

Differentiation of Type 2 Autoimmune Pancreatitis Presenting as Clinical Acute Pancreatitis

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See “Type 2 Autoimmune Pancreatitis (Idiopathic Duct-Centric Pancreatitis) Highlighting Patients Presenting as Clinical Acute Pancreatitis: A Single-Center Experience” by Dongwook Oh, et al. on page 461, Vol. 13, No. 4, 2019

Autoimmune pancreatitis (AIP) is known to be a chronic fibrosis-inflammatory disease of the pancreas that responds to steroids. In 1995, Yoshida *et al.*¹ introduced the term AIP to describe an inflammatory pancreatic disease reminiscent of autoimmune hepatitis. Since the establishment of diagnostic criteria for AIP in Japan in 2002, the concept of AIP has been increasingly recognized and nationwide diagnostic criteria have been proposed. Also, in South Korea, since the introduction of the diagnostic criteria of Kim *et al.*² in 2006, concern over AIP has increased.

The diagnosis of AIP requires pancreatic parenchymal and ductal imaging, determination of the serum immunoglobulin G4 (IgG4) level, the presence of characteristic pathologic findings, and a response to steroid therapy. The serum IgG4 level is characteristically elevated in type 1 AIP (~66%) but this is not a confirmative diagnostic marker because the serum IgG4 level is elevated in <25% of patients with type 2 AIP.³ Based on an enhanced understanding of its clinical characteristics, AIP is divided into histological type 1 (lymphoplasmacytic sclerosing pancreatitis, LPSP) and type 2 (idiopathic duct-centric pancreatitis, IDCP). LPSP and IDCP share histopathologic and clinical features, and the term AIP came to be used for both diseases; LPSP was termed type 1 AIP and IDCP, type 2 AIP.⁴

However, definitive diagnosis of type 2 AIP is still difficult because the imaging findings of the pancreatic parenchyma and the steroid response are similar to those of type 1 AIP; therefore, a pathologic diagnosis is required for confirmation. The guidelines of the International Association of Pancreatology (IAP) provide level 1 and 2 diagnostic criteria for type 2 AIP (Table

1).⁵ A histologic evaluation of the pancreas is also important for diagnosis of type 2 AIP. In patients presenting with obstructive jaundice and/or diffuse pancreatic enlargement/mass, if serology does not indicate type 1 AIP and there is no involvement of other organs, type 2 AIP can be diagnosed by IDCP and the diagnosis confirmed by pancreatic biopsy after exclusion of malignancy. Therefore, until pathologic confirmation of IDCP, use of the term AIP can result in confusion. On this basis, it was recently proposed that the term “AIP” be used only for LPSP (currently type 1 AIP), and “IDCP” only for IDCP (currently type 2 AIP). However, the term “type 2 AIP” is more familiar to physicians.

Over the past decade, type 1 AIP has been investigated extensively in South Korea, but type 2 AIP may be mislabeled as AIP (without subtype specification). Type 2 AIP predominates in Western countries, and has a younger age of onset and no gender deviation.⁶ Also, in 16% to 30% of cases, type 2 AIP presents together with an inflammatory bowel disease (IBD) such as ulcerative colitis (UC).^{7,8}

Although Oh *et al.*⁹ of *Gut and Liver* is a retrospective single-center study, results showed that the prevalence of type 2 AIP was not low in Korea. In that study, based on clinical, radiologic, and histologic evaluations the subjects were classified as “definite” or “probable” type 2 AIP according to the International Consensus Diagnostic Criteria. Among the 244 patients with AIP, 11.1% had type 2 AIP. All patients who received steroids but not surgical resection showed complete clinical and radiological remission.⁹ Endoscopic retrograde cholangiopancreatography and pathologic analysis can provide confirmative

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Table 1. International Association of Pancreatology Criteria for Type 2 Autoimmune Pancreatitis⁵

Criterion	Level 1	Level 2
Parenchymal imaging	Typical: diffuse enlargement with delayed enhancement (sometimes associated with rim-like enhancement)	Indeterminate (including atypical): segmental/focal enlargement with delayed enhancement
Parenchymal imaging	Long (>1/3 length of the main pancreatic duct) or multiple strictures without marked upstream dilatation	Segmental/focal narrowing without marked upstream dilatation (duct size, <5 mm)
Other organ involvement		Clinically diagnosed inflammatory bowel disease
Histology of the pancreas (core biopsy/resection)	IDCP, both of the following: (1) Granulocytic infiltration of duct wall (GEL) with or without granulocytic acinar inflammation (2) Absent or scant (0–10 cells/HPF) IgG4-positive cells	Both of the following: (1) Granulocytic and lymphoplasmacytic acinar infiltrate (2) Absent or scant (0–10 cells/HPF) IgG4-positive cells
Response to steroid	Diagnostic steroid trial Rapid (≤ 2 weeks) radiologically demonstrable resolution or marked improvement in manifestations	

IDCP, idiopathic duct-centric pancreatitis; HPF, high-power field; IgG4, immunoglobulin G4.

information, but the risk of adverse events may preclude further examination of patients with idiopathic pancreatitis, particularly young patients. For this reason, they compared the image findings of computed tomography (CT) and magnetic resonance cholangiopancreatography (MRCP). In younger patients with idiopathic pancreatitis, and particularly in cases of a first attack, obtaining a biopsy for diagnostic purposes is associated with a risk of complications.

Clinically, type 1 AIP typically presents as painless obstructive jaundice, and type 2 AIP as acute pancreatitis in ~50% of patients. Therefore, type 2 AIP can be mistakenly classified as idiopathic pancreatitis. Therefore, a histologic evaluation of the pancreas is needed for a definitive diagnosis of type 2 AIP presenting as acute pancreatitis, as its clinical diagnosis is problematic. To diagnose type 2 AIP, attention should be paid to a specific patient subpopulation (e.g., IBD). Type 2 AIP reportedly develops in younger patients (median, 29 years; 70.6% males) and all patients with type 2 AIP require analgesics for pain control. Before their diagnosis with type 2 AIP presenting as acute pancreatitis, nine patients (52.9%) had a medical history of idiopathic acute pancreatitis, and all of them had clinically mild pancreatitis. Also, the frequency of UC as a co morbidity was higher than type 1 (n=8, 47.1%).⁹

CT and MRCP can provide meaningful diagnostic information for type 2 AIP. Compared with gallstone pancreatitis, CT findings of multifocal lesions, focal mass, capsule-like low-density rim, delayed enhancement, and focal or segmental main pancreatic duct dilatation are more common in cases of type 2 AIP. Indeed, multifocality (35.3% vs 0%, $p < 0.01$), peripancreatic halo (11.8% vs 0%, $p = 0.01$), and delayed enhancement (81.3% vs 0%, $p < 0.01$) are found only in patients with type 2 AIP.⁹ However, patients with type 1 AIP may have similar features and it might be argued to compare with gallstone pancreatitis which also has its characteristics determined by image studies. Therefore, AIP should be diagnosed by stepwise exclusion of other types of

pancreatitis and needs pathological diagnosis in type 2 AIP for differentiation.

In conclusion, type 2 AIP is not rare in South Korea and should be suspected in young UC patients who present with clinical acute pancreatitis of unknown etiology. Also, larger nationwide studies involving pathologic findings are required to improve the diagnosis of AIP.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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