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Review article

Clinical validation of the international consensus diagnostic criteria and algorithms for autoimmune pancreatitis: Combined IAP and KPBA meeting 2013 report

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A B S T R A C T

There have been great developments in the diagnosis and treatment of autoimmune pancreatitis (AIP) in the last decade. Most significantly, the international consensus diagnostic criteria (ICDC) proposed in 2011 were the first attempt to provide unified diagnostic criteria incorporating most features of the previously existing national criteria. However, the ICDC have not yet been prospectively validated using evidence-based studies since their introduction. An international symposium on the diagnosis of AIP was held in Seoul, South Korea on September 6, 2013, in cooperation with the International Association of Pancreatology and the Korean Pancreatobiliary Association meeting. In contrast to other symposia in the past, which had primarily focused on the diagnostic criteria themselves, expert panels in this symposium discussed how the diagnostic criteria and algorithms had been embraced in clinical settings to diagnose AIP in each country and conducted a comprehensive evaluation of these criteria and algorithms. It was acknowledged that there was a room for improvement in the ICDC and their algorithms and that further modifications might be required in the future. Prospective clinical validation in larger series is needed for confirmation.

1. Introduction

During the last decade, there has been growing recognition of a peculiar type of chronic pancreatitis known as autoimmune pancreatitis (AIP). Although the concept, characterization and treatment of AIP have evolved significantly, the diagnosis of AIP remains challenging in clinical practice. Since 2002, when the Japan Pancreas Society (JPS) first proposed diagnostic criteria for AIP based on pancreatic imaging, serology and histology [1], several sets of diagnostic criteria for AIP have been advocated around the world, including the revised JPS criteria (2006 and 2011) [2,3], the original and revised HISORt criteria (2006 and 2009) [4,5], the Korean criteria (2007) [6], the Asian diagnostic criteria (2008) [7], the Verona criteria (2009) [8] and the Mannheim criteria (2009) [9]. The diversity of diagnostic criteria for AIP in various countries may reflect differences in practice patterns in the use of various tests (e.g., diagnostic endoscopic retrograde pancreatography [ERP]), local expertise (e.g., endoscopic ultrasound [EUS]-guided pancreatic core biopsy [PCB]), and clinical epidemiology (e.g., type 1 vs. type 2 AIP).

The international consensus diagnostic criteria (ICDC) formulated under the influential leadership of Drs. Chari and Shimosegawa in 2011 have marked a significant step forward in the diagnosis of AIP (Table 1). The ICDC unified multiple diagnostic criteria from different countries. Eastern and Western experts have reached a consensus on diagnostic criteria for AIP in response to the need to diagnose AIP regardless of the practice patterns in the use of various tests and to incorporate the two different subtypes (type 1 and type 2) of AIP [10].

In the ICDC, the entity of AIP consists of two distinct clinical and histopathological forms of pancreatitis; type 1 and type 2. In

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contrast to type 2 AIP that appears to exclusively affect the pancreas, type 1 AIP is now viewed as the pancreatic manifestation of a systemic fibroinflammatory disease referred to as IgG4-related disease. To diagnose AIP, the ICDC use varying combinations of the five cardinal features of AIP; pancreatic imaging (parenchymal and ductal), serology (immunoglobulin G4; IgG4), other organ involvement (OOI), histopathology and immunostaining, and steroid responsiveness. The ICDC feature a grading for each category as level 1 or level 2, depending on the strength of the association with AIP. The criteria and algorithms for types 1 and type 2 AIP were developed separately. How these recent advances have been embraced in general practice, however, is not clearly known, especially with regard to the algorithmic approach. It is time to validate the ICDC and their algorithms using more objective evidence.

2. Seoul symposium on the diagnosis of AIP

The Joint Meeting of the International Association of Pancreatology and the Korean Pancreatobiliary Association was held in Seoul, South Korea, between September 4 and 7, 2013. An international symposium on the diagnosis of AIP was held on September 6 during which experts from Japan, Korea, the U.S., Germany and Italy (see Appendix) engaged in vigorous debate on the diagnostic criteria and algorithms for AIP and discussed future directions to improve them. In contrast to other international symposia in the past, which mainly dealt with diagnostic criteria themselves, this symposium aimed to assess how the international consensus diagnostic algorithms have been integrated in each country to diagnose AIP in clinical practice. This meeting provided a good opportunity to evaluate the current use of the ICDC and their algorithms in clinical settings and to identify their potential limitations that may require further clarifications and modifications in the future.

Herein, we report a brief summary of the discussions regarding the current use of the ICDC and their algorithms as a diagnostic tool in clinical settings.

3. Controversies in the ICDC

3.1. Issues related to other organ involvement

3.1.1. Grading of OOI

Under the ICDC, for type 1 AIP, proximal bile duct stricture and retroperitoneal fibrosis are classified as level 1 (highly suggestive of) OOI, while enlarged salivary glands and renal involvement are classified as level 2 (only supportive) OOI. Level 1 OOI constitutes findings that strongly suggest AIP, such as imaging findings that are very rarely observed in pancreatic cancer and do not require histological verification. However, it is not clear why renal involvement is classified as level 2 OOI [11–13]. It could be argued that both retroperitoneal fibrosis and renal involvement provide clues for diagnosing AIP and permit reliable distinction between AIP and pancreatic cancer. As pancreatic cancer rarely metastasize to the kidney or retroperitoneum, the findings of renal involvement or retroperitoneal fibrosis would favor the diagnosis of AIP when differentiating between pancreatic cancer and AIP. Moreover, both findings can be recognized on abdominal CT which is part of the routine workup for AIP, and the retroperitoneum is not easily accessible for nonsurgical biopsy. On the other hand, the imaging features of lymph nodes involvement are non-specific and require histological confirmation to exclude pancreatic cancer-related lymphadenopathy. It was therefore suggested to classify lymph node involvement as lower level of evidence compared to proximal bile duct stricture, retroperitoneal fibrosis and renal involvement in terms of strength of association with AIP. Two organs/sites (proximal bile duct and retroperitoneal fibrosis) do not seem to have more evidence of strength to be superior to kidney involvement in the diagnosis and differential diagnosis of AIP. Renal involvement could be of the same level as retroperitoneal fibrosis.

Grading (level 1 vs. level 2) of each criterion (pancreatic ductal imaging, serum IgG4, OOI and histology) may not be established based on high-level of evidence.

3.1.2. Bile duct stricture as OOI (IgG4-related sclerosing cholangitis)

It remains controversial among experts whether isolated distal bile duct stricture represents a part of pancreatic lesion or OOI (IgG4-related sclerosing cholangitis [IgG4-SC]). In the ICDC, proximal (hilar/intrahepatic) bile duct stricture are classified as level 1 OOI whereas an isolated distal bile duct stricture confined to the intrapancreatic portion is not included in OOI as the distal bile duct stricture may be caused by extrinsic compression by pancreatic inflammation. Distal bile duct stricture is therefore regarded as a part of AIP and is not included in IgG4-SC. Recently, experts in Japan have established separate criteria for the diagnosis of IgG4-SC [14]. In contrast to the ICDC, the Japanese consensus criteria included isolated distal common bile duct stricture as IgG4-SC, because resection specimens of these patients with isolated intrapancreatic common bile duct stricture often show that ductal wall thickening spreads continuously from intrapancreatic common bile duct to the suprapancreatic middle bile duct [14]. Japanese investigators suggested that both IgG4-related biliary inflammation and pancreatic head swelling affect lower bile duct stricture, which may be included in IgG4-SC [15]. Therefore, consensus on an accurate definition of bile duct involvement as OOI would be necessary.

3.2. Diagnostic groups according to the ICDC

In the ICDC, AIP diagnosis was stratified by the strength of the supporting evidence for AIP into definite and probable. Thus the diagnosis of type 1 and type 2 AIP can be definite or probable, and AIP cases clinically indistinguishable between type 1 and type 2 AIP

Table 1
The international consensus diagnostic criteria for autoimmune pancreatitis.

Diagnosis	Imaging evidence	Collateral evidence
Definitive type 1 AIP	Typical/indeterminate	Histologically confirmed LPSP (level 1 H)
	Typical	Any non-D level 1/level 2
	Indeterminate	Two or more from level 1 (+level 2 D)
	Indeterminate	Level 1 S/OOI + Rt or level 1 D + level 2 S/OOI/H + Rt
Probable type 1 AIP	Indeterminate	Level 2 S/OOI/H + Rt
Definitive type 2 AIP	Typical/indeterminate	Histologically confirmed IDCP (level 1 H) or clinical inflammatory bowel disease + level 2 H + Rt
Probable type 2 AIP	Typical/indeterminate	Level 2 H/clinical inflammatory bowel disease + Rt
AIP-not otherwise specified	Typical/indeterminate	D1/2 + Rt

LPSP, lymphoplasmacytic sclerosing pancreatitis; H, histology of the pancreas; D, ductal imaging; S, serology; OOI, other organ involvement; Rt, steroid responsiveness; IDCP, idiopathic duct-centric pancreatitis.

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