EDITORIAL

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Cell block created from pancreatic duct lavage is another jigsaw puzzle to diagnose early pancreatic ductal adenocarcinoma

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See "Pancreatic duct lavage cytology combined with a cell-block method for patients with possible pancreatic ductal adenocarcinomas, including pancreatic carcinoma *in situ*" by Hiroaki Kusunose, Shinsuke Koshita, Yoshihide Kanno, et al., Clin Endosc 2023;56:353–366.

Pancreatic ductal adenocarcinoma (PDAC) usually presents as a mass, pancreatic ductal stricture, or recurrent pancreatitis. Endoscopic ultrasound (EUS) with tissue acquisition, including fine needle aspiration (FNA) and fine needle biopsy (FNB), is the preferred technique for diagnosing PDACs with masses. However, in suspected PDAC without a mass, cytology of pancreatic lavage and brushing is the only method for evaluating ductal malignancy. Unfortunately, the diagnostic yield of cytology is suboptimal (<50%).[1] The paucity of cells in the obtained fluid is the main obstacle in achieving a reliable level of sensitivity. Like assembling jigsaw puzzles, by centrifuging the lavage fluid to make a cell block (CB), the tumor cells could aggregate sufficiently to embed in the paraffin block that can be cut for cellular evaluation and architectural analysis. In addition, immunocytochemical staining can be performed on CB. In the study by Kusunose et al.,[2] Ki-67, p53 protein, and MUC1 glycoprotein were important stains for facilitating diagnosis. They performed pancreatic duct lavage in 41 patients deemed unfit for EUS-FNA/B. Of these, 36 (87.8%) had sufficient CB specimens for histopathological analysis. They demonstrated the sensitivity, specificity, and accuracy of CB in detecting PDAC to be 94.1%, 100%, and 96.8%, respectively. Interestingly, the sensitivity in those without a mass did not drop by more than 10%, showing a sensitivity of 87.5% while maintaining perfect specificity at 100%. The authors should be commended for this pioneering work because they can assemble cells in a block as a jigsaw of a tumor.

Previously, direct pancreatoscopy with targeted biopsy was the only additional asset of diagnostic endoscopic retrograde cholangiopancreatography (ERCP). El Hajj et al.[3] performed direct peroral pancreatoscopy in patients with indeterminate pancreatic duct strictures using visual impression and targeted biopsy as the gold standard for diagnosis; they reported a sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of 91%, 95%, 94%, 93%, and 94%, respectively. However, the high accuracy observed in this study was derived from expert centers with extensive experience in pancreatoscopy. The CB technique welcomes back diagnostic pancreatography as it is traditionally valued for image interpretation alone; however, pancreatic duct lavage can now be performed as part of this diagnostic ERCP. Unlike direct pancreatoscopy, CB does not require endoscopic expertise in reading indeterminate strictures, as it is the work of a cytopathologist. In addition, the cytopathologist who reads the specimen has additional support for accurate reading by adding immunocy-

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tochemical staining. Nevertheless, pancreatic lavage and direct peroral pancreatoscopy carry a significant risk of post-procedural pancreatitis. The risk of post-ERCP pancreatitis with pancreatic lavage reported in this study[2] remained at 9.8%, despite strong suction applied after irrigation during lavage, and the majority of patients received pancreatic stent placement and nonsteroidal anti-inflammatory drug prophylaxis. Notably, the amount of saline injected during lavage was approximately 40 mL. In comparison with pancreatic lavage for CB, pancreatoscopy with periodic suction of the content in the pancreatic duct in 102 patients resulted in 4% post-procedural pancreatitis cases.[3] Thus, decompression of the pancreatic duct during lavage to obtain a CB should be considered to reduce the risk of pancreatitis.

EUS with FNA requires rapid on-site evaluation (ROSE) to ensure the adequacy of the specimen and reduce the chance of re-examination. In contrast, the adequacy of CB specimens after pancreatic lavage is sufficient. To date, no study has evaluated the requirements for ROSE using this technique. The current study reported that only 12% of the cases had inadequate specimens for CB.[2] Another idea for evaluating the adequacy of specimens for CB may have to be extrapolated from a recent study from Florida, United States that used the EUS-FNA specimen to make a centrifuged clot-like CB that demonstrated an extremely high satisfactory outcome of 94% on the adequacy of specimens from 282 patients.[4] The next question is how much lavage is needed before terminating the procedure to obtain the CB specimen since one of the main concerns is the significant risk of pancreatitis from over-irrigation and inadequate CB production from a small volume of lavage.

In the future, the CB technique can be standardized after confirmation in a well-conducted prospective study. This technique would be the next jigsaw piece to complete the puzzle in patients with suspected PDAC without a pancreatic mass on imaging, and those with undiagnosed pancreatic tumors, even after multiple EUS attempts with FNA or FNB.

Conflicts of Interest

Rungsun Rerknimitr is currently serving as an associate editor of *Clinical Endoscopy*; however, he had not involved in the peer reviewer selection, evaluation, or decision process of this manuscript.

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