDCP.[1,2,24,26] **Table 1** summarizes the key similarities and differences between type and type 2 AIP.

Immune Check Point Inhibitor-induced Pancreatitis

Immune check point inhibitors (ICIs) are monoclonal antibodies that block cytotoxic T lymphocyte-associated protein 4 (CTLA-4), programmed cell death receptor 1 (PD-1), and programmed cell death ligand 1.[32–34] ICIP is a pancreatic immune-related adverse event (irAE) related to administration of ICIs.[32–34]

Recent reports have referred to ICIP as type 3 autoimmune pancreatitis, primarily due to the suspected immune-mediated pathophysiology. The demographic profile of ICIP is not well described given the rarity of this entity. It is has been shown that irAEs generally are more likely to occur in the sixth decade of life and among Caucasian men.[32] Combination therapy with anti-CTLA-4 and anti-PD-1 is associated with a higher incidence and severity of ICIP compared to monotherapy. ICIP has varied clinical presentations including asymptomatic pancreatic enzyme elevation in two-thirds of cases, and painful pancreatitis in only about 20% of cases. Radiologically, unlike other forms of AIP, there is no characteristic imaging appearance of the acute episode. However, the pancreas eventually develops parenchymal atrophy without ductal changes or calcification, a radiologic progression that mimics AIP.[32–34]

Differential Diagnosis

Patients with type 1 AIP commonly present with a pancreatic mass and/or obstructive jaundice, making it difficult to distinguish from PaC.[1,2,11,31–36] AIP can also coexist with PaC.[25] The presence of a previously undiagnosed PaC should be considered in patients undergoing the initial evaluation for AIP. Given that AIP is less common than PaC, it has been recommended that the diagnosis of AIP should be considered only after PaC has been definitively excluded.[1,2]

AIP has been found to have a distinct pattern of enhancement from PaC on dual-CT imaging.[29] A comparative study was performed for patients with AIP and PaC to help physicians distinguish these 2 entities and provide a strategy for workup of patients on the basis of CT features, serology, and other organ involvement.[11] The patients were stratified into 3 groups namely group 1, highly suggestive of AIP; group 2, which is indeterminate, and group 3, highly suggestive of PaC.[11] However, approximately 30% of patients with AIP will still require pancreatic core biopsy, steroid trial, and rarely surgical pathology to establish the diagnosis.[11] In patients presenting with a pancreatic mass, the absence of pancreatic duct dilation and absence of vascular involvement generally favors a diagnosis of AIP. Concomitant presence of other organ involvement with characteristic features of IgG4-RD can be useful for the diagnosis of AIP.

MEDICAL MANAGEMENT OF AUTOIMMUNE PANCREATITIS

International recommendations for the management of AIP outline a primarily medical approach to treatment.[37] Aims of medical therapy include reducing pancreatic inflammation, alleviating associated symptoms, and possibly reducing subsequent disease complications. Steroid therapy may not only improve structural abnormalities but also exocrine and endocrine abnormalities.[25–27] Other agents used in the treatment of AIP include RTX and immunomodulators such as azathioprine or mycophenolate mofetil (MMF).[25,27,37]

Treatment of AIP is typically reserved for patients who are symptomatic with clinical signs of pancreatic involvement (eg, obstructive jaundice and abdominal pain) or other

biliary involvement (eg, biliary stricture leading to jaundice).[27,37] Indications for treatment of asymptomatic patients include a persistent mass of the pancreas on imaging or persistent abnormalities in liver tests in IgG4-related sclerosing cholangitis.[27,37] It remains unclear if treatment of asymptomatic pancreatic disease prevents future development of endocrine or exocrine dysfunction.

Given that both subtypes are dramatically steroid-responsive, the use of corticosteroids remains the mainstay of therapy for both LPSP and IDCP.[37] This is both diagnostic and therapeutic, with a lack of response to steroids considered to be an indication to consider alternative diagnoses.[37] Response to steroids is determined by clinical, radiological, and biochemical changes on follow-up and should be used cautiously for establishing a diagnosis, typically reserved in cases with high likelihood of AIP based on other diagnostic criteria.[25]

Spontaneous resolution of AIP in the absence of any therapy has been observed in approximately 10% to 25% of AIP, supporting a "watchful waiting" approach among asymptomatic patients.[37] Though patients with IgG4-RD may experience spontaneous resolution without treatment, patients with AIP who receive steroid therapy have a significantly higher remission rate than those who do not receive steroid therapy.[38] There is also emerging evidence that timely diagnosis and treatment can reduce long-term organ dysfunction.

Induction of Remission

Steroids remain the cornerstone of treatment of AIP. The recommended dose to induce remission is prednisolone 0.6 to 0.8 mg/kg/d or prednisone 40 mg/d.[1,2,25,27,37] This dose is administered for 4 weeks while evaluating response to treatment with clinical findings, biochemical tests, and imaging. A minimum dose of 20 mg/d is generally required to induce remission. Patients typically exhibit response within 2 to 4 weeks.[25] Tapering the dose before 4 weeks is avoided to prevent recrudescence. In patients with poorly controlled diabetes mellitus, a shorter initial course of high-dose steroids may need to be considered under expert guidance. Decreases in serum IgG4 can be seen within 4 weeks with a downward trend that spans several months. In patients demonstrating a response to therapy, induction is followed by a gradual steroid taper. The recommended taper is a reduction in dose by 5 mg every 1 to 2 weeks, for a total treatment of at least 12 weeks.[25,37]

Lower doses of prednisone have been trialed for induction of remission.[37,38] In a study comparing low dose (10–20 mg/d), medium dose (30 mg/d), and high dose (40–60 mg/d) prednisone in AIP, there was comparable symptomatic, radiological, and laboratory improvement.[39] However randomized trials have not been performed to validate these findings. Another recent retrospective study from Europe indicated that higher corticosteroid doses ($\geq$0.4 mg/kg/d) were no more effective in remission induction compared to lower doses and the risk of relapse within 6 months was independent of steroid tapering duration, induction treatment duration, and total cumulative dose.[40] There is some evidence that steroids may prevent progression to CP, especially in patients with pancreatic head swelling and dilation of the main pancreatic duct, but more data are necessary to understand the long-term impact of treatment on pancreatic function.[41]

RTX is a chimeric monoclonal antibody against CD20, a B-cell-specific antigen.[27] RTX is the only other steroid-sparing monotherapy that can be used for induction therapy for AIP.[25,27,37,42–45] RTX can be considered in patients with contraindications to steroids, patients who do not tolerate steroids, and to induce remission in patients with refractory or relapsing disease.[25,37] The recommended dose to induce remission for AIP is either RTX 375 mg/m^2 once weekly for 4 weeks or RTX 1000 mg

administered as 2 doses on day 0 and 14. RTX has been shown to achieve a remission rate as high as 97% at 6 months.[27]

Management of Relapse and Maintenance of Remission

Maintenance therapy should be considered for patients who are at high risk of relapse or who exhibit evidence of recrudescence or relapse with tapering or cessation of steroid therapy. Relapse is more common in LPSP than IDCP.[24] Approximately 30% to 50% of patients with LPSP experience a relapse, compared to less than 10% of patients with IDCP.[25,26] Other identified risk factors for relapse include initial high levels of serum IgG4, IgG4-related sclerosing cholangitis, more than 2 other organs involved, and delayed radiological remission with treatment.[24,25,37] Relapses of type 2 AIP are infrequent and typically managed with a repeat course of corticosteroids similar to treatment of the index presentation, and there is no proven role of maintenance therapy or use of immunomodulators or RTX in type 2 AIP. The following section describes the management of relapses in type 1 AIP.

Treatment options for relapses include (1) high-dose steroids similar to the management of the index episode with or without low-dose long-term steroid maintenance therapy, (2) high-dose steroids combined with immunomodulator therapy with eventual steroid taper and discontinuation, and (3) RTX induction with or without maintenance.[26,37,43] Maintenance therapy with steroids when used should be administered at a low dose of 2.5 to 10 mg/d.[25] Continuation of low-dose steroid therapy for up to 36 months has been demonstrated to reduce the rate of relapse compared to steroid cessation in a randomized controlled trial for patients with AIP.[25] In patients who initially receive RTX for induction only, a higher relapse rate is observed when compared to patients who receive RTX induction followed by maintenance therapy and RTX maintenance therapy prolongs remission.[27,46] Though relapses can occur in patients treated with RTX, these relapses can be effectively managed with repeat administration of RTX and relapses are distinctly uncommon in patients while on RTX maintenance therapy. Elevated alkaline phosphatase at baseline especially if levels remain elevated after RTX induction, higher IgG4 responded index score, and patients who are younger at time of diagnosis are at a greater risk of relapse.[46] The presence or absence of these factors can, therefore, guide decision-making on the need for maintenance therapy while considering the increased risk of infection with long-term immunosuppressive therapy.

Azathioprine (AZA), MMF, 6-mercaptopurine, cyclosporine A, tacrolimus, methotrexate, and cyclophosphamide have been used as steroid sparing agents in patients with AIP.[26,27,37,47] Use of these agents may be helpful in reducing long-term risks of steroid therapy in patients who required a more prolonged course of immunosuppression to maintain remission especially in patients who cannot receive RTX.[26,45] There is variation on the choice of steroid sparing agent, with AZA being the most commonly used in clinical practice followed by MMF, with other agents rarely used in clinical practice.[37] In type 1 AIP, higher doses of AZA (2.0–2.5 mg/kg), similar to that used in the management of inflammatory bowel disease, are recommended for AIP.[27] A 6 to 8 week overlap with steroid treatment is recommended for immunomodulators to allow adequate time for steroids to induce remission.[37] Unfortunately, nearly half of the patients with type 1 AIP will relapse while on immunomodulator therapy limiting their efficacy as a maintenance strategy.[42]

Emerging Therapies

There are several emerging therapies for IgG4-RD targeting both B-cell and T-cell lineages.[48] Abatacept (CD80/86 inhibitor) and XmAb5871 (humanized anti-CD19 with

Fcγ-RIIb antibody) are among new therapies being trialed.[27] A recent open-label study of abatacept in active IgG4-RD demonstrated variable response with sustained response in only half of the patients in the absence of concomitant glucocorticoid therapy.[48,49] In a single-arm phase 2 pilot study with Xmab5871, now referred to as obexelimab, 80% of patients achieved the primary response endpoint and a randomized, placebo-controlled trial is in progress to further evaluate the role of this promising novel agent in the management of IgG4-RD. A phase 2 proof-of-concept trial for elotuzumab (anti-SLAMF7 monoclonal antibody) in IgG4-RD is also in progress.[27] The results of these trials may expand the therapeutic options for this rare disease beyond corticosteroids and B-cell-depleting agents.

Role of Endoscopy in the Management of Autoimmune Pancreatitis

Endoscopy has a diagnostic and therapeutic role in the management of AIP.[50–52] Biliary brushing and cytology can help differentiate IgG4-SC from biliary malignancy. Endoscopic biliary stenting standalone does not resolve biliary strictures in active AIP and stenting needs to be accompanied with medication to induce remission, typically steroids. Endoscopic biliary stent placement can be safely performed while patients are on steroid therapy and typically removed within 4 weeks of steroid initiation.[50] Traditionally biliary stenting has been the primary modality of treating obstructive jaundice in AIP. However, when the diagnosis of AIP is established definitively and the patient is under the care of a pancreatologist with experience in managing AIP, biliary obstruction can be managed medically with oral corticosteroids alone, without concomitant need for biliary stenting.[53] Endoscopic ultrasound (EUS)-guided fine needle biopsies, when available and clinically appropriate, can greatly facilitate the diagnosis of AIP, whereas the role of EUS fine-needle aspiration is rather limited for diagnostic purposes.[54,55] While a diagnosis of type 1 AIP does not mandate histologic confirmation in the appropriate clinical context supported by imaging and serology, a pancreatic biopsy should be strongly considered in suspected type 2 AIP as histologic confirmation is essential to definitively establish a diagnosis.[24,25,27] Additionally, though characteristic features of AIP have been identified on EUS and endoscopic retrograde cholangiopancreatography (ERCP), the ability to diagnose AIP using these modalities alone remains limited.[30,56] There is emerging evidence to indicate that artificial intelligence algorithms applied to EUS images may be highly accurate in differentiating a malignant pancreatic mass from AIP.[57]

Long-term Consequences of Autoimmune Pancreatitis

Chronic inflammation of the pancreas in patients with AIP can lead to associated complications. Exocrine insufficiency is estimated to affect about 45% of patients with AIP at the time of diagnosis and 36% of patients with AIP during follow-up.[58] Exocrine insufficiency is more common in patients with disease activity within the head of the pancreas.[59] Recovery of pancreatic exocrine function has been observed after initiation of steroid therapy.[59]

Endocrine insufficiency has been estimated to affect 36% of patients with AIP at the time of diagnosis and 44% of patients with AIP during follow-up.[58] Endocrine insufficiency is also much higher in LPSP than IDCP.[60] Steroid therapy has also been associated with an increased rate of diabetes.[61]

Other complications that have been described include pancreatic stone formation, though this occurs less often in AIP than with other forms of CP. There are emerging data indicating an increased risk of cancers in patients with AIP, especially gastric cancer and PaC, which generally involves the area of the pancreas affected by AIP and has been more frequent in the LPSP subtype.[61,62] Interestingly, while long-term

steroid maintenance may adversely impact glycemic function and bone health, it appears to reduce the risk of cancer and improve survival. These findings need to be confirmed in larger cohorts.[61]

FUTURE DIRECTIONS

Further research on AIP is key to better refine understanding of this clinical entity, specifically to identify genetic, environmental, and immunologic factors that contribute to the pathogenesis of AIP. There is a need to develop noninvasive biomarkers that differentiate AIP from pancreaticobiliary malignancies and other forms of CP. While steroids remain the mainstay of treatment, the optimal dose and duration of induction therapy as well as patient selection for maintenance therapy warrants further prospective study. Exploration of novel medical therapies is ongoing with several promising candidates emerging. Future studies should focus on standardizing treatment options, selection of first-line therapy, duration of treatment, need for maintenance, and selection of alternative agents in patients with relapsing disease.

SUMMARY

AIP is a chronic, fibroinflammatory disease for which 2 distinct subtypes, LPSP and IDCP, have been identified. Differentiating AIP from other conditions such as PaC is key. Medical management involves induction of remission, management of relapse, and maintenance of remission. This is most often achieved with the use of steroid therapy, which can acutely reduce inflammation and alleviate symptoms. More recently, there has been evidence to support the use of RTX, immunomodulators, and emerging therapies targeting both B-cell and T-cell lineages.[48] Though AIP is typically characterized by a benign clinical course, the burden of disease can be high especially in patients with refractory type 1 AIP and complications such as pancreatic exocrine insufficiency, endocrine insufficiency and malignancy can occur. These patients should ideally be managed in centers with medical pancreatology expertise.

CLINICS CARE POINTS

- Autoimmune pancreatitis may mimic pancreatic cancer and the diagnosis of cancer needs to be definitively excluded prior to initiating treatment for AIP.
- Corticosteroids are the mainstay of AIP treatment.
- In patients with relapsing disease maintainence therapy with immunomodulators or Rituximab may need to be considered.
- Long term consequences of AIP include exocrine pancreatic insufficiency, diabetes mellitus and increased risk of cancer. Early effective treatment may lower the risk..

DISCLOSURE

The authors have no disclosures relevant to the content of this article.

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