Endoscopic Ultrasound-Guided Fine Needle Aspiration for Solid Pancreatic Masses. Optimizing the Diagnostic Yield

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Pancreatic cancer is one of the most lethal malignancies. It is considered as the tenth most commonly diagnosed cancer, ranking 4th in estimated annual cancer death. Early detection remains a big challenge, with only 10-20% of patients being diagnosed with potentially resectable disease. In spite of several improvements in the treatment of this disease, the average 5-year survival is still under 10%.

Over the past decades, endoscopic ultrasound (EUS) has evolved to become a crucial tool for the evaluation of pancreatic diseases. Specifically, EUS plays a critical role in the evaluation of patients with known or suspected pancreatic masses. Published literature supports the superiority of EUS compared with cross-sectional imaging for tumor detection [1]. It is not only that the high sensitivity for tumor detection is high, which is important, but also because of the very high negative predictive value. This has important implications for the clinician because it means that EUS can reliably exclude pancreatic cancer, especially in the setting of a low or indeterminate pretest probability. Another important advantage of EUS is its ability to target and place a needle into suspicious lesions, in order to obtain a cyto-histological sample for establishing the final diagnosis of lesions evaluated.

Up to now, due to the universal drawback considered for all sampling techniques available for the pancreas, preoperative sampling has not been generally advised (i.e., for potentially resectable pancreatic tumors in operable patients). However, differential diagnosis of solid pancreatic masses includes many different types of lesions, like ductal adenocarcinoma, neuroendocrine tumors, metastases, acinar cell carcinomas, lymphomas, mass forming chronic pancreatitis (including autoimmune pancreatitis), and very rare diseases such as pancreaticoblastomas and solid pseudopapillary tumors. In this setting, pancreatic solid masses suspicious for cancer may be classified into masses that will not be resected because they are locally advanced, associated with metastases, or they are present in patients with a poor physical condition, and potentially resectable solid pancreatic lesions. For the first category, sampling in order to obtain a definitive diagnosis is usually desirable to assist with counseling and planning palliation. However, in the second group, it is generally accepted that the procedure is not needed, since the results of any nonsurgical sampling technique are unlikely to affect further management due to the relatively low negative predictive value of sampling techniques for cancer diagnosis. However, there are increasing arguments for performing biopsies in potentially resectable pancreatic tumors. An established protocol of preoperative neoadjuvant therapy, a patient demand for a conclusive diagnosis of cancer before surgery and, lastly, exclusion of unusual tumors (e.g., lymphoma, some pancreatic metastases, autoimmune pancreatitis) that would not benefit from surgery are becoming usual indications for sampling solid pancreatic lesions. In summary, obtaining cyto-histological samples from pancreatic solid lesions is becoming mandatory in many circumstances.

When sampling of these pancreatic lesions is necessary, EUS-guided fine needle aspiration (EUS-FNA) is nowadays considered as the most accurate and safe technique, and the principal to establish the diagnosis of malignancy of pancreatic tumors. A number of retrospective and prospective case series studying EUS-FNA of solid pancreatic lesions have been published. Reported diagnostic accuracy ranges between 62%
and 96% [2]. A recent meta-analysis by Hewitt et al showed great diagnostic value of EUS-FNA for solid pancreatic lesions, 98% in specificity and 95% in accuracy [3]. And when looking at complications, EUS-FNA is considered safe, with a reported rate of morbidity between 0.35 and 2.8%, with almost no cases of death related to the procedure [4]. Thus, EUS-FNA is recommended as the first-line procedure for sampling solid pancreatic lesions.

However, and although it is invaluable as a diagnostic tool, it is not uncommon to encounter inconclusive diagnosis at the initial EUS-FNA. There are several known factors for inconclusive result of EUS-FNA, such as existence of concurrent chronic pancreatitis, small size of the lesions, difficult access to the lesions, etc. In these patients, with a high clinical suspicion for pancreatic cancer and indeterminate or negative findings at the initial sampling procedure, including EUS-FNA, EUS-FNA (possibly repeated) is strongly advised. In fact, a retrospective review of 24 consecutive patients showed that repeating EUS-FNA facilitated determination of the true status of disease in 20 patients (84%) with inconclusive findings at initial EUS-FNA [5]. It is crucial to analyze factors influencing these first negative results. Above of all these factors, expertise of facilities seems to be the significant factor maximizing diagnostic accuracy of EUS-FNA. For instance, the existence of experienced endosonographers and cytopathologists who can provide rapid on-site cytological evaluation has shown to be essential for improving the diagnostic accuracy of EUS-FNA of pancreatic solid lesions [6]. We have also demonstrated in a multicenter trial that the success of EUS-FNA seems to be dependent on the involvement of a pathologist with experience in handling and dealing with materials obtained by fine needle aspiration or fine needle biopsy [7]. A study from DeWitt et al [8] stressed the importance of repeating the EUS-FNA at a tertiary referral center, showing that diagnostic sensitivity increased from 68% to 92%. Similar data are presented by Suzuki et al in the present issue of the Journal of Gastrointestinal and Liver Diseases [9]. Authors reported that repeating EUS-FNA at a tertiary referral center after inconclusive EUS-FNA result at referring facilities, had the ability to confirm the diagnosis in 82.1% of patients, mostly adenocarcinoma (67.9%), in whom first EUS-FNA was inconclusive or negative for malignancy. Hence, a new puncture in well-equipped, high-volume centers with experienced endosonographers and pathologists seems mandatory in order to exclude malignancy in cases where the first EUS-FNA has been nonmalignant or inconclusive.

In conclusion, EUS-FNA is an excellent tool, playing a pivotal role in the study of solid pancreatic lesions. Sampling pancreatic lesions is becoming essential to optimize the management of pancreatic solid tumors, both in resectable and unresectable cases. Probably, although EUS-FNA is widely available, after a first negative result in selected patients, with a high clinical suspicion for pancreatic malignancy, repeating EUS-FNA at highly experience centers is strongly advised.

REFERENCES