Comparison of cytological and histological preparations in the diagnosis of pancreatic malignancies using endoscopic ultrasound-guided fine needle aspiration

Dong Kee Jang, Sang Hyub Lee, Jun Kyu Lee, Woo Hyun Paik, Kwang Hyun Chung,

Ban Seok Lee, Jun Hyuk Son, Jae Woo Lee, Ji Kon Ryu, Yong-Tae Kim and Kyoung-Bun Lee

Seoul, Korea

BACKGROUND: Endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) has become a crucial diagnostic technique for pancreatic malignancies. The specimen obtained by EUS-FNA can be prepared for either cytological or histological examinations. This study was to compare diagnostic performance of cytological and histological preparations using EUS-FNA in the same lesions when pancreatic malignancies were suspected.

METHODS: One hundred and eighteen patients who underwent EUS-FNA for suspected pancreatic malignancies were consecutively enrolled. All procedures were conducted by a single echoendoscopist under the same conditions. Four adequate preparations were obtained by 22-gauge needles with 20 to-and-fro movements for each pass. The 4 preparations included 2 cytological and 2 histological specimens. The pathologic reviews of all specimens were conducted independently by a single experienced cytopathologist. Sensitivity, specificity, and accuracy of the 2 preparations were compared.

RESULTS: The enrolled patients consisted of 62 males (52.5%), with the mean age of 64.6±10.5 years. Surgery was performed in 23 (19.5%) patients. One hundred and sixteen (98.3%) lesions were classified as malignant, while 2 (1.7%) were benign. Sensitivity of cytology and histology were 87.9% and 81.9%, respectively, with no significant difference (P=0.190). Accuracy was also not significantly different. Cytological preparation was more sensitive when the size of lesion was <3 cm (86.7% vs 68.9%, P=0.033).

CONCLUSIONS: Our results suggested that the diagnostic performances of cytological and histological preparations are not significantly different for the diagnosis of pancreatic malignancies. However, cytological preparation might be more sensitive for pancreatic lesions <3 cm.

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KEY WORDS: endoscopic ultrasound-guided fine needle aspiration; pancreatic neoplasms; cytology; pathology; histology

Author Affiliations: Department of Internal Medicine, Dongguk University Ilsan Medical Center, Goyang-si, Gyeonggi-do, Korea (Jang DK and Lee JK); Department of Internal Medicine and Liver Research Institute, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea (Jang DK, Lee SH, Paik WH, Chung KH, Lee BS, Lee JW, Ryu JK and Kim YT); Department of Internal Medicine, Inje University Ilsan Paik Hospital, Goyang-si, Gyeonggi-do, Korea (Son JH); Department of Pathology, Seoul National University College of Medicine, Seoul, Korea (Lee KB)

Corresponding Author: Sang Hyub Lee, MD, PhD, Department of Internal Medicine, Seoul National University Hospital, 101 Daehak-ro, Jongno-gu, Seoul 03080, Korea (Tel: +82-2-2072-4892; Fax: +82-2-762-9662; Email: gidoctor@snuh.org)

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Introduction

Currently, endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) is an established standard method for tissue diagnosis in patients with suspected pancreatic neoplasm.[1-3] The recently reported sensitivity, specificity, and accuracy of EUS-FNA were 77%-94.3%, 85.9%-100% and 80%-95%, respectively.[4-7] Many factors such as the sample size, definition of positive results, types of neoplasm, and methods of tissue sampling may affect these values. Accurate, prompt diagnosis of pancreatic neoplasms is essential in directing surgical or medical treatment of patients,

because pancreatic cancer has a poor prognosis. Hence, there have been various efforts to improve the diagnostic performance of EUS-FNA, including development of needles or helpful techniques, and accompanying on-site cytopathologists.[8-13]

The two methods of tissue sampling with the same needle in EUS-FNA differ in the way the samples are processed. In cytological preparation, an aspirate of cells is smeared on a slide and fixed in alcohol; while in histological preparation, aspirated cells fixed in formalin are sectioned from a paraffin block. The quantity and quality of the collected materials often affect the preference. Smear cytological examination is a traditional and standard method for cytological diagnosis, which should be interpreted by an experienced cytopathologist.[3, 11, 12] Histological preparations provide more pathological information, especially when combined with immunohistochemistry (IHC). The IHC is remarkably useful for the discovery of non-morphological markers.[14-17] These two methods are considered complementary, according to previous studies.[18-20] However, little is known about the specific contribution of each method in the same target lesion. The aim of this study was to compare diagnostic performance of cytological and histological preparations using EUS-FNA in the same lesions when pancreatic malignancies were suspected. We also attempted to determine the superior method under certain circumstances.

Methods

Patients and study design

The patients who underwent EUS-FNA for suspected pancreatic malignancies at Seoul National University Hospital between September 2013 and February 2015 were consecutively enrolled. Patients who had pure cystic neoplasms or specimens obtained by methods other than our study protocol were excluded. We reviewed patients' entire medical records, EUS-FNA results, and pathology reports. This study was approved by the Institutional Ethics Review Board of Seoul National University Hospital and conducted in accordance with the *Declaration of Helsinki* (IRB No. 1505-033-670).

EUS-FNA procedures and cytopathological examinations

All EUS-FNA procedures in the included patients were performed by a single, experienced echoendoscopist (Lee SH) according to the following protocol with the same types of instruments. Linear array echoendoscope (GF-UCT240; Olympus Ltd., Tokyo, Japan) was used for EUS. FNA was performed with a 22-gauge needle (EchoTip® Ultra; Wilson Cook Medical, Winston-Salem, NC, USA) regardless of the lesions' location. A transduodenal approach was applied for proximal lesions located in the head or uncinate process of the pancreas; whereas, a transgastric approach was used for distal lesions in the pancreatic body or tail. Each session included at least 4 needle passes to make 4 adequate preparations without an exception, and aspirated material by each pass was subjected to cytological (C) or histological (H) preparation in the pre-set order of C-H-H-C or H-C-C-H. The order of preparations was alternately assigned to each patient, making the final proportion the same. In the cytological preparation, an aspirate was thinly smeared on microscope glass slides and immediately fixed in 95% alcohol solution. In the histological preparation, aspirated material was placed in a container with 10% formaldehyde solution, which was then interpreted after appropriate staining such as hematoxylin and eosin stain. Needles were washed after each pass and flushed with air before reinsertion. Fanning technique was applied if possible, as described previously,[8] and 20 to-and-fro movements were performed in each needle pass with negative pressure created by a 10 mL syringe. There was no available on-site cytopathologists at our institution. The collected specimens were sent to the department of pathology for microscopic analysis. Pathologic reviews of all specimens were independently conducted and confirmed by a single experienced cytopathologist (Lee KB) after all of the patients were enrolled.

Definitions

Malignancy or suspicion of malignancy in the pathologic review was categorized as malignancy, while atypical or benign cells were categorized as benign. Final diagnosis was determined by the result of EUS-FNA itself or another biopsy of metastatic lesions or pathologic analysis of surgically resected specimens. Size was defined by the longest diameter measured by EUS. Lesions in the head or uncinate process of the pancreas were classified as proximal lesions, while those in the body or tail were regarded as distal lesions.

Statistical analysis

Continuous data was expressed as mean±standard deviation, while categorical variables were presented as frequencies and percentages. Sensitivity, specificity, and accuracy of the two preparations were compared by the McNemar Chi-square test.[21] All analyses were calculated with the statistics program IBM SPSS version 21.0 (IBM Corp., Armonk, NY, USA). A two-sided P value of <0.05 was considered to indicate statistically significant.