Diagnosis of autoimmune pancreatitis by EUS-guided FNA using a 22-gauge needle: a prospective multicenter study CME

Atsushi Kanno, MD, PhD,[1] Atsushi Masamune, MD, PhD,[1] Fumiyoshi Fujishima, MD, PhD,[2] Takuji Iwashita, MD, PhD,[3] Yuzo Kodama, MD, PhD,[4] Akio Katanuma, MD,[5] Hirotaka Ohara, MD, PhD,[6] Masayuki Kitano, MD, PhD,[7] Hiroyuki Inoue, MD, PhD,[8] Takao Itoi, MD, PhD,[9] Nobumasa Mizuno, MD, PhD,[10] Hiroyuki Miyakawa, MD, PhD,[11] Rintaro Mikata, MD, PhD,[12] Atsushi Irisawa, MD, PhD,[13] Satoko Sato, MD, PhD,[2] Kenji Notohara, MD, PhD,[14] Tooru Shimosegawa, MD, PhD[1]

Sendai, Gifu, Kyoto, Sapporo, Nagoya, Osaka, Tsu, Tokyo, Chiba, Aizu-wakamatsu, Kurashiki, Japan

Background and Aims: Histopathologic examination is critical for diagnosing autoimmune pancreatitis (AIP). However, specimens obtained using EUS-guided FNA (EUS-FNA) are not recommended for histopathologic diagnosis because of inadequate sample size volume. We evaluated EUS-FNA efficacy for AIP diagnosis using a 22G needle.

Methods: Seventy-eight patients exhibiting the imaging characteristics indicative of AIP in the pancreatic parenchyma and pancreatic duct underwent EUS-FNA with a 22G needle at 12 institutions between February 2013 and March 2014. Samples were evaluated for tissue sampling conditions, CD38- and IgG4-positive plasma cell counts, storiform fibrosis (SF), and obliterative phlebitis (OP).

Results: Tissue specimens containing >10, 5 to 10, and 1 to 4 high-power fields (HPFs) were obtained from 29 (37.2%), 18 (23.1%), and 15 (19.2%) of 78 patients, respectively. The mean ± standard deviation (SD) CD38- and IgG4-positive plasma cell counts were 23.2 ± 18.8/HPF and 5.1 ± 6.7/HPF, respectively. SF was detected in 49 of 78 patients (62.8%) and OP in 38 of 78 patients (48.7%). According to the International Consensus Diagnostic Criteria (ICDC), histopathologic levels corresponded to level 1 in 32, level 2 in 13, and unclassifiable in 17 patients. Hence, 45 of 78 patients (57.7%) could be diagnosed with lymphoplasmacytic sclerosing pancreatitis according to ICDC.

Conclusions: Pancreatic tissues with at least 1 HPF were obtained by EUS-FNA from approximately 80% of patients, and nearly 60% of patients were diagnosed with ICDC level 2 or higher. Our findings indicate that EUS-FNA with a 22G needle may be useful for the histopathologic diagnosis of AIP. (Clinical trial registration number: UMIN000010097.) (Gastrointest Endosc 2016;84:797-804.)

Abbreviations: AIP, autoimmune pancreatitis; HPF, high-power field; ICDC, International Consensus Diagnostic Criteria; IgG, immunoglobulin G; LPSP, lymphoplasmacytic sclerosing pancreatitis; OP, obliterative phlebitis; SF, storiform fibrosis; SD, standard deviation.

DISCLOSURE: *The following author received research support for this study from a Grant-in-Aid from the Japan Society for the Promotion of Science (no. 25461020): A. Kanno. All authors disclosed no financial relationships relevant to this publication. The following authors received research support from the Ministry of Health, Labor, and Welfare of Japan (Principal Investigators: Tsutomu Chiba, Tsuneyo Mimori, and Yoshifumi Takeyama): A. Masamune, H. Ohara, M. Kitano, T. Itoi, A. Irisawa, K. Notohara, and T. Shimosegawa.*

See CME section; p. 833.

0016-5107/$36.00
http://dx.doi.org/10.1016/j.gie.2016.03.1511

Received August 16, 2015. Accepted March 30, 2016.

Current affiliations: Division of Gastroenterology (1), Department of Pathology (2), Tohoku University Graduate School of Medicine, Sendai, Japan; First Department of Internal Medicine, Gifu University Hospital, Gifu, Japan (3), Department of Gastroenterology and Hepatology, Kyoto University Graduate School of Medicine, Kyoto, Japan (4), Center for Gastroenterology, Teine-Keijinkai Hospital, Sapporo, Japan (5), Department of Gastroenterology and Metabolism, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan (6), Department of Gastroenterology and Hepatology, Kinki University Faculty of Medicine, Osaka, Japan (7), Department of Gastroenterology and Hepatology, Mie University School of Medicine, Tsu, Japan (8), Department of Gastroenterology and Hepatology, Tokyo Medical University, Tokyo, Japan (9), Department of Gastroenterology, Aichi Cancer Center Hospital, Nagoya, Japan (10), Department of Gastroenterology, Sapporo Kosei Hospital, Sapporo, Japan (11), Department of Gastroenterology and Nephrology, Chiba University Graduate School of Medicine, Chiba, Japan (12), Department of Gastroenterology, Fukushima Medical University Aizu Medical Center, Aizu-wakamatsu, Japan (13), Department of Anatomic Pathology, Kurashiki Central Hospital, Kurashiki, Japan (14).

Reprint requests: Atsushi Kanno, MD, PhD, Division of Gastroenterology, Tohoku University Graduate School of Medicine, 1-1 Seiryo-machi, Aoba-ku, Sendai, Miyagi 980-8574, Japan.

Autoimmune pancreatitis (AIP) is a rare type of pancreatitis with a hypothesized autoimmune mechanism and distinctive clinical characteristics. AIP is currently regarded as a pancreatic manifestation of systemic immunoglobulin G (IgG)4-related disease[1] and has several distinct clinical, serologic, and morphologic characteristics. Histologically, lymphoplasmacytic sclerosing pancreatitis (LPSP) is a characteristic feature of type 1 AIP,[2] whereas idiopathic duct-centric chronic pancreatitis and granulocytic epithelial lesions are of type 2 AIP.[3-5] Compared with Western countries, type 2 AIP is extremely rare in Japan.[6-8] The world's first clinical diagnostic criteria for AIP were released by the Japan Pancreas Society in 2002.[9] Subsequently, diagnostic criteria for AIP have been proposed in several other countries.[10-14] To standardize the diagnostic criteria of AIP, the International Consensus Diagnostic Criteria (ICDC) were proposed in 2011.[15] EUS-guided FNA (EUS-FNA) is not included in ICDC as a method for histopathologic diagnosis of AIP because of the difficulty in obtaining adequate specimens for histopathologic analysis. However, several reports have suggested that EUS-FNA is useful for the diagnosis of AIP.[16-18] Therefore, we conducted a prospective multicenter study to investigate whether EUS-FNA is useful for the histopathologic diagnosis of AIP.

METHODS

This multicenter study was prospectively conducted between February 2013 and March 2014 at 12 tertiary care referral centers. The inclusion criteria included patients exhibiting the imaging characteristics, such as diffuse or segmental/focal enlargement with delayed enhancement and diffuse or segmental/focal or multiple irregular narrowing of the main pancreatic duct without marked upstream dilatation, indicative of AIP in the pancreatic parenchyma and pancreatic duct according to the ICDC. These findings were detected by cross-sectional images via CT and/or magnetic resonance imaging techniques. Exclusion criteria were as follows: (1) patients less than 20 years old, (2) patients in whom EUS-FNA is difficult (eg, cases with surgically altered anatomy), (3) patients with a performance status > 2 as defined by the Eastern Cooperative Oncology Group, (4) patients with malignant tumors, and (5) patients who declined to participate. Patients with surgically altered anatomy were excluded because it was difficult to acquire clear EUS images from the stomach or duodenum in such cases. All patients who participated in this study provided written informed consent. The study was approved by the institutional review board at all participating institutions and was registered on February 22, 2013 at the University Hospitals Medical Information Network (UMIN000010097).

A linear echoendoscope with an Expect 22G needle (Boston Scientific Japan, Tokyo, Japan) was used to perform EUS-FNA. EUS-FNA processing of histologic samples and immunostaining were performed as previously described.[18] Endosonographers punctured the enlarged region in segmental or focal type AIP. In patients with a diffusely enlarged pancreas, the endosonographer determined the puncture site. Endosonographers did not change the pancreatic region for puncture in each session of EUS-FNA. After the puncture, a needle was moved up and down 10 to 20 times within the enlarged pancreas by pulling the needle stylet slowly and steadily (slow-pull method) or by aspiration under 20 mL of negative pressure (aspiration method). The endosonographer at each institution decided whether to use the slow-pull or aspiration method.

The number of punctures was 3.4 ± 1.3 (mean ± standard deviation [SD]; range, 1-7). Tissue samples were fixed in formalin and embedded in paraffin, and several thin serial sections were prepared at each institution. The sliced sections were subsequently sent to the Tohoku University Hospital for histologic examination. Hematoxylin and eosin, Masson's trichrome, and Elastica-Masson staining were performed on each section. Immunohistochemical staining was performed using antibodies against IgG4 (Invitrogen, Gaithersburg, Md) and CD38 (Novocastra, Newcastle upon Tyne, UK).

An expert pathologist (F.F.), who was blinded to all clinical information, reviewed the histopathologic specimens. An average of >10 IgG4- and CD38-positive plasma cells per high-power field (HPF, 400×) was defined as IgG4-positive and lymphocyte-plasma cell infiltration, respectively. Tissue samples were also examined for the presence of storiform fibrosis (SF), obliterative phlebitis (OP), and granulocytic epithelial lesions. OP was diagnosed by Elastica-Masson staining. Because the arteries and veins are usually found next to each other in the pancreas, OP unaccompanied by arteries was judged to be a suspected diagnosis.

Statistics

Statistical analysis was performed using SPSS, version 20.0 (SPSS Inc., Chicago, Ill). A P value < .05 was considered to be statistically significant.

RESULTS

Clinical findings

Eighty-one patients were assessed for eligibility, and 3 patients were excluded because of pancreatic cancer (n = 1) or surgically altered anatomy (n = 2). Table 1 summarizes the clinical characteristics of the 78 enrolled patients. A male-to-female ratio of 60:18 and a mean ± SD age of 65.8 ± 11.1 years were observed. Seventy-seven of the 78 patients (98.7%) showed pancreatic enlargement; 39.7% (31/78), 33.3% (26/78), and 25.6% (20/78) had diffuse, segmental, and focal enlargement, respectively. Only 1 patient did not exhibit pancreatic enlargement. In this patient the endosonographer