https://www.cytojournal.com/

CytoJournal

Editor-in-Chief:
Miaoqing Zhao, PhD., MD (Shandong First Medical University, Jinan, China)
He Wang, MD, PhD (Yale University School of Medicine, New Haven, Connecticut, USA)
Founding Editor & Editor-in-chief Emeritus:
Vinod B. Shidham, MD, FIAC, FRCPath (WSU School of Medicine, Detroit, USA)

OPEN ACCESS

Research Article

Endoscopic ultrasound-guided fine-needle aspiration value in suspected autoimmune pancreatitis malignancy diagnosis

Yue Liu, MS[1#], Dongling Wan, MS[1#], Chang Wu, MD[1], Deyu Zhang, MD[1], Jiaheng Xu, MS[1], Wanshun Li, MD[1], Zhenghui Yang, MD[1], Jiayu Li, MS[1], Ying Chen, MD[1], Zhendong Jin, MD[1*], Haojie Huang, MD[1*]

[1]Department of Gastroenterology, Changhai Hospital, Second/Navy Military Medical University, Shanghai, China.
[#]Yue Liu and Dongling Wan are co-first authors of this article.

***Corresponding authors:**

Haojie Huang,
Department of Gastroenterology, Changhai Hospital, Second/Navy Military Medical University, Changhai Hospital, Shanghai, China.
Hhuanghaojie@163.com

Zhendong Jin
Department of Gastroenterology, Changhai Hospital, Second/Navy Military Medical University, Changhai Hospital, Shanghai, China.
zhendongjin@163.com

Received: 16 October 2024
Accepted: 2 April 2025
Published: 2 June 2025

DOI
10.25259/Cytojournal_214_2024

Quick Response Code:

ABSTRACT

Objective: Histopathology examination is important for diagnosing autoimmune pancreatitis (AIP), which is suspected to be pancreatic cancer based on imaging findings. Although the validity of endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) in the diagnosis of AIP is still debated globally, this study aimed to evaluate the efficacy of EUS-FNA in the diagnosis of AIP with suspected pancreatic cancer.

Material and Methods: From January 2021 to June 2024, 30 AIP patients with radiographically diagnosed pancreatic cancer were enrolled and underwent EUS-FNA. Sex, age, symptoms, CA199, serum immunoglobulin G4 (IgG4), and treatment outcome were included. Tissue sampling conditions, puncture sites, storiform fibrosis, CD38- and IgG4-positive plasma cell counts, and obliterans phlebitis were evaluated.

Results: Thirty patients, 24 males and six females, with an average age of 60.53 ± 11.72 years (32-79 years), were included in the study. Thirty patients had their serum IgG4 and CA199 levels tested. Tissue samples containing ≥10 were obtained from 19 (63.33%) patients. CD38+ plasma cell infiltration and laminar fibrosis were detected in 22 (73.33%) and 10 (33.33%) patients. According to the International Consensus Diagnostic Criteria (ICDC), 12 patients had histopathological levels of Grade 1, 15 of Grade 2, and three patients could not be classified. The accuracy, sensitivity, and specificity of EUS-FNA in diagnosing AIP with suspected pancreatic cancer on imaging were 96.66% (29/30), 96.42% (27/28), and 100% (2/2), respectively. The area under the curve value of EUS-FNA for patients with AIP who were radiologically suspected of having pancreatic cancer was 0.957.

Conclusion: Approximately 90% of patients with EUS-FNA results are diagnosed with an ICDC level of 2 or higher. Our results suggest that for cases where malignant tumors are suspected after imaging or cannot be ruled out, obtaining pancreatic tissue through EUS-FNA puncture for pathological diagnosis is recommended.

Keywords: Autoimmune pancreatitis, Endoscopic ultrasound-guided fine-needle aspiration, Histopathologic diagnosis

INTRODUCTION

Autoimmune pancreatitis (AIP) is a special type of chronic pancreatitis, first proposed by Sarles *et al*. in 1961.[1] Its main features include obstructive jaundice with or without a pancreatic mass, lymphoplasmacytic cell infiltration, and fibrosis. Based on histopathology, AIP can be divided into type 1 (AIP-1), also known as lymphoplasmacytic sclerosing pancreatitis (LPSP), and type 2 (AIP-2), also known as idiopathic duct-centric pancreatitis (IDCP). Type 1 disease is characterized by abundant immunoglobulin G4 (IgG4)-positive plasma cells, storiform fibrosis (SF), extensive periductal lymphoplasmacytic infiltration, obliterative phlebitis, and acinar atrophy if

intralobular inflammation is severe enough to cause more prominent fibrotic changes.[2] Type 2 AP is characterized mainly by idiopathic duct-centric chronic pancreatitis and granulocytic epithelial lesions.[3] The diagnosis of AIP requires comprehensive assessment, including pancreatic imaging, serological, histopathology, and other organ involvement, among which pancreatic imaging plays an important role.[4] In clinical practice, some cases of AIP are often misdiagnosed as pancreatic cancer based on imaging findings. At present, the treatment approaches for these two diseases differ significantly with opposite prognoses: AIP relies primarily on long-term steroid therapy for management; pancreatic cancer necessitates timely surgical intervention followed by adjuvant chemotherapy or radiation therapy, with a 5-year survival rate still <5%.[5] Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) biopsy is diagnostically important in differentiating between suspected malignant tumors and AIP while assessing fibrosis progression.[6] Therefore, we retrospectively analyzed the characteristics of patients initially misdiagnosed with pancreatic cancer based on imaging findings but later diagnosed with AIP to evaluate the diagnostic value of EUS-FNA for suspected malignant tumors associated with AIP.

MATERIAL AND METHODS

Study design

This retrospective, single-center study was conducted at one of the top three hospitals in coastal China.

Study population

Between January 2021 and June 2024, 30 patients with suspected AIP who were ultimately treated with EUS-FNA were enrolled. The enrolment criteria were as follows: Pancreatic cancer was diagnosed by computed tomography (CT) or/and enhanced CT, magnetic resonance imaging (MRI), or/and enhanced MRI. They are often characterized by a pancreatic space with partial pancreatic duct amputation, slight dilation of the distal pancreatic duct, and possibly large pancreatic cancer. The exclusion criteria were as follows: (1). EUS-FNA biopsy pathology suggestive of pancreatic cancer; (2). patients who refused EUS-FNA; (3). patients who refused to undergo EUS-FNA and chose surgery directly; and (4). patients who cannot safely receive EUS-FNA, such as those with coagulation disorders, mental disease, cardiorespiratory dysfunction, or other conditions such as drug addiction.

EUS-FNA

The ultrasonic endoscopy procedure was performed via a UMG20-29R ultrasonic probe (frequency: 20 MHz; Olympus Corporation, Tokyo, Japan), a high-frequency probe designed for detailed imaging. For tissue sampling, the puncture needles (COOK Echo Tip Procore and COOK Echo Tip Ultra; specific model details: ECHO-22, ECHO-25, ECHO-HD-22-C, and ECHO-HD-25-C) used were models manufactured by Bovie Medical Corporation (Clearwater, FL, USA) or Boston Scientific Corporation (Marlborough, MA, USA). All puncture surgeries were conducted by professors with an associate senior professional title or above, and intravenous-assisted anesthesia was adopted. The ultrasonic probe was positioned at the lower part of the gastric body on the lesser curvature side or the greater curvature side of the gastric antrum to scan the head, tail, and body of the pancreas. The pancreas size, shape, internal echoes, and margins were observed. Moreover, attention was given to whether the lesion has invaded the surrounding blood vessels, whether the surrounding lymph nodes are enlarged, and whether there is dilation, distortion, or stenosis in the pancreatic and common bile ducts. Simultaneously, acoustic contrast imaging was carried out to determine the blood supply. Then, blood vessels, the appropriate puncture path, and depth were chosen to avoid blood vessels. In general, repeated insertions and withdrawals were performed 3-5 times under 10 mL of negative pressure. The puncture needle was subsequently withdrawn. The aspirated tissue fluid and fragments were subjected to smear and cytological examinations. The tissue strips were placed in a formaldehyde solution for fixation and sent for pathological examination. To prevent insufficient tissue strips from being used for subsequent immunohistochemistry, 2-3 punctures were selected. After the puncture was completed, the puncture site was observed for immediate complications such as active bleeding and pancreatic fistula. Then, the ultrasonic endoscope was gradually withdrawn. Based on the swelling condition of the duodenal papilla, a decision was made on whether to conduct a biopsy of the duodenal papilla. The operation was completed. After surgery, the patient fasted for 24 h, vital signs, abdominal signs, and blood amylase levels were monitored, and symptomatic and supportive treatments such as enzyme inhibition, acid suppression, and fluid infusion were provided. Complications such as delayed bleeding and acute pancreatitis were observed in the post-operative patients.

Histological biopsy

Tissue samples obtained through EUS-FNA were fixed with formalin and then embedded with paraffin wax. Paraffin sections were made, and the tissues were stained with hematoxylin and eosin. Histological evaluation of the biopsy samples was performed by two experienced pathologists with over 10 years of expertise in pancreatic pathology. The observations were independently reviewed to ensure accuracy and reliability; this was performed by each pathologist, and any differences were resolved through

discussion with a pathologist with over 20 years of experience. The tissues were analyzed by experienced pathologists according to the International Consensus Diagnostic Criteria (ICDC) histological standards.[7] If necessary, the degree of plasma cell infiltration was determined through an anti-IgG4 antibody. The histological diagnostic criteria for LPSP were as follows: (1) perivascular lymphocytic plasma cell infiltration without granulocyte infiltration; (2) SF; (3) obliterative venous angiitis; and (4) the presence of more than 10 positive IgG4 cells per high-power field (HPF). The level 1 criteria had 3 or more positive results out of the 4 LPSP criteria, and the level 2 criteria had 2 positive results. The IDCP results were as follows: (1) granulocyte infiltration, with or without granulocyte follicular inflammation; (2) granulocyte and lymphocytic plasma cell follicular infiltration; and (3) the absence or lack of IgG4-positive cells (0-10 cells per HPF). The result needs to be positive for items (1) and (3) if they meet the Grade 1 standard and positive for items (2) and (3) if they meet the Grade 2 standard.

Observation scale

(1) The lesion detection rate of EUS-FNA in suspected patients; (2) the diagnosis results of lesion location by EUS-FNA; (3) the sensitivity, accuracy, and specificity of EUS-FNA pathological diagnosis results in patients with AIP diagnosed with pancreatic cancer based on the final clinical diagnosis. According to the ICDC criteria, those with a grade of 2 or above were positive, whereas the others were negative.

Adverse events

No patients experienced adverse events (e.g., pancreatitis, perforation, and hemorrhage) during or after EUS-FNA.

Statistical analysis

Statistical analysis was performed through IBM Statistical Package for the Social Sciences Statistics (Version 27.0; IBM Corporation, Armonk, NY, USA), a comprehensive software package for statistical analysis. $P < 0.05$ was considered statistically significant.

RESULTS

Clinical findings

Thirty-six patients with suspected AIP were enrolled between January 2021 and June 2024. One patient refused to undergo an EUS-FNA examination, three patients underwent surgery due to imaging findings of pancreatic cancer, and two patients underwent an EUS-FNA examination, which revealed pathological findings of pancreatic malignancies. In total, 30 patients were enrolled in this study.

The patient characteristics are shown in Table 1. Thirty patients, 24 males and six females, were included, with an average age of 60.53 ± 11.72 years (32-79 years). Thirty patients had their serum IgG4 and CA199 levels tested. The extrapancreatic manifestations of type I AIP were sclerosing cholangitis in two patients and no cases of sialadenitis or interstitial nephritis. All patients ultimately had no ulcerative colitis or Crohn's disease. No patients had immediate complications, such as active bleeding or pancreatic fistula, and no delayed complications, such as delayed bleeding or acute pancreatitis. Six patients (20%) received steroids after EUS-FNA, eight underwent endoscopic retrograde cholangial pancreatography (ERCP) biliary drainage after EUS-FNA, and two received immune-modulating therapy.

EUS and EUS-FNA findings

AIP is often misdiagnosed as pancreatic cancer. We selected images that were misdiagnosed as pancreatic cancer by enhanced pancreatic CT in the imaging department of our hospital [Figure 1a and b], mainly because both AIP and pancreatic cancer can present with focal pancreatic

Table 1: Clinical features of the 30 enrolled patients.

Characteristics	Values (%)
Sex, male-to-female	24:6
Age, y (mean±SD)	60.53±11.72
Symptom	
Jaundice	18/30 (60.00)
Celialgia	7/30 (23.33)
Physical examination finding	3/30 (10.00)
Wight loss	2/30 (6.67)
Pancreatic imaging	
Diffuse enlargement	2/30 (6.67)
Segmental enlargement	28/30 (93.33)
Serology (IgG4)	
>2 upper limit of the normal value	8/30 (26.67)
1-2 upper limit of the normal value	15/30 (50.00)
Within the normal value	7/30 (23.33)
Tumor marker (CA199)	
Within the normal value	22/30 (73.33)
Above the normal value	8/30 (26.67)
Other extrapancreatic organ involvement, no. (%)	
Sclerosing cholangitis associated with IgG4	2/30 (6.67)
Sialadenitis, interstitial nephritis	0/30 (0.00)
Treatment	
Steroid administration	6/30 (20.00)
Effective cases	6/6 (100)

IgG4: Immunoglobulin G4, SD: Standard deviation

enlargement, low attenuation of contrast-enhanced imaging, and stenosis of the main pancreatic duct (MPD). These similarities often lead to diagnostic challenges, especially when clinical symptoms and laboratory test results are not specific. Focal pancreatic lesions: Both AIP and pancreatic cancer can present as focal masses, making it difficult to distinguish inflammatory and malignant processes based on imaging alone. Catheter changes: Stenosis or obstruction of the MPD is a common feature of both conditions, further complicating differential diagnosis. Vascular involvement: Imaging may reveal vascular encapsulation or compression in AIP and pancreatic cancer, such as malignancy. Moreover, there is a lack of specific markers and imaging criteria to distinguish between AIP and pancreatic cancer. Thus, it is critical to clarify the diagnosis of AIP.[8] Compared with imaging examination, EUS can observe the substance and duct characteristics of the pancreas more clearly, observe whether there are other abnormal features, such as vascular involvement, described in the imaging results [Figure 2a and b], and perform elastography and contrast-enhanced ultrasound in low-echo areas, which play important roles in differentiating pancreatic cancer.[9] According to the EUS results, 26 of the 30 patients were diagnosed with AIP, and four of the 30 patients were diagnosed with lesions occupying the pancreatic space. Two patients experienced narrowing of the MPD, and one patient experienced dilation of the MPD. However, since measuring the entire pancreatic duct through EUS is difficult, it is impossible to judge the level accurately. In contrast, two of the 30 patients were found to have sclerosing cholangitis associated with IgG4, with thickened biliary walls and distal and proximal biliary strictures. The selection of a 22G needle for EUS-FNA is primarily attributed to its optimal balance between sample acquisition and procedural safety. The 22G needle provides sufficient tissue yield to meet the requirements of histological and cytological analysis, which is crucial for accurate diagnosis. In addition, its smaller gauge reduces the risk of complications such as bleeding and pain during the procedure. The needle's design ensures precise targeting and maneuverability under ultrasound guidance, facilitating accurate puncture and sampling. Moreover, the moderate sample volume obtained with a 22G needle ensures diagnostic accuracy without increasing procedural complexity.[10] EUS-FNA was performed through a 22-G EUS biopsy needle for all 30 patients with pancreatic lesions [Table 2]. The puncture frequency range of the above patients was 2-4. Twenty-six of the 30 punctures were performed in the head, one in the neck, and five in the body/tail.

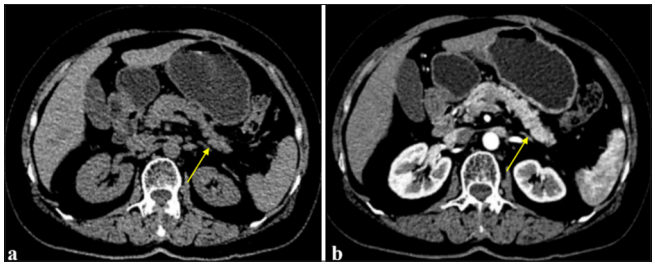

Figure 1: Pancreatic enhanced computed tomography scan of a patient misdiagnosed with pancreatic cancer. (a) shows the mass found during the normal scan; (b) shows the mass found during the enhancement phase. The arrow indicates the lesion site.

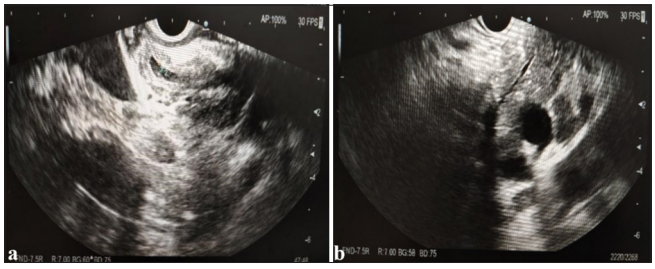

Figure 2: Endoscopic ultrasonography of a patient with autoimmune pancreatitis. (a) shows that the pancreas is hypoechoic; (b) shows that a biopsy of the hypoechoic part was performed to obtain pathology.

Histopathologic examination

Cytological and histological assessments did not reveal malignant or atypical cells in 30 patients. The histological results of EUS-FNA are shown in Table 2. Among the 30 patients, 22 (73.33%) and 10 (33.33%) had CD38+ plasma cell infiltration [Figure 3a] and SF, respectively. In 19 of the 30 patients (63.33%), IgG4-positive plasma cell infiltration ≥10/HPF was detected [Figure 3b]. The characteristic features of occluded veins were not detected in this study.

Histopathologic diagnosis according to the International Classification of Disease Criteria (ICDC)

Among the 30 patients, the histologic findings of 12 and 15 patients were grade level 1 and level 2, respectively. Three patients could not be classified. Figure 4 shows the ROC curve of EUS-FNA for evaluating suspected patients with puncture pathology results. A patient was considered a true positive by the final clinical diagnosis of AIP, and the pathological results of EUS-FNA were also positive. If a patient was clinically diagnosed with AIP, but EUS-FNA results were negative, the patient was considered a false-negative. If the patient was not clinically diagnosed with AIP and EUS-FNA results were negative, the patient was considered a true negative. If the patient was clinically undiagnosed with AIP but EUS-FNA results were positive, the patient was considered a false-positive. Table 3 summarizes the sensitivity, specificity, and accuracy of EUS-FNA in diagnosing AIP with imaging suspicion of pancreatic cancer as 96.42% (27/28), 100% (2/2), and 96.66% (29/30), respectively. The area under the curve value of EUS-FNA for patients with AIP who were

Table 2: Pathological features of AIP patients.

Case	Sex	Punctures	Range	Region	OP	SF	CD38	IgG4	Grade
1	M	3	Focal	Head	−	+	+	+	1
2	M	3	Focal	Head	−	−	+	+	2
3	M	2	Focal	Head	−	−	+	+	2
4	M	3	Focal	Head	−	−	−	−	−
5	M	4	Focal	Head	−	−	−	−	2
6	M	3	Focal	Body/tail	−	+	+	+	1
7	M	3	Focal	Head	−	−	+	+	2
8	M	4	Diffuse	Neck	−	−	+	+	2
9	M	4	Focal	Head	−	−	+	+	1
10	F	2	Focal	Body/tail	−	−	−	−	2
11	F	3	Focal	Head	−	−	+	+	1
12	F	3	Focal	Head	−	−	+	−	2
13	F	2	Focal	Head	−	−	−	−	−
14	F	2	Focal	Head	−	+	+	+	1
15	M	4	Focal	Head	−	+	+	+	1
16	M	3	Focal	Body/tail	−	−	+	+	2
17	M	3	Focal	Head	−	−	+	+	1
18	M	3	Focal	Head	−	−	−	−	−
19	M	3	Focal	Head	−	−	+	+	1
20	M	2	Focal	Head	−	−	+	+	2
21	M	3	Focal	Body/tail	−	−	−	−	2
22	M	3	Focal	Head	−	+	+	+	1
23	F	2	Focal	Head	−	+	+	+	1
24	M	3	Focal	Head	−	−	−	−	2
25	M	4	Diffuse	Head	−	+	+	−	2
26	M	2	Focal	Head	−	+	+	−	2
27	M	2	Focal	Body/tail	−	−	+	+	2
28	M	3	Focal	Head	−	+	+	+	1
29	M	3	Focal	Head	−	+	+	+	1
30	M	3	Focal	Head	−	−	−	−	2

F: Female, M: Male, Range: Range of enlarged pancreas, Punctures: Number of pancreas punctures, OP: Obliterative phlebitis, Region: Region punctured, HPF: High-power field, SF: Storiform fibrosis, IgG4: ≥10 cells per HPF, Grade: Grade of the histological diagnostic criteria of the, ICDC: International consensus diagnostic criteria, AIP: Autoimmune pancreatitis, +: Presence of the feature, −: Absence of the feature.

Table 3: Comparison of the pathological results of EUS-FNA with the final clinical results.

EUS-FNA	Final clinical results		Total
	Positive	Negative	
Positive	27	0	27
Negative	1	2	3
Total	28	2	30

EUS-FNA: Endoscopic ultrasound-guided fine needle aspiration

radiologically suspected of having pancreatic cancer was 0.957. The results were consistent with the final clinical diagnosis.

DISCUSSION

AIP is a type of immune-inflammatory, benign fibrotic disease. Many patients with AIP have painless jaundice, abdominal pain, and weight loss.[7] This disease is more common in middle-aged and elderly men. When the affected area is the head of the pancreas, and there is obvious compression of the common bile duct, causing liver and extrahepatic bile duct dilatation, the clinical manifestation of jaundice without pain may easily lead to misdiagnosis as pancreatic cancer.[11] This disease often presents as diffuse pancreatic enlargement or enhanced soft-tissue margins on imaging modalities such as CT and MRI, resembling sausages,

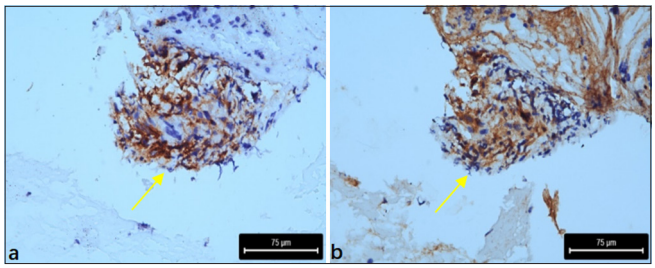

Figure 3: Immunohistochemical results of autoimmune pancreatitis. (a): Immunohistochemical staining of CD38. Abundant CD38-positive plasma cells were found in high-power fields (HPF) (orig. ×400) (scale bar: 75 μm). The yellow arrow indicates that the brown cells are CD38-positive plasma cells. (b): Many immunoglobulin G4-positive cells were found in the HPF (orig. ×400) (scale bar: 75 μm). The yellow arrow indicates that the brown cells are immunoglobulin G4-positive cells.

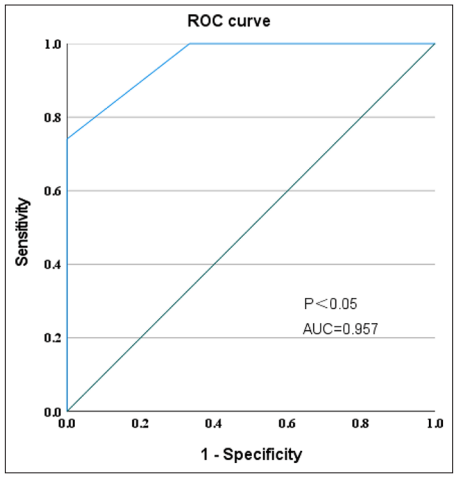

Figure 4: Receiver operating characteristic (ROC) curves of suspected patients evaluated by endoscopic ultrasound-guided fine needle aspiration puncture pathology. The area under the curve value was 0.957.

commonly known as "sausage-like." A low-density marginal area exists around the pancreas due to inflammation, fibrosis, etc., forming a "capsule." In the parenchymal phase, a low-enhanced capsular-like edge is visible, with spotted enhancement of the pancreatic parenchyma. During the delayed phase, the pancreatic parenchyma shows enhanced intensity.[12] Simultaneously, it may also manifest as a focal pancreatic mass, which is located mainly in the head of the pancreas. Approximately 25-50% of patients with AIP have imaging reports suggesting possible compression, occlusion, or thrombosis of the splenic vein and mesenteric vein, which is highly similar to pancreatic cancer, resulting in an elevated misdiagnosis rate.[13] Deshpande *et al.* reported that approximately 25% of patients with benign lesions who underwent pancreaticoduodenectomy were diagnosed with AIP postoperatively.[14] The diagnostic criteria for AIP mainly encompass five aspects: (1) Serum indicators. (2) Imaging manifestations. (3) Pathological results. (4) Sensitivity to steroid drug treatment. (5) Involvement of extrapancreatic organs, such as sclerosing cholangitis, retroperitoneal fibrosis, or renal-related impairments.[7] Therefore, the accurate diagnosis and discrimination of AIP from other diseases, such as pancreatic cancer, holds significant clinical importance. For patients who cannot be diagnosed through laboratory tests and imaging examinations or those suspected or unable to be excluded from malignancy, pancreatic tissue can be obtained through EUS-FNA for pathological diagnosis. The ICDC emphasizes the importance of histological diagnosis in diagnosing AIP.[15] EUS-FNA can directly acquire the tissue cells of pancreatic space-occupying lesions, providing technical support for differentiating benign and malignant lesions. A previous meta-analysis indicated that the specificity of EUS-FNA in diagnosing solid pancreatic space-occupying lesions was 98%, and the sensitivity was 85%.[16] De Pretis *et al.* evaluated the diagnostic efficacy of EUS-FNA with a 22G needle in diagnosing type I and type II AIP and reported that among 47 patients, nine achieved level 1 LPSP, and five achieved level 2 LPSP.[17] These results are similar to those of this study. A total of 30 patients were included in this study. Twelve patients had histopathological levels of Grade 1, 15 had histopathological levels of Grade 2, and three patients could not be classified. Morishima *et al.* conducted a multicenter prospective study on the effectiveness of EUS-FNA in diagnosing AIP and reported that the final diagnostic sensitivity was 90%.[18] The sensitivity of diagnosis in this study was 96.42%. The results are similar to those of previous studies. The pathological reports of the three cases that could not provide a pathological diagnosis were analyzed, all of which suggested a small number of cells and a large number of blood clots, indicating that a small amount or even no lesion tissue might have been obtained during the puncture process. At present, the diagnostic accuracy of EUS-FNA is believed to be influenced by numerous factors, such as the location and size of the lesion, the quality and quantity of the sample, the technical level of the operator, and the level of the pathologist.[19] Previous studies have suggested that pancreatic puncture might lead to complications such as bleeding, pancreatitis, and pancreatic fistula. Common potential risks and complications associated with surgery include infection, bleeding, and acute pancreatitis. To minimize these risks, surgical specialists performed pre-operative coagulation tests on all patients. In addition, they used ultrasound guidance to locate the lesion precisely, selected the shortest puncture path, and reduced damage to the pancreatic parenchyma or pancreatic duct, thereby reducing the risk of post-operative pancreatitis.[20] No adverse events, such as pancreatitis or bleeding, were observed in the

30 enrolled patients during or after EUS-FNA in this study. Wang *et al*. reported that the incidence of complications, such as pancreatitis, after EUS-FNA was approximately 0.44% (36/8246), which was significantly lower than that after ERCP. The mortality rate due to the specific incidence of EUS-FNA was 0.02%.[21] With the continuous maturation of this technology and the continuous improvement of puncture needles, many randomized controlled studies have confirmed its safety. Kanno *et al*. conducted a prospective multicenter study and reported that no adverse events (such as pancreatitis) were observed in the 78 enrolled patients during or after EUS-FNA.[22] Thus, based on these results, the authors recommend that clinicians use EUS-FNA for pathological diagnosis in patients suspected of having AIP. This study demonstrated that EUS-FNA has high accuracy (96.66%), sensitivity (96.42%), and specificity (100%) in diagnosing AIP. For patients suspected of having pancreatic cancer based on imaging but ultimately diagnosed with AIP, EUS-FNA can directly obtain tissue cells from pancreatic lesions, providing technical support for distinguishing between benign and malignant lesions. However, due to the small number of samples included in this study, the sample distribution is uneven, and the number of inflection points in the image is limited. Although the results of this study indicate that it has high sensitivity and specificity in diagnosing AIP, the diagnostic accuracy of EUS-FNA is influenced by various factors. These findings help avoid misdiagnosis of pancreatic cancer and unnecessary surgery, optimizing the diagnostic process and improving diagnostic efficiency and accuracy. These results are expected to prompt updates to clinical guidelines, increasing the recommended status of EUS-FNA in the diagnosis of AIP and enhancing clinicians' awareness and application standards of EUS-FNA technology.

This study has several limitations. One is that the number of patients enrolled was small. Second, our study was a single-center retrospective study. Third, the experts performing the ultrasound puncture were not uniform, with certain technical differences, which may influence the accuracy of the results. Finally, we did not compare EUS-FNA with other diagnostic modalities, such as ERCP or percutaneous FNA. In the future, we will expand the scope of the study and collaborate with other medical institutions to increase the sample size and diversity to improve the generality and reliability of the results. In future studies, comparative experiments should be designed to compare existing diagnostic methods directly with traditional methods, such as ERCP and percutaneous FNA, to evaluate their accuracy, sensitivity, and specificity. In long-term follow-up, more clinical data should be collected to verify the long-term efficacy and stability of the diagnostic method. Uniform diagnostic criteria and operational procedures should be developed to ensure data comparability between different centers and reduce bias.

SUMMARY

This study demonstrated that for cases where malignancy is suspected or cannot be excluded through imaging, pancreatic tissue can be obtained through EUS puncture for pathological diagnosis. Moreover, our retrospective analysis revealed that EUS-FNA is safe and feasible for diagnosing pancreatic space-occupying lesions and has high diagnostic value. Moreover, with the continuous development of technology, the rate of histological diagnosis of AIP is also increasing. Especially for patients with suspected AIP whose radiographic and serological diagnosis is uncertain, misdiagnosis of pancreatic cancer and unnecessary surgery should be avoided. At the same time, a key area for future research is integrating artificial intelligence (AI) to potentially increase the accuracy of EUS-FNA or further distinguish AIP from pancreatic cancer. Ongoing research and technological advancements in AI and enhanced imaging hold promise for more precise and personalized patient care. AI can assist in analyzing EUS images and FNA samples, potentially improving diagnostic accuracy. This technology can provide predictive analysis and personalized treatment plans based on a patient's unique medical history, genetic information, and lifestyle. In addition, AI can enhance diagnostic capabilities by analyzing medical images to identify abnormalities that may be missed by the human eye. As AI continues to evolve, it will become an indispensable tool for doctors, helping them make more efficient and accurate diagnoses and thus providing more appropriate and timely treatment plans.

AVAILABILITY OF DATA AND MATERIALS

During this study, datasets generated and/or analyzed have been obtained from corresponding author on reasonable request.

ABBREVIATIONS

AIP: Autoimmune pancreatitis
EUS-FNA: EUS-guided fine-needle aspiration
LPSP: Lymphoplasmacytic sclerosing pancreatitis
IDCP: Idiopathic duct-centric pancreatitis
HE: Hematoxylin and eosin
CT: Computed tomography
MRI: Magnetic resonance imaging
OP: Obliterans phlebitis
SF: Storiform fibrosis
HPF: High-power field
MPD: Main pancreatic duct
F: Female
M: Male
Range: Range of enlarged pancreas
Region: Region punctured
ICDC: International consensus diagnostic criteria

AUTHOR CONTRIBUTIONS

YL and DLW: Responsible for the data curation and writing-original draft; CW, DYZ, JHX, LWS, and YC: Responsible for the investigation and formal analysis; ZHY and JYL: Responsible for the resources and validation; and ZDJ and HJH: Responsible for the conceptualization and project administration. All authors meet the authorship status of ICMJE.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethics approval number: CHEC2025-114, Ethics Committee of Changhai Hospital (Shanghai, China). This study is a retrospective study and does not involve patient privacy, so we have applied to the research Institute of Shanghai Changhai Hospital for exemption of patient informed consent, and this study is in line with the Declaration of Helsinki.

ACKNOWLEDGMENT

Not applicable.

FUNDING

Not applicable.

CONFLICT OF INTEREST

Given his role as an editorial member, Zhendong Jin had no involvement in the peer-review of this article and had no access to information regarding its peer-review.

EDITORIAL/PEER REVIEW

To ensure the integrity and highest quality of CytoJournal publications, the review process of this manuscript was conducted under a **double-blind model** (authors are blinded for reviewers and vice versa) through an automatic online system.

REFERENCES

1. Sarles H, Sarles JC, Muratore R, Guien C. Chronic inflammatory sclerosis of the pancreas--an autonomous pancreatic disease? Am J Dig Dis 1961;6:688-98.
2. Cao L, Wang Y, Wang J, Guo Q, Chen Q, Wu X, *et al*. The role of EUS-guided fine needle aspiration in autoimmune pancreatitis: A single center prospective study. Scand J Gastroenterol 2018;53:1604-10.
3. Hart PA, Zen Y, Chari ST. Recent advances in autoimmune pancreatitis. Gastroenterology 2015;149:39-51.
4. Hart PA, Kamisawa T, Brugge WR, Chung JB, Culver EL, Czakó L, *et al*. Long-term outcomes of autoimmune pancreatitis: A multicentre, international analysis. Gut 2013;62:1771-6.
5. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, JemalA. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68:394-424.
6. Kamisawa T, Zen Y, Nakazawa T, Okazaki K. Advances in IgG4-related pancreatobiliary diseases. Lancet Gastroenterol Hepatol 2018;3:575-85.
7. Okazaki K, Kawa S, Kamisawa T, Ikeura T, Itoi T, Ito T, *et al*. Amendment of the Japanese consensus guidelines for autoimmune pancreatitis, 2020. J Gastroenterol 2022;57:225-45.
8. Lopes Vendrami C, Shin JS, Hammond NA, Kothari K, Mittal PK, Miller FH. Differentiation of focal autoimmune pancreatitis from pancreatic ductal adenocarcinoma. Abdom Radiol (NY) 2020;45:1371-86.
9. Guo T, Xu T, Zhang S, Lai Y, Wu X, Wu D, *et al*. The role of EUS in diagnosing focal autoimmune pancreatitis and differentiating it from pancreatic cancer. Endosc Ultrasound 2021;10:280-7.
10. Oh D, Kong J, Ko SW, Hong SM, So H, Hwang JS, *et al*. A comparison between 25-gauge and 22-gauge Franseen needles for endoscopic ultrasound-guided sampling of pancreatic and peripancreatic masses: A randomized non-inferiority study. Endoscopy 2021;53:1122-9.
11. Vitali F, Strobel D, Frulloni L, Heinrich M, Pfeifer L, Goertz RS, *et al*. The importance of pancreatic inflammation in endosonographic diagnostics of solid pancreatic masses. Med Ultrason 2018;20:427-35.
12. Sandrasegaran K, Menias CO. Imaging in autoimmune pancreatitis and immunoglobulin G4-related disease of the abdomen. Gastroenterol Clin North Am 2018;47:603-19.
13. Wang G, Du L, Lu X, Chen S, Bi X, Zhang M, *et al*. Multiparameter diagnostic model based on ^{18}F-FDG positron emission tomography and serological examination for differentiating focal autoimmune pancreatitis from pancreatic ductal adenocarcinoma. Quant Imaging Med Surg 2023;13:5653-63.
14. Deshpande V, Mino-Kenudson M, Brugge W, Lauwers GY. Autoimmune pancreatitis: More than just a pancreatic disease? A contemporary review of its pathology. Arch Pathol Lab Med 2005;129:1148-54.
15. Notohara K, Kamisawa T, Furukawa T, Fukushima N, Uehara T, Kasashima S, *et al*. Concordance of the histological diagnosis of type 1 autoimmune pancreatitis and its distinction from pancreatic ductal adenocarcinoma with endoscopic ultrasound-guided fine needle biopsy specimens: An interobserver agreement study. Virchows Arch 2022;480:565-75.
16. Hewitt MJ, McPhail MJ, Possamai L, Dhar A, VlavianosP, Monahan KJ. EUS-guided FNA for diagnosis of solid pancreatic neoplasms: A meta-analysis. Gastrointest Endosc 2012;75:319-31.
17. De Pretis N, Crinò SF, Frulloni L. The Role of EUS-guided FNA and FNB in autoimmune pancreatitis. Diagnostics (Basel) 2021;11:1653.
18. Morishima T, Kawashima H, Ohno E, Yamamura T, Funasaka K, Nakamura M, *et al*. Prospective multicenter study on the usefulness of EUS-guided FNA biopsy for the diagnosis of autoimmune pancreatitis. Gastrointest Endosc 2016;84:241-8.
19. Levy MJ, Oberg TN, Campion MB, Clayton AC, Halling KC,

Henry MR, *et al*. Comparison of methods to detect neoplasia in patients undergoing endoscopic ultrasound-guided fine-needle aspiration. Gastroenterology 2012;142:1112-21.e2.
20. Lai Y, Pan J, Peng K, Wu D, Wen L. Rare cause of recurrent acute pancreatitis in teenage man. eGastroenterology 2024;2:e100105.
21. Wang KX, Ben QW, Jin ZD, Du YQ, Zou DW, Liao Z, *et al*. Assessment of morbidity and mortality associated with EUS-guided FNA: A systematic review. Gastrointest Endosc 2011;73:283-90.
22. Kanno A, Masamune A, Fujishima F, Iwashita T, Kodama Y, Katanuma A, *et al*. Diagnosis of autoimmune pancreatitis by EUS-guided FNA using a 22-gauge needle: A prospective multicenter study. Gastrointest Endosc 2016;84:797-804.e1.

How to cite this article: Liu Y, Wan D, Wu C, Zhang D, Xu J, Li W, *et al*. Endoscopic ultrasound-guided fine-needle aspiration value in suspected autoimmune pancreatitis malignancy diagnosis. CytoJournal. 2025;22:58. doi: 10.25259/Cytojournal_214_2024

HTML of this article is available FREE at:
https://dx.doi.org/10.25259/Cytojournal_214_2024