Tissue Acquisition for Histologic Diagnosis

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Introduction

Autoimmune pancreatitis (AIP) is recognized as a distinct clinical entity, and it is also identified as a chronic inflammatory process of the pancreas in which the autoimmune mechanism is involved. The diagnosis of AIP is clinically challenging because it is a rare disease, which closely mimics more common pancreaticobiliary malignancies in its presentation such as obstructive jaundice and pancreatic mass. Type 1 AIP has dense periductal lymphoplasmacytic infiltrate with storiform fibrosis and obliterative phlebitis, whereas type 2 is distinguished from type 1 by granulocyte epithelial lesion, less prominent lymphoplasmacytic infiltrate, and less prominent storiform fibrosis [1]. The international consensus diagnostic criteria (ICDC) for AIP were developed based on the agreement of an international panel of experts and ICDC include both type 1 and 2 AIP [2].

The histological criteria of type 1 AIP are categorized as level 1, if more than three of the four criteria are met (lymphoplasmacytic infiltrate without granulocytic infiltration, obliterative phlebitis, storiform fibrosis, and >10 IgG4-positive plasma cells per HPF). If at least two of the criteria are met, the findings are categorized as level 2. Level 1 histological criterion for type 2 AIP is the presence of granulocytic epithelial lesions and the absence or scant presence of IgG4-positive cells. Level 2 histological criteria for type 2 AIP are the presence of granulocytic epithelial lesions with lymphoplasmacytic acinar infiltrate and the absence or scant presence of IgG4-positive cells. Therefore, adequate tissue acquisition is very important for a definite diagnosis of AIP.

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Indication for Tissue Acquisition

Although histopathological features are considered as the gold standard for a diagnosis of AIP, adequate tissue acquisition for a diagnosis of AIP is clinically difficult without surgical resection. So, we should know the indication of tissue acquisition. Because the most important decision for the differential diagnosis of pancreatic mass is to differentiate AIP from pancreatic cancer, endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) is usually performed to exclude the pancreatic cancer. However, a histological diagnosis of AIP using the small samples obtained by EUS-FNA is somewhat difficult. Another problem is that some AIP cases are difficult to distinguish as type 1 or type 2 AIP with small samples because these cases show less intense lymphoplasmacytic infiltration but more fibrosis, venulitis without obliterative phlebitis, and scattered neutrophils are present but granulocytic epithelial lesions are not.

Type 1 AIP can be diagnosed frequently without histological analysis. According to ICDC diagnostic algorithm, a diagnosis of type 1 AIP is possible with additional one non-ductal level 1/2 criteria if the pancreatic parenchymal image is typical. Non-ductal level 1/2 criteria include serology and other organ involvement. However, if the pancreatic parenchymal image is indeterminate or atypical, work-up for cancer is recommended. If there are two or more level 1 criteria such as ductal imaging, serology (IgG4, >2X upper limit of normal value), and other organ involvement, a definite diagnosis is possible without histology. Therefore, tissue acquisition should be done in all cases if there is no enough evidence of AIP. Of course, for the exact diagnosis of type 2 AIP, histology is always necessary because serum IgG4 level is normal and there is no other organ involvement except inflammatory bowel disease in type 2 AIP.

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Method of Tissue Acquisition

Percutaneous transabdominal ultrasonography-guided pancreatic tissue acquisition was a standard method before the era of EUS-FNA. The success rate and diagnostic yield are known to be higher in EUS-FNA for the diagnosis of pancreatic cancer. In addition, the problem of percutaneous approach is the high risk of cancer seeding. Micames et al. reported that the risk of peritoneal seeding was significantly lower with EUS-FNA (2.2 %) than with ultrasound-guided transabdominal FNA (16.3 %) [3]. Therefore, EUS-FNA is the standard method for the histologic diagnosis of possible pancreatic cancer, and percutaneous approach should not be done in patients with potentially resectable pancreatic cancer. Although EUS-FNA is sufficient to diagnose the pancreatic cancer, EUS-guided core biopsy is essential to obtain specimens of adequate size that preserves tissue architecture and permits an exact histological diagnosis of AIP. Usually, the primary role of EUS-FNA of the pancreas in patients with suspected AIP may be to exclude malignancy rather than to provide definitive evidence for a diagnosis of AIP. We should keep in mind that a negative biopsy/cytology is not a guarantee of non-malignancy. So, a short-term follow-up imaging to assess corticosteroid responsiveness is needed. If the patient does not respond to a diagnostic corticosteroid trial, a definitive diagnosis should always be pursued by core biopsy or resection. The ICDC suggest that negative work-up for pancreatobiliary malignancies is a prerequisite for a corticosteroid trial [2]. It should be emphasized that repeated EUS-FNA is warranted in patients with continued suspicion of pancreatobiliary malignancies despite indeterminate or negative findings at initial EUS-FNA. We should be aware that AIP is much less common than pancreatic cancer or cholangiocarcinoma.

In 2009, Detlefsen S et al. reported the role of core biopsy samples for the diagnosis of AIP [4]. The core needle biopsy specimens could be able to recognize AIP in 22 of 29 (76 %) specimens. In that study, most of core biopsy samples were obtained by percutaneous methods. However, another study concluded that percutaneous needle biopsy of pancreas was not satisfactory for the diagnosis of AIP even after IgG4-immunostaining because diagnostic sensitivity was only 47 % among 15 core biopsy samples [5]. Whereas FNA with a small caliber (22 or 25 gauge) provides material only for cytological review, a 19-gauge trucut biopsy (TCB) needle (Cook Endoscopy Inc, Winston-Salem, NC) acquires larger tissue samples to allow a histological diagnosis of AIP by preserving tissue architecture. Levy et al. reported the results of their retrospective study using EUS-TCB in patients with AIP [6]. The specimens obtained were adequate for histologic analysis in all 14 AIP patients and revealed diagnostic findings or abundant IgG4-positive plasma cells in 57 % of the patients (8 of 14). Mizuno et al. performed both EUS-TCB and EUS-FNA with a 22-gauge needle in 11 patients who were given a final diagnosis of AIP [7]. They reported that pancreatic specimens obtained by EUS-TCB showed full-spectrum lymphoplasmacytic sclerosing pancreatitis in 50 % (4 of 8) of the patients and probable lymphoplasmacytic sclerosing pancreatitis in another 4 patients (50 %, 4 of 8). However, EUS-FNA result showed that three out of eight patients with AI had full-spectrum lymphosplasmacytic sclerosing pancreatitis. One was reported as normal and 4 cases were inconclusive.

The complication rates of EUS-FNA for pancreatic mass were reported to be 0–2 % [8]. The complication rate of EUS-TCB is comparable to that of EUS-FNA. Although a TCB needle obtains the specimen on the tissue tray after cutting the tissue with only one sliding movement of the outer sheath, the FNA needle suctions the specimen inside of the needle after multiple movements of the needle inside the lesion. Theoretically, these differences in the specimen collection method might cause more distortions in the FNA specimen than that obtained by a TCB needle. However, the EUS-TCB has a technical limitation with regard to needle manipulation in the duodenum and in the approach to the pancreatic head because a puncture from the duodenum to the head of the pancreas usually requires an angulated scope position, endoscopic tip angulation, and the use of an elevator function, which makes the passage of the TCB needle difficult. So, overall diagnostic accuracy of EUS- trucut biopsy is known to be 50–72 % (Table 14.1). In addition, EUS-TCB is available in only a few specialized tertiary-care centers. Iwashita T et al. evaluated the samples collected by EUS-FNA with a conventional 19-gauge needle by histologic analysis, to look for features of AIP from 44 patients who were diagnosed with AIP [9]. EUS-FNA was performed successfully in all patients using a 19-gauge needle for the pancreatic lesions. However, 19 patients (43 %) were diagnosed with AIP based on histologic analysis.

In order to overcome the limitation of the 19-gauge needle, a EUS-guided fine-needle biopsy (EUS-FNB) device (Echotip Procore; Wilson Cook Medical Inc., Winston-Salem, North Carolina, USA) was developed. In a randomized trial, diagnostic sufficiency, technical performance, and safety profiles of the 22-gauge biopsy needle were comparable to those of the conventional 22-gauge aspiration needle for sampling of pancreatic mass [12]. In another prospective comparison study, the correct diagnosis rate of EUS-FNB was higher than that of EUS-FNA in the pancreatic mass group (86.8 % vs. 75 %, $P=0.046$) [13]. Larghi et al. reported the prospective result of EUS-FNB in 61 patients with pancreatic masses [14]. EUS-FNB was technically feasible in 98 % of patients with a solid pancreatic mass. A suitable sample for histological evaluation was obtained in 88.5 % of the cases after only one single needle pass. However, no article was published on the yield of

Table 14.1 Diagnostic yields of pancreatic biopsies in patients with AIP

Author (year)	Nation	Number	Technique	Diagnostic yield
Levy (2006) [6]	United States	14	EUS-trucut	Diagnostic 57 % (8/14) Suggestive 29 % (4/14) Inconclusive 14 % (2/14)
Hirano (2009) [5]	Japan	15	Percutaneous	Diagnostic 47 % (7/15) Suggestive 20 % (3/15) Inconclusive 33 % (5/15)
Mizuno (2009) [7]	Japan	8	EUS-trucut	Diagnostic 50 % (4/8) Suggestive 50 % (4/8) Inconclusive 0 % (0/8)
Detlefsen (2009) [4]	Germany Denmark	26	Percutaneous Intraoperative EUS-trucut	Diagnostic 81 % (21/26) Suggestive 19 % (5/26) Inconclusive 0 % (0/26)
Iwashita (2012) [9]	Japan	44	EUS-FNA (19G)[a]	Diagnostic 43 % (19/44) Suggestive 43 % (19/44) Inconclusive 7 % (3/44) Analysis impossible 7 % (3/44)
Song (2012) [10]	Korea	54	Percutaneous EUS-trucut	Diagnostic 72 % (39/54) Suggestive 0 % (0/54) Inconclusive 28 % (15/54
Fujii (2013) [11]	United States	7	EUS-trucut	Diagnostic 72 % (5/7) Suggestive 14 % (1/7) Inconclusive 14 % (1/7)

[a]EUS-guided tissue acquisition by using a conventional 19-gauge needle

EUS-FNB using the new needle for AIP diagnosis. Further studies are required to assess the diagnostic performance of EUS-FNB and comparison study between EUS-TCB and EUS-FNB for the better histologic diagnosis of AIP is necessary.

Summary

Type 1 AIP can be diagnosed frequently without histological analysis if image is typical and there are additional criteria. However, if the pancreatic parenchymal image is indeterminate or atypical, work-up for cancer is recommended. Therefore, tissue acquisition should be done in all cases if there is no enough evidence of AIP. Even if percutaneous transabdominal ultrasonography-guided pancreatic tissue acquisition was a standard method before the era of EUS-FNA, nowadays EUS-guided tissue acquisition is recommended because diagnostic yield is high and the risk of peritoneal seeding is low if the mass has possibility of pancreatic cancer. Theoretically, EUS-TCB seems to be a better method for obtaining core tissue; however, there are some technical limitations and diagnostic yield that are not satisfactory till now. The better needle should be developed to obtain the core tissue without technical limitation, and further studies are required to find the ideal and standard tissue acquisition method.

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