EDITORIAL

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CLINICAL ENDOSCOPY

A multidisciplinary approach is essential for differentiating autoimmune pancreatitis from pancreatic adenocarcinoma

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See "Diagnostic value of homogenous delayed enhancement in contrast-enhanced computed tomography images and endoscopic ultrasound-guided tissue acquisition for patients with focal autoimmune pancreatitis" by Keisuke Yonamine, Shinsuke Koshita, Yoshihide Kanno, et al., Clin Endosc 2023;56:510–520.

Autoimmune pancreatitis (AIP) is a glucocorticoid-responsive form of pancreatitis that can mimic pancreatic ductal adenocarcinoma (PDAC).[1] AIP can manifest as either a diffuse or focal type, depending on the affected portion of the pancreas. In some instances, unnecessary major pancreatic surgeries have been performed for AIP, particularly the focal type, when suspicion of malignant lesions cannot be ruled out after a comprehensive diagnostic workup.[2] In the current issue of *Clinical Endoscopy*, Yonamine et al.[3] explored the clinical differences between focal-type AIP (23 patients) and PDAC (44 patients) and also assessed the impact of endoscopic ultrasound (EUS)-guided tissue acquisition on the diagnosis of focal-type AIP.

The authors chose candidate factors to differentiate focal-type AIP and PDAC as follows: (1) serologic findings (carbohydrate antigen 19–9, immunoglobulin G4 [IgG4]), (2) computed tomography (CT) findings (contrast enhancement pattern, capsule-like rim), (3) endoscopic retrograde pancreatography (ERP) findings (length of the main pancreatic duct [MPD] stenosis, the diameter of the upstream MPD from the stricture, and visibility of the side branches arising from the MPD stenosis), and (4) EUS findings.[3] A multivariate analysis showed that only homogenous delayed enhancement on CT (odds ratio, 10.2; p=0.015) was a significant factor indicative of AIP compared to PDAC. Serum IgG4 level (>135 mg/dL) was not a significant factor, albeit with a relatively high odds ratio of 10.2 (p=0.096).

Although the study by Yonamine et al.[3] identified homogenous delayed enhancement as the only significant indicator of AIP, it is important to consider all the characteristic imaging features of AIP.[4] While this study did not utilize magnetic resonance imaging (MRI), dynamic contrast-enhanced MRI should be used in clinical practice to differentiate focal-type AIP from PDAC due to its superior tissue contrast resolution and the availability of diffusion-weighted imaging or magnetic resonance cholangiopancreatography.[1,4] The imaging features of AIP on CT or MRI may include the capsule-like rim, diffuse pancreatic enlargement, homogenous delayed enhancement, speckled enhancement, multiple pancreatic masses, absence of MPD dilatation, multiple MPD strictures, penetrating duct sign, and enhanced duct sign.[1,4] Additionally, it is crucial to evaluate extrapancreatic organ involvement in AIP since it is a pancreatic manifestation of an IgG4-related disease. Assessing the involvement of the bile duct, kidney, retroperitoneal fibro-

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sis, lachrymal gland, salivary gland, and lung is necessary when distinguishing between AIP and PDAC.[4]

This study reported ERP performance in 15 of 23 patients with focal-type AIP and all 44 patients with PDAC, which may reflect the practice pattern of Japanese pancreatologists who consider ERP crucial for diagnosing AIP. Although ERP was previously mandatory in Japanese diagnostic criteria, it is no longer considered essential in the revised Japanese clinical diagnostic criteria from 2018.[5] Instead, ERP has been adjusted to be equivalent to the combination of magnetic resonance cholangiopancreatography and negative malignancy demonstrated by EUS-guided sampling.[5]

In actual practice, diagnosing focal-type AIP requires tissue acquisition and adherence to diagnostic criteria.[6-8] Histopathologic examination has a dual role in diagnosing focal-type AIP: first, to exclude malignancy, and second, to provide pathological evidence supporting the diagnosis of AIP. In this study, 17 patients with AIP underwent EUS-tissue acquisition using various fine-needle aspiration and fine-needle biopsy (FNB) needles; 59% (*n*=10) and 12% (*n*=2) achieved levels 1 and 2 histology for AIP, respectively.[3] The authors demonstrated excellent histopathologic results using diverse needles; FNB needles are favored over fine-needle aspiration needles, as a recent meta-analysis showed superior diagnostic yield with FNB needles for diagnosing AIP.[9] Storiform fibrosis and obliterative phlebitis were observed in 65% (*n*=11) and 24% (*n*=4) of cases, respectively, aided by Elastica-Masson staining. Previous studies have reported varying rates of storiform fibrosis (0%-86%) and obliterative phlebitis (0%–49%) in samples obtained via EUS.[9] Consequently, the elastic stain and IgG4 immunohistochemistry should be incorporated for histological samples requiring differentiation of AIP.[10]

According to the international consensus diagnostic criteria for AIP, at least two level 1 collateral evidences are required to diagnose indeterminate imaging of AIP, including focal-type AIP.[6] These level 1 collateral evidences include serology (>2×upper limit of normal value), ductal imaging via ERP, extrapancreatic organ involvement (typical radiological evidence [multiple proximal or proximal and distal bile duct strictures, or retroperitoneal fibrosis]; and typical histology of extrapancreatic organs), and distinctive pancreatic histology.[6] Pancreatic histology must exhibit at least three of the following features: (1) periductal lymphoplasmacytic infiltrate; (2) obliterative phlebitis; (3) storiform fibrosis; and (4) abundant IgG4-positive cells.[6] Hence, a multidisciplinary approach, incorporating all diagnostic criteria, including serology, histology, other organ involvement, and steroid responsiveness, is essential for diagnosing focal-type AIP.

Over the past decade, researchers have extensively investigated the utility of various modalities for diagnosing AIP. However, a single, definitive modality for the diagnosis of AIP remains elusive, necessitating the continued use of the complicated diagnostic algorithm in the evaluation of AIP.[5,6]

In conclusion, there is no holy grail for the diagnosis of AIP. The differential diagnosis process of focal-type AIP may present challenges and concerns for pancreatologists, underscoring the importance of a multidisciplinary approach.

Conflicts of Interest

The author has no potential conflicts of interest.

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