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ORIGINAL ARTICLE—LIVER, PANCREAS, AND BILIARY TRACT

Histological diagnosis of autoimmune pancreatitis using EUS-guided trucut biopsy: a comparison study with EUS-FNA

Nobumasa Mizuno · Vikram Bhatia · Waki Hosoda · Akira Sawaki · Noriyuki Hoki · Kazuo Hara · Tadayuki Takagi · Shigeru B. H. Ko · Yasushi Yatabe · Hidemi Goto · Kenji Yamao

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Abstract
Purpose The aim of this study was to evaluate the feasibility and safety of endoscopic ultrasonography (EUS)-guided trucut biopsy (TCB) for diagnosis of autoimmune pancreatitis (AIP).
Methods Fourteen patients with suspected AIP based on imaging studies underwent both EUS-guided fine-needle aspiration (FNA) and EUS-TCB for diagnosis of AIP and exclusion of pancreatic cancer (PC). According to the revised Japanese clinical diagnostic criteria, AIP was diagnosed in eight while the remaining six patients had pancreatitis of other etiologies. Pathologically, AIP was defined as lymphoplasmacytic sclerosing pancreatitis (LPSP), and sub-divided into two types: definite LPSP (d-LPSP) showing fulspectrum of LPSP and probable LPSP (p-LPSP) without obliterative phlebitis or abundant (>10 cells/hpf) IgG4-positive plasmacytes infiltration.
Results PC was excluded in all patients. EUS-FNA resulted in three of eight patients with AIP were reported as p-LPSP, one was reported as normal, and 4 were inconclusive. One of six with non-autoimmune pancreatitis was diagnosed as p-LPSP on EUS-FNA, one as idiopathic chronic pancreatitis (ICP) and four were inconclusive. By using EUS-TCB, all AIP patients were diagnosed as LPSP (4 d-LPSP and 4 p-LPSP). Of the six patients with non-autoimmune pancreatitis, three were diagnosed as LPSP (1 d-LPSP and 2 p-LPSP) and three showed ICP on TCB. No complications were identified in any patient with either EUS-FNA or TCB.
Conclusion EUS-TCB is a safe and accurate procedure for obtaining a histological diagnosis in patients with suspected AIP. EUS-TCB can serve as a rescue technique in cases of AIP lacking typical findings.

Keywords AIP · LPSP · EUS-TCB · Pancreatic cancer

N. Mizuno (✉) · A. Sawaki · N. Hoki · K. Hara · T. Takagi · K. Yamao
Department of Gastroenterology, Aichi Cancer Center Hospital, 1-1 Kanokoden, Chikusa-ku, Nagoya 464-8681, Japan
e-mail: nobumasa@aichi-cc.jp

V. Bhatia
Department of Medical Hepatology, Institute of Liver and Biliary Sciences (ILBS), New Delhi, India

W. Hosoda · Y. Yatabe
Department of Pathology and Molecular Diagnostics, Aichi Cancer Center Hospital, 1-1 Kanokoden, Chikusa-ku, Nagoya 464-8681, Japan

S. B. H. Ko · H. Goto
Department of Gastroenterology, Nagoya University Graduate School of Medicine, Nagoya, Japan

Introduction

Autoimmune pancreatitis (AIP) is now being increasingly diagnosed based on its unique clinical features, radiological images and serological findings [1–3]. Histopathological findings of AIP have typically been described in resected specimens since most cases of AIP are initially misdiagnosed as pancreatic cancer (PC), and obtaining adequate pancreatic tissue using non-surgical approaches is difficult [4–7]. Endoscopic ultrasonography (EUS)-guided fine-needle aspiration (FNA) is now widely accepted as a safe and effective modality for obtaining pancreatic tissue samples [8]. The diagnostic accuracy of FNA for PC is reported to be between 60% and 90%, but conclusive diagnosis of AIP is often difficult due to the small size of specimens obtained by

FNA [7, 9]. In view of this limitation, large-caliber cutting biopsy (trucut biopsy [TCB]) needles have been developed to acquire samples with preserved tissue architecture, thus allowing histological examination [10].

To date, several diagnostic criteria for AIP have been proposed from many countries such as Japan [11], Korea [12], United States (Mayo Clinic) [13], and countries of the European Union. Asian diagnostic criteria for AIP based on Japanese and Korean consensus were also proposed recently [14]. Among these, only the Mayo Clinic criteria (HISORt criteria) allow a conclusive diagnosis of AIP based on pancreatic histology without any radiological features or serological testing, when specific features of lymphoplasmacytic sclerosing pancreatitis (LPSP) are found on histology [13]. Although the HISORt criteria require a "core" biopsy for the diagnosis of LPSP, whether EUS-TCB is effective for providing an adequate histological core of the pancreas is unclear [15].

In May 2004, EUS-TCB of the pancreas was introduced at our hospital to obtain core pancreatic tissue from patients with suspected AIP. To date there is no study comparing EUS-FNA and EUS-TCB for diagnosis of AIP. Thus, the aim of this study was to evaluate the feasibility and safety of EUS-guided TCB (EUS-TCB) for the diagnosis of AIP, comparing it with the conventional EUS-FNA.

Patients and methods

This study was a retrospective case review of all patients who underwent both EUS-FNA and EUS-TCB for diagnosis of AIP and exclusion of PC. Between January 1997 and February 2008, we evaluated 36 patients in whom AIP was suspected because of pancreatic enlargement and narrowing of the main pancreatic duct (MPD) on computed tomographic (CT) imaging, magnetic resonance imaging (MRI), and/or endoscopic retrograde cholangiopancreatography (ERCP). After EUS-TCB was introduced at the Aichi Cancer Center, 14 of the above-mentioned patients underwent a pancreatic TCB to differentiate AIP from PC. All of the patients were non-drinkers with no family history of pancreatitis. Fourteen patients with PC who underwent both EUS-FNA and TCB were included in this study as control subjects.

Informed consent was obtained from all patients before the procedure. Collection of data for this study was approved by our Institutional Review Board. EUS-FNA of the pancreas was done with a disposable 22-gauge needle (EZ-Shot^{TM}, Olympus, Tokyo, Japan) advanced through a 2.8-mm channel linear echoendoscope (GF-UCT240, Olympus). A part of FNA sample was placed onto a glass slide and fixed in absolute alcohol solution for staining. Rest of FNA sample was fixed in formalin and embedded in paraffin. When the on-site cytologic examination was negative for malignancy, then, a core biopsy specimen was obtained by EUS-TCB using a disposable 19-gauge trucut needle (QuickCore^{TM}, Wilson-Cook, Winston-Salem, NC) [16]. All tissue samples obtained by TCB were routinely fixed in formalin and embedded in paraffin. Deparaffinized sections 4-μm thick were stained with hematoxylin and eosin. For immunohistochemical staining, a monoclonal anti-human immunoglobulin (IgG)4 antibody (Binding Site, Birmingham, UK) was used with standard immunohistochemical techniques. The extent of IgG4-positive plasma cells were scored as none, mild, moderate and marked according to the number of immunohistochemically identified positive staining plasma cells per high-power field (hpf) in each specimen. Tissues with less than 5 positive cells/hpf were scored as none, 5–10 cells/hpf were scored as mild, 11–30 cells/hpf scored as moderate, and tissues with >30 positive cells/hpf were scored as marked [17].

In this study, patients who met both criterion 1 and 2 of the revised clinical diagnostic criteria of AIP 2006 (revised Japanese criteria) were diagnosed with AIP. The following are the criteria: (1) typical pancreatic imaging features, (2) typical laboratory abnormalities and (3) histopathological examinations. First, we compared histopathological findings obtained by EUS-FNA and EUS-TCB with the clinical features. All tissue slides were reviewed by the same pathologist (W.H.), who was blinded to the clinical information. The histology of AIP, termed LPSP is characterized histologically by a dense lymphoplasmacytic infiltrate centered around the pancreatic ducts and ductules, accompanied by obliterative phlebitis, acinar atrophy and interstitial fibrosis (storiform fibrosis) [4, 18, 19]. LPSP was divided into two types: (1) definite LPSP, showing the full spectrum of LPSP changes with obliterative phlebitis (Fig. 1), and (2) probable LPSP when obliterative phlebitis was absent or abundant (>10 cells/hpf) IgG4 positive plasmacytes infiltration. Chronic pancreatitis with the presence of granulocyte epithelial lesion (GEL) was defined as idiopathic duct-centric chronic pancreatitis (IDCP) [4, 7]. When features of chronic pancreatitis were found pathologically, but findings of LPSP or IDCP were absent, it was defined as idiopathic chronic pancreatitis (ICP, Fig. 2). Second, we assessed the diagnostic usefulness of EUS-TCB in diagnosis of AIP comparing EUS-FNA, imaging examinations, laboratory findings and the revised Japanese criteria. Third, we evaluated the usefulness of EUS-FNA and TCB for differentiating between focal pancreatitis and PC.

Statistical analysis

The diagnostic performance of EUS-FNA and TCB were compared with the chi-squared test (using JMP version

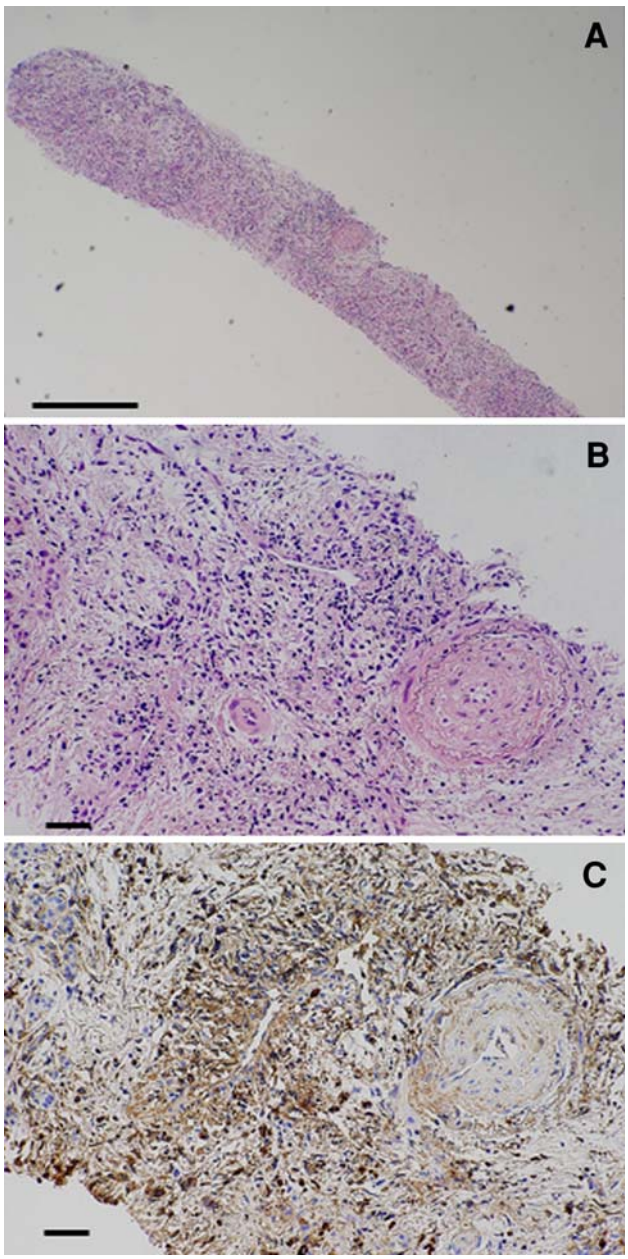

Fig. 1 Histopathology of lymphoplasmacytic sclerosing pancreatitis (LPSP). **a**, **b** The pancreatic acinar structure is replaced by fibrosis with lymphoplasmacytic infiltration. Obliterative phlebitis is observed adjacent to an intact artery (hematoxylin and eosin (H&E); *bars* **a** 500 μm, **b** 50 μm). **c** Numerous plasma cells show positive immunoreactivity for IgG4 (C); *bar* 50 μm

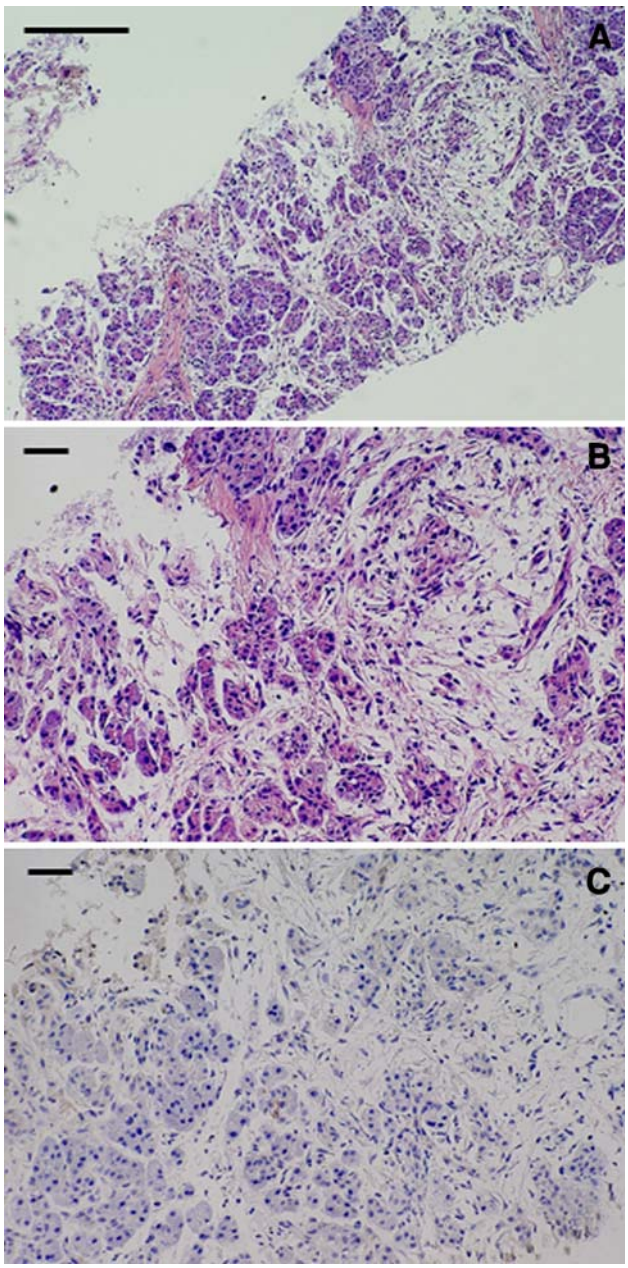

Fig. 2 Histopathology of idiopathic chronic pancreatitis (ICP). **a**, **b** The pancreatic acinar structure is replaced by fibrosis with little lymphoplasmacytic infiltration. Obliterative phlebitis is not observed (H&E; *bars* **a** 200 μm, **b** 50 μm). **c** No IgG4 (C)-positive plasma cells are apparent; *bar* 50 μm

6.0.3 software); A P-value of <0.05 was considered significant.

Results

Demographics and presentation

Table 1 summarizes the clinical features of the 14 patients (12 men, 2 women), who underwent both EUS-FNA and EUS-TCB for suspected AIP. The patients ranged in age from 41 to 76 years (median 67 years). Serum levels of total γ-globulin (normal levels <2.0 g/dl) and IgG (normal levels <1,800 mg/dl) were elevated in five and six patients, respectively. IgG4 levels were elevated (≥135 mg/dl) in 10 patients and normal in the other four patients. Two of the 14 patients were positive for auto-antibodies. ERCP showed diffuse irregular narrowing of the MPD in ten patients and segmental narrowing of the MPD that met

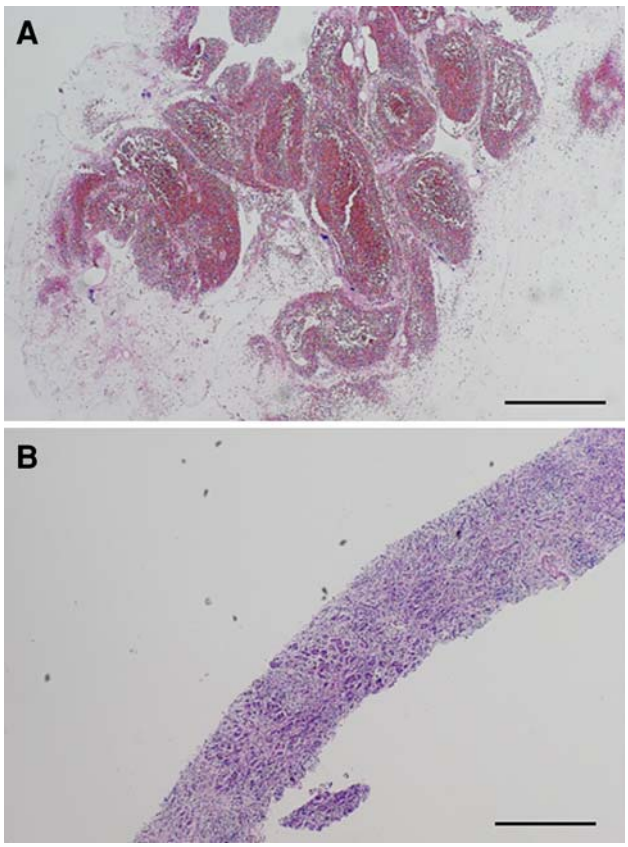

Fig. 3 Comparison of pancreatic tissue obtained by EUS-FNA and EUS-TCB. Most tissue samples obtained by EUS-FNA are small, making conclusive diagnosis of AIP difficult (**a**). Conversely, EUS-TCB allows preservation of tissue architecture and histological examination (**b**). *Bars* 500 μm

criterion 1 of the revised Japanese criteria in two other patients. One patient showed a focal stricture of the MPD that did not fulfill the criterion 1. Pancreatography was unavailable in one patient because a biliary metal stent had been placed after misdiagnosis of unresectable PC at the previous hospital. Of these 14 patients, eight were diagnosed as AIP according to the revised Japanese criteria, and the other six were diagnosed as pancreatitis of other etiologies (Table 1).

EUS-guided fine needle aspiration

The EUS-FNA specimens were adequate for cytology in all 14 patients. EUS-FNA showed negative cytological results for PC in all patients. The EUS-FNA specimens were adequate for additional histological evaluation in six of 14 cases (43%), while the FNA specimens did not yield an adequate tissue core for histological diagnosis (Fig. 3a) in the remaining eight patients (Table 2). Among the eight patients with AIP, the results of EUS-FNA were reported as probable LPSP in three, normal in one, and inconclusive in four patients. Among the six patients with non-autoimmune pancreatitis, the results of EUS-FNA were reported as probable LPSP in one, ICP in one, and inconclusive in four patients.

EUS-guided trucut biopsy

Pancreatic tissue specimens were successfully obtained by EUS-TCB in all 14 patients. All pancreatic biopsies had preserved tissue architecture and permitted a histological review (Fig. 3b). A dense lymphoplasmacytic infiltration was present in every case (Table 3). Nine of the 14 patients showed abundant IgG4-positive plasma cells, while obliterative phlebitis was found in five patients. Although neutrophil infiltration was observed in three patients, none of the 14 patients showed GEL which is a characteristic feature of IDCP [4, 7]. Dense fibrosis, representing storiform fibrosis, was apparent in 13 of the 14 patients.

Among the eight patients diagnosed with AIP according to the first two criteria, four patients had definite LPSP (Fig. 1) and four had probable LPSP on EUS-TCB. By contrast, one of the six patients with non-autoimmune pancreatitis was diagnosed with definite LPSP, two were probable LPSP, and three were ICP (Fig. 2). IgG4 immunostaining yielded positive results in all five patients who showed the full spectrum of LPSP changes and was also positive in four of the six patients with probable LPSP. None of the three patients who showed pathological ICP had IgG4-positive cells. In our study, 11 of 14 patients showed LPSP (five definite, six probable), but no patient was diagnosed with IDCP.

Table 4 summarizes a comparison of EUS-FNA and EUS-TCB for the diagnosis of LPSP. Although 6 of 14 samples obtained by EUS-FNA were diagnostic, more than half of the samples were inconclusive. On the other hand, all samples obtained by EUS-TCB were diagnostic. All eight patients clinically diagnosed with AIP were diagnosed as having definite or probable LPSP by EUS-TCB. Conversely, among the 6 patients diagnosed with non-autoimmune pancreatitis, three had definite or probable LPSP on EUS-TCB and three were diagnosed with ICP. The sensitivity of EUS-TCB for diagnosing LPSP (100%) was significantly higher than that of EUS-FNA (36%; $P = 0.004$). The specificity of EUS-TCB (100%) tended to be higher than that of EUS-FNA (33%; $P = 0.0833$). The diagnostic accuracy of EUS-TCB (100%) was significantly higher than that of EUS-FNA (36%; $P = 0.0006$).

EUS-FNA and TCB for focal pancreatitis and pancreatic cancer

The EUS-FNA specimens were adequate for cytology and positive for PC in all 14 patients. The EUS-FNA specimens were adequate for additional histological evaluation in 12

Table 1 Patients characteristics

Case		Irregular MPD narrowing	γ-Globulin (g/dl)	IgG (mg/dl)	IgG4 (mg/dl)	Auto antibodies	Clinical diagnosis
1	72/M	Diffuse	1.6	1,823	366	(–)	AIP
2	76/M	Diffuse	1.8	1,604	227	(–)	AIP
3	58/M	Segmental	1.4	1,355	201	(–)	AIP
4	76/M	Diffuse	1.7	1,652	495	(–)	AIP
5	70/M	Diffuse	3.0	3,180	223	(–)	AIP
6	59/M	Diffuse	3.5	3,650	1,550	(–)	AIP
7	75/M	Diffuse	3.9	4,091	1,070	(+)	AIP
8	41/F	Diffuse	1.3	1,545	414	(+)	AIP
9	68/M	N/A[a]	2.4	2,346	640	(–)	Other
10	66/M	Focal	2.1	2,060	342	(–)	Other
11	55/F	Diffuse	1.5	1,404	127	(–)	Other
12	62/M	Segmental	1.2	1,449	93	(–)	Other
13	68/M	Diffuse	0.9	1,156	65	(–)	Other
14	62/M	Diffuse	1.2	1,318	79	(–)	Other

[a] Placement of metal stent due to misdiagnosis of pancreatic cancer at the previous hospital

Table 2 Histological features obtained by EUS-FNA

Case	Clinical diagnosis	Histological diagnosis	LP infiltrate	IgG4 (+)ve plasmacytes	Neutrophils	GEL	Storiform fibrosis	Obliterative phlebitis
1	AIP	Normal	±	–	–	–	–	–
2	AIP	Inconclusive	IN	IN	–	IN	IN	IN
3	AIP	Probable LPSP	++	+	–	–	+	–
4	AIP	Inconclusive	IN	IN	IN	IN	IN	IN
5	AIP	Inconclusive	IN	IN	IN	IN	IN	IN
6	AIP	Inconclusive	IN	IN	IN	IN	IN	IN
7	AIP	Probable LPSP	++	–	–	–	+	–
8	AIP	Probable LPSP	+	–	–	IN	+	–
9	Other	Probable LPSP	+	+	–	–	+	–
10	Other	Inconclusive	+	IN	IN	IN	±	IN
11	Other	Inconclusive	+	–	–	IN	+	–
12	Other	Inconclusive	IN	IN	IN	IN	IN	IN
13	Other	Inconclusive	IN	IN	IN	IN	IN	IN
14	Other	ICP	+	–	+	–	+	–

LP lymphoplasmacytes, *GEL* granulocytic epithelial lesion, *ICP* idiopathic chronic pancreatitis, *IN* inconclusive

of 14 cases. Among 12 patients with PC, EUS-FNA showed cancer cells in eight patients and atypical cells in four patients. By contrast, EUS-TCB specimens were adequate for histological evaluation in 11 patients, while the TCB specimens did not yield an adequate tissue core for histological diagnosis in the remaining three patients. Among 11 patients, 10 had cancer cells, and one had atypical cells. Table 5 summarizes diagnostic performance of EUS-FNA and TCB for differential diagnosis of focal pancreatic mass. Overall diagnostic accuracy was not different between EUS-FNA and TCB ($P = 0.3683$). However, for diagnosis of pancreatitis, the sensitivity of EUS-TCB (100%) tended to be higher than that of EUS-FNA (33%; $P = 0.0833$). By contrast, the specificity of EUS-FNA (100%) was higher than that of EUS-TCB (71%; $P = 0.0308$).

Complications

No complications such as gastrointestinal bleeding, perforation or acute pancreatitis were encountered with either EUS-FNA or EUS-TCB.

Discussion

With recent advances and the proposal of several diagnostic criteria for AIP in various countries, most cases of

Table 3 Histological features obtained by EUS-TCB

Case	Clinical diagnosis	Histological diagnosis	LP infiltrate	IgG4 (+)ve plasmacytes	Neutrophils	GEL	Storiform fibrosis	Obliterative phlebitis
1	AIP	Definite LPSP	++	+	–	–	++	+
2	AIP	Definite LPSP	++	+	+	–	++	+
3	AIP	Definite LPSP	++	+	–	–	++	+
4	AIP	Definite LPSP	++	+	–	–	++	+
5	AIP	Probable LPSP	++	+	–	–	++	–
6	AIP	Probable LPSP	++	–	–	–	+	–
7	AIP	Probable LPSP	++	+	–	–	++	–
8	AIP	Probable LPSP	++	+	–	–	++	–
9	Other	Definite LPSP	++	+	–	–	++	+
10	Other	Probable LPSP	++	+	–	–	±	–
11	Other	Probable LPSP	++	–	–	–	++	–
12	Other	ICP	++	–	–	–	+	–
13	Other	ICP	+	–	+	–	+	–
14	Other	ICP	+	–	+	–	+	–

LP lymphoplasmacytes, *GEL* granulocytic epithelial lesion, *ICP* idiopathic chronic pancreatitis

Table 4 Comparison of EUS-FNA and -TCB to clinical features

Case	Imaging	Serology	Imaging/ Serology	FNA histological diagnosis	TCB histological diagnosis	Final diagnosis
1	(+)	(+)	(+)	Normal	d-LPSP	AIP
2	(+)	(+)	(+)	Inconclusive	d-LPSP	AIP
3	(+)	(+)	(+)	p-LPSP	d-LPSP	AIP
4	(+)	(+)	(+)	Inconclusive	d-LPSP	AIP
5	(+)	(+)	(+)	Inconclusive	p-LPSP	AIP
6	(+)	(+)	(+)	Inconclusive	p-LPSP	AIP
7	(+)	(+)	(+)	p-LPSP	p-LPSP	AIP
8	(+)	(+)	(+)	p-LPSP	p-LPSP	AIP
9	(–)[a]	(+)	(–)	p-LPSP	d-LPSP	AIP
10	(–)	(+)	(–)	Inconclusive	p-LPSP	AIP
11	(+)	(–)	(–)	Inconclusive	p-LPSP	AIP
12	(+)	(–)	(–)	Inconclusive	ICP	ICP
13	(+)	(–)	(–)	Inconclusive	ICP	ICP
14	(+)	(–)	(–)	ICP	ICP	ICP

[a] Placement of metal stent at the previous hospital; d-LPSP, definite LPSP; p-LPSP, probable LPSP

AIP are diagnosed based on a combination of pancreatic imaging and laboratory data [11, 12]. However, with increasing experience, it has been seen that some patients with AIP do not fulfill both the typical imaging and laboratory features [20]. In these patients, the biggest problem is how to distinguish AIP from PC and achieve a conclusive diagnosis of AIP, as has been emphasized by the revised Japanese criteria. AIP can be defined as chronic inflammatory changes of the pancreas due to autoimmune mechanisms [2, 3]. AIP occasionally mimics PC, both clinically and radiologically. Therefore many patients with AIP have undergone pancreatectomy based on a misdiagnosis of PC [18, 19].

EUS-FNA is an established and widely used technique to evaluate pancreatic masses. EUS-FNA safely provides high diagnostic accuracy, ranging from 60% to 90% for pancreatic neoplasms. EUS-FNA is a sensitive method for diagnosing PC, but, lymphoma, mesenchymal tumors, well-differentiated or highly desmoplastic pancreatic neoplasms are difficult to diagnose by using cytology alone [21, 22]. Deshpande et al. reported that FNA cytology can suggest a diagnosis of AIP in addition to excluding the possibility of carcinoma [9]. However, the presence of abundant IgG4-positive plasmacytes in the pancreas is not a specific finding for AIP [23], despite the high sensitivity of serum IgG4 in diagnosing AIP. Tissue samples collected

Table 5 Comparison of diagnostic performance of EUS-FNA and -TCB in focal pancreatic mass

	EUS-FNA	EUS-TCB	*P* value
Final diagnosis			
Pancreatitis ($n = 3$)	1/3	3/3	
LPSP ($n = 2$)	1/2	2/2	
ICP ($n = 1$)	0/1	1/1	
PC ($n = 14$)	14/14	10/14	
Sensitivity[a]	33%	100%	0.0833
Specificity[a]	100%	71%	0.0308
Accuracy[a]	88%	76%	0.3683

ICP idiopathic chronic pancreatitis, *PC* pancreatic cancer

[a] Sensitivity, specificity and accuracy for diagnosis of pancreatitis

via FNA do not have a preserved tissue architecture, which most pathologists consider as necessary for the diagnosis of AIP. The small tissue sample obtained by EUS-FNA is usually insufficient for a conclusive diagnosis of AIP.

TCB of solid lesions arising in soft tissue, breast, lung, lymph node, liver, kidney, adrenal, spleen, prostate and other sites is a safe, accurate, and established method [15]. EUS-TCB needle is a 19-gauge needle with a tissue tray and a sliding sheath that permits collection of a histological core. Levy et al. studied a small number of patients with AIP and reported that EUS-TCB is safe, and may provide a sufficient tissue sample for a histological diagnosis of AIP [15]. In our study, the sample obtained by EUS-FNA was inadequate for a histological evaluation in more than half of the cases (8 of 14), whereas all tissue samples obtained by TCB were sufficient for histological review. Of the six cases diagnosed as non-autoimmune pancreatitis, three showed LPSP (one definite, two probable). Our results thus confirmed that EUS-TCB is superior to FNA for diagnosing AIP.

According to the HISORt criteria, the characteristic histological finding, (1) full spectrum of changes of LPSP or (2) lymphoplasmacytic infiltrate with storiform fibrosis showing abundant ($\geq$10 cells/hpf) IgG4 positive cells, is solely diagnostic for AIP [13]. Our results showed that EUS-TCB, not FNA, can provide the histological diagnosis of AIP regardless of imaging or serological findings.

Bang et al. [24] reported that transabdominal ultrasound-guided core biopsy may not provide enough tissue to evaluate the characteristic histopathological features of AIP. In their study, although all surgically resected specimens (4/4) of AIP patients showed a full spectrum of LPSP, histological examination with transabdominal ultrasound-guided core biopsy specimens found LPSP (equivalent to definite LPSP in our study) in only 5 of 19 AIP patients (26%). They also reported that nine of the other 16 patients lacking full-spectrum LPSP showed both lymphoplasmacytic infiltration and loose fibrosis without obliterative phlebitits (equivalent to probable LPSP in our study). By contrast, five (45%) of 11 patients in our study who were finally diagnosed with AIP showed full-spectrum LPSP, and the other six patients showed probable LPSP.

EUS-TCB is technically difficult when the lesion is located in the pancreatic head, as the scope angulation while imaging the pancreatic head does not allow easy passage of the TCB needle. All EUS-TCB samples were obtained from the pancreatic body in this study. Conversely, EUS offers superior resolution and can improve the accuracy of lesion targeting. Furthermore, EUS showed the diffuse hypoechoic lesion in most cases of AIP even CT or transabdominal US had only demonstrated focal or segmental lesion [25]. For example in patients 3, 10 and 12, in whom ERCP and CT showed only focal or segmental lesions, EUS revealed diffuse pancreatic lesions. In these cases, transgastric EUS-TCB was performed after exclusion of pancreatic head cancer by transduodenal EUS-FNA. The complication rate associated with US-guided transabdominal pancreatic biopsy is comparable to that for EUS-FNA, at 0–5%, although Matsubara et al. [26] recently reported a complication rate of 21.4% for US-guided biopsy. By contrast, several authors have mentioned that the safety of EUS-TCB is comparable to that of EUS-FNA [27–29]. No complications such as bleeding or acute pancreatitis were encountered in our series. Moreover, EUS-TCB as well as EUS-FNA offer the advantage of a shorter needle tract and might result in a lower frequency of peritoneal seeding, as compared to percutaneous image guided biopsies. Micames et al. [30] reported that the risk of peritoneal seeding was significantly lower with EUS-FNA (2.2%) than with ultrasound-guided transabdominal FNA (16.3%), and concluded that EUS-FNA should be the preferred method for obtaining tissue diagnosis in PC, particularly in patients with potentially resectable disease. The complication rate of EUS-TCB is comparable to that of EUS-FNA. The actual frequency of peritoneal dissemination by EUS-TCB in patients with PC has not been established. According to our data, although EUS-FNA alone could provide accurate diagnosis of PC, EUS-TCB is essential for the histological assessment of LPSP. These results indicate that the sequential sampling strategy, involving EUS-FNA first, followed by EUS-TCB when on-site cytologic examination is negative for PC in case of suspected AIP, is a reasonable diagnostic algorithm. This sequential sampling strategy results in fewer needle passes, and may reduce the incidence of peritoneal dissemination in patients with PC.

IDCP is frequently complicated with ulcerative colitis or Crohn's disease in younger patients. However, the true incidence of IDCP is still unclear in Japanese patients. Cases 12, 13 and 14 were compatible with criterion 1

without fulfill of criterion 2. In these cases who did not have concomitant ulcerative colitis or Crohn's disease, typical findings of not only LPSP but also IDCP such as GEL [4, 7] were not observed in the tissue samples obtained by EUS-TCB. As GEL is patchy lesion, one possibility in these cases is sampling error. Another possibility is the existence of as yet undefined idiopathic chronic pancreatitis, other than LPSP or IDCP, with typical imaging findings of AIP.

In conclusion, despite the technical limitations of existing EUS-TCB needles in the duodenum, EUS-TCB is an accurate and safe procedure for the diagnosis of AIP. EUS-TCB can serve as a rescue technique in cases of AIP lacking typical imaging or serological findings. Furthermore, EUS-TCB can provide histological diagnosis of AIP regardless imaging or serological findings. Considering the risk of peritoneal dissemination, a sequential strategy, involving EUS-FNA first, followed by EUS-TCB, is a rational diagnostic algorithm.

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