Douglas G. Adler MD, FACG, AGAF, FASGE, Series Editor

Avoiding Misses and Near Misses: Improving Accuracy in EUS

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"Real knowledge is to know the extent of one's ignorance." – Confucius

"The first step in avoiding a trap is knowing of its existence." – Thufir Hawat (Dune, Frank Herbert)

INTRODUCTION

Endoscopic ultrasound (EUS) has proven to be an indispensable tool for diagnosis and management of a wide variety of disorders. Mastery of EUS takes considerable time, dexterity, effort, and perseverance. A steady and wide-ranging caseload of EUS procedures is critical for maintaining competence and the development of new skills in this field. Even expert endoscopists can miss significant lesions during an EUS examination.

One of the most challenging aspects of EUS is that scope manipulation is driven by the real-time gray-scale images on the EUS screen, and not the view on the color video monitor used for standard endoscopic procedures. Evaluation and interpretation of ultrasound images are unfamiliar to most endoscopists, particularly in the United States, because formal training in transabdominal ultrasound imaging is not part of their GI curriculum, as it might be in Europe or Asia.

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Manipulation of the echoendoscope is driven by the images on the EUS monitor, and the usual "up, down, left, right" movement will not produce the same effect as it would on the endoscopic video monitor. Mastery of the movements necessary to optimize EUS imaging is "as much done by the cerebellum as by the cerebrum", and for real experts, the scope movements seem to be commanded subliminally.

Obtaining comprehensive EUS images of a given area of interest takes practice and skill, but the influence of factors that cannot be controlled by the endoscopist should not be underestimated. A patient's body habitus, luminal anatomy, and the anatomic variations that can be encountered from one patient to another must be factored in to the ability of any endosonographer to arrive at the correct diagnosis. It must be recognized that the ability of EUS to visualize lesions is imperfect, even in the hands of the most experienced endosonographer. There are many potential pitfalls for EUS and EUS-FNA, which have been exhaustively summarized.[1]

Adverse effects (AEs) of EUS are remarkably low, even with the addition of fine needle aspiration. However, missing a diagnosis of malignancy remains

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one of the most feared complications of EUS. In distinction to ERCP, in which AEs are often acts of commission (for example, actively doing things that cause pancreatitis or a perforation), AEs in EUS are most commonly acts of omission ("missing things").

It should be stressed that all EUS operators are human, and thus imperfect. Even the most skilled and experienced endosonographer can miss a clinically significant lesion.

The consequences of missing a cancer diagnosis are among the most difficult in all of procedural gastroenterology. However, missing other findings (even non-malignant ones), can result in increased health care costs and patient discomfort or inconvenience and can create medicolegal issues for physicians. We recognize that EUS, like all human endeavors, is an imperfect science and that even the most experienced endosonographer can miss a critically important finding. In this article, we will analyze potential causes for "misses and near misses" in EUS, and suggest how the endosonographer can minimize these occurrences.

Patient Dependent Factors in EUS Imaging of The Pancreas

Certain patient-dependent factors may have a significant impact on the ability to visualize the pancreas (Table 1). In patients with increased intra-abdominal fat, pancreatic imaging may be very challenging, as the pancreas might be hyperechoic due to fatty infiltration, or be atrophic which could be related to diabetes and/or metabolic syndrome. Fatty infiltration of the pancreas can occur in patients with a normal body habitus as well. Dense shadowing from inflammation, scarring, or calcifications in chronic pancreatitis can leave large portions of the pancreas, typically the head and genu, unseen. In the immediate period following acute pancreatitis, inflammatory changes can mask significant findings or be misinterpreted as a mass. EUS evaluation of the pancreas is often pursued in cases of idiopathic recurrent acute pancreatitis, but many endosonographers will wait for several weeks prior to doing a diagnostic EUS to allow these inflammatory changes to clear. Performing EUS of the pancreas in the time period just after an episode of acute pancreatitis can often be a fruitless endeavor.

Usually the presence of a biliary stent does not interfere with the ability to see a pancreatic mass with EUS, although in unusual cases, ultrasonographic shadowing in the pancreatic head from a biliary stent may make it difficult to see or fully delineate a small mass lesion. The literature is mixed on the influence of pancreatic cancer staging accuracy with or without a biliary stent in place.[3,4] Three studies have looked at cytologic yields of EUS-FNA of pancreatic masses after a stent has been placed. The concern is that cytology yields could be diminished due to the aforementioned stent effect (which could affect targeting of tissue for FNA sampling), or that false positive cytology could result. One of the 3 studies demonstrated a diminished yield of FNA in the presence of a stent,[5] while another showed more indeterminate results if the biliary stent was placed less than 1 day prior to EUS.[6] The third study compared EUS FNA in patients who had previously received metal or plastic biliary stent.[7] The yields were very high and comparable in both groups (all patients had stents). A single false positive FNA was found in a patient with a plastic stent).

One of the few available studies to analyze factors accounting for missed pancreatic masses was the **N**o **E**ndo**S**onographic detection of **T**umor (NEST) study.[7] In this retrospective analysis, 9 expert endosonographers retrospectively identified 20 patients in whom a pancreatic neoplasm was missed. The goal was to try to understand factors that led to the missed diagnosis. Twelve of the 20 missed malignancies had EUS features of chronic pancreatitis, again emphasizing the limitations of EUS in this setting. Three patients had diffusely infiltrating carcinoma, which was not mass forming. Other unusual causes of missed pancreatic neoplasms were "prominent ventral dorsal split" in two

Table 1. Patient-related Factors for Inadequate Pancreatic Imaging by EUS

a. Body habitus (i.e. obese)
b. Fatty infiltration or atrophy of the pancreas
c. Shadowing from calcifications in chronic pancreatitis
d. Shadowing from previously placed biliary stent
e. Following acute pancreatitis
f. Altered gastric or duodenal anatomy
g. Prior pancreatic surgery
h. Prior necrotizing pancreatitis

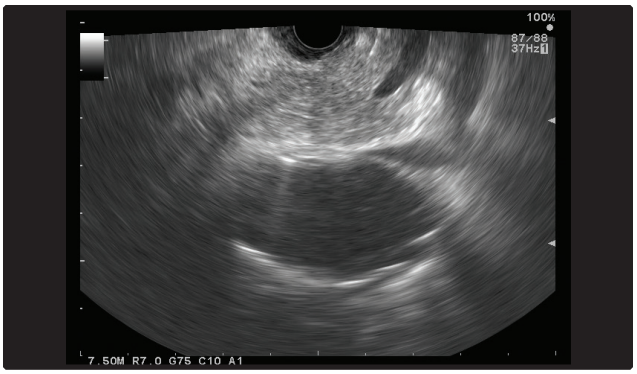

Figure 1. Jaundiced patient without mass on CT underwent EUS, showing no mass, but caliber change in the CBD and PD (shown here). FNA done (needle indicated by arrow) diagnostic for pancreatic adenocarcinoma.

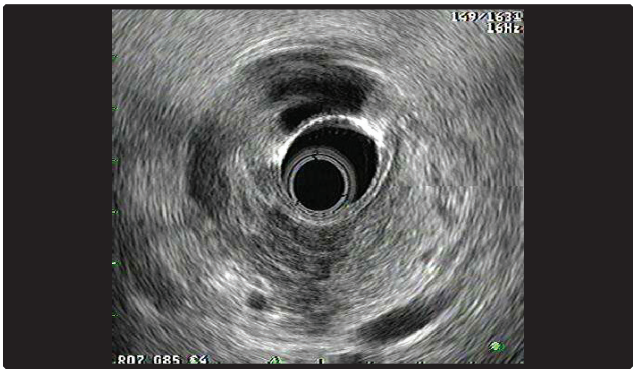

Figure 2a. Prominent dorsal-ventral pancreatic split interpreted on initial EUS to be normal uncinate.

Figure 2b. A CA 19-9 was sent on the same day as the first EUS and was elevated. Repeat EUS was done and this time, the uncinate was perceived to be more "mass-like". FNA confirmed pancreatic malignancy.

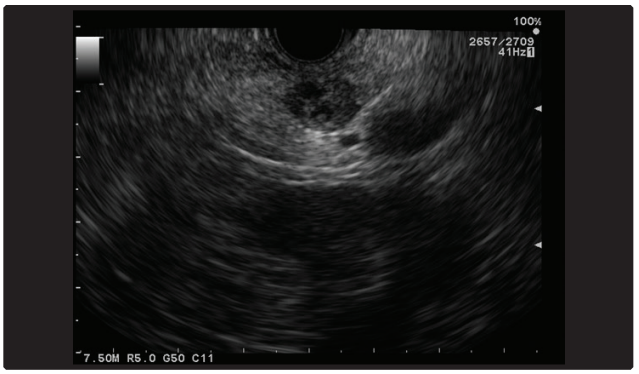

Figure 3a. Small neuroendocrine tumor (confirmed by FNA) found in the body/tail of the pancreas during EUS examination to work-up elevated serum chromogranin level.

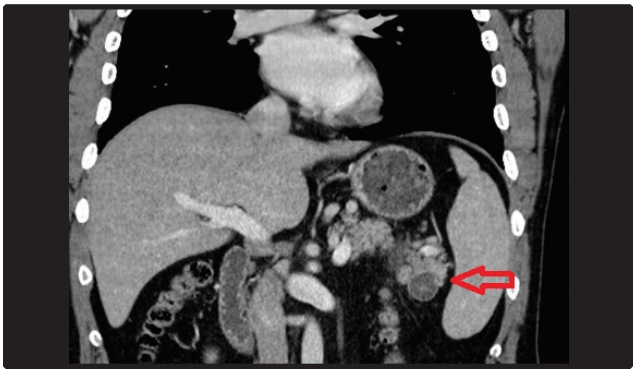

Figure 3b. CT done after the EUS showed an additional lesion in the far pancreatic tail.

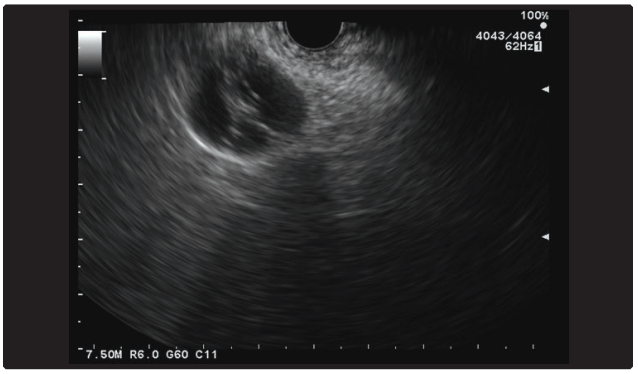

Figure 3c. Repeat EUS was done and FNA performed on the tail lesion. Subsequent pathology showed multifocal neuroendocrine carcinoma.

patients and recent acute pancreatitis in one patient.

We have encountered cases of "invisible" pancreatic masses, in which only a caliber change of the bile and/or pancreatic ducts was the sole clue to the presence of malignancy (Figure 1).[8] In other cases, the mass is "isoechoic" and subtle. An example of a patient with pancreatic adenocarcinoma that mimicked the usual difference in echogenicity seen between the dorsal and ventral anlagen in the uncinate process is shown in Figure 2. In this patient, the mass lesion was missed and the images were initially interpreted as showing a normal uncinate process.

Table 2. Endosonographer Related Factors in Suboptimal Endosonographic Examination

a. Operator inexperience
b. Narrow examination without attending to other important structures
c. Rushing

The "Hidden" Areas in Pancreatic Imaging

Given the relationship of the pancreas to the adjacent stomach and duodenum, the entire gland can be reproducibly imaged by EUS. However, the endosonographer must assure that the whole pancreas has, in fact, been imaged. While this sounds simple, in practice this can sometimes be hard to do and it can often be difficult to be sure that one has seen the entire pancreas.

The distal extremity of the pancreatic tail, often in very close approximation to the splenic hilum, can be easily overlooked or incompletely imaged, particularly if another finding has caught the eye (Figure 3). Even concerted attempts to evaluate the entire tail can result in an incomplete examination in some patients.

The pancreatic neck (near the region of the portal confluence) is an area that some feel is seen better with the linear echoendoscope[9] although data on this point is limited and it is wholly acceptable to view this area with a radial scope. When using a radial scope, some feel that this region may be better imaged by tracing the pancreas back from the pancreatic head, rather than pushing the scope forward from the pancreatic body towards the head of the pancreas.

The uncinate process may be hard or impossible to reach in some patients due to variations in gastric or duodenal anatomy, and, again, it can be difficult to ensure that the entire uncinate process has been seen. Inability to visualize all parts of the pancreas must be distinguished from reporting that "nothing abnormal was seen in the pancreas", even though these two disparate concepts seem similar.

Operator Dependent Factors in EUS Imaging

There are also endoscopist related factors that may factor into the quality of an EUS examination (Table 2). Operator experience is probably the most important one. The variation in EUS imaging from patient to patient and the wide range of anatomic locations that must be familiar to the endosonographer are unlike any other facet of advanced endoscopic practice. The endoscopist must maintain an organized approach to EUS imaging to prevent missing pathologic findings.

Doing a so-called "directed examination" i.e. performing EUS just to FNA a pancreatic mass that was identified on a pre-procedure CT scan without

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Figure 4a. Submucosal lesion seen in gastric body, referred for EUS characterization.

Figure 4b. EUS shows a small round lesion, arising from 4th hypoechoic layer (muscularis propria) consistent with stromal tumor.

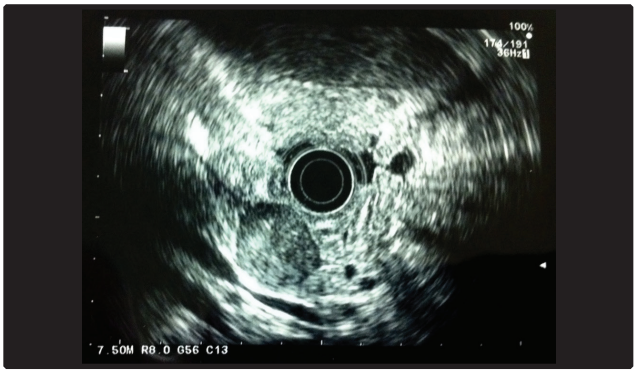

Figure 4c. While completing a screening examination with the radial echoendoscope, a second stromal lesion (larger than the first) is found.

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thoroughly evaluating the rest of the gland, may lead to missing important additional findings, such as liver metastases, the presence of ascites, malignant adenopathy, and other important pathology (Figures 4,5).

Competence and comfort in using both the radial and linear echoendoscope is vital to procedural success as one or both instruments may be required in a single patient. For example, the mediastinum is often easier to fully scan with the radial instrument than the linear, which requires careful, staged rotation to perform a complete exam (Figures 6,7). With experience, and the willingness to spend a little more time, a comprehensive examination can be conducted with the linear echoendoscope.

Endosonographer, (Attempt To) Know Thyself

In studying learning, social psychologists have identified factors that can influence perception of visual information. A person's motivational state in regards to their wishes and preference can influence their processing of visual stimuli.[10] Humans often "see what they want to see", despite clear objective findings. An example might be the endosonographer minimizing the findings on EUS because, for example, he doesn't "want the patient to have cancer", or has already concluded that the findings are not consistent with malignancy (Figure 8). An endosonographer who is overscheduled may also minimize a particular finding because of the additional time burden associated with performing a fine needle aspiration. Overscheduling can also lead to rushing or distraction that could result in a missed lesion.

Another psychological phenomenon that could influence the quality of an EUS examination is the so-called "Dunning-Kruger effect".[11] This describes a cognitive bias in which unskilled individuals mistakenly overestimate their abilities in a given field. Their very lack of skill leads them to fail to recognize that they lack skill, and tends to inflate their perception of their own competence. In another way of phrasing it, they "don't know what they don't know."

An EUS trainee who works with an expert that provides active proctoring (rather than passive teaching) may be less likely to fall victim to this effect. One example of active proctoring would be to help the student learn how to find relevant anatomy, and then the mass, which is the target of the examination, rather

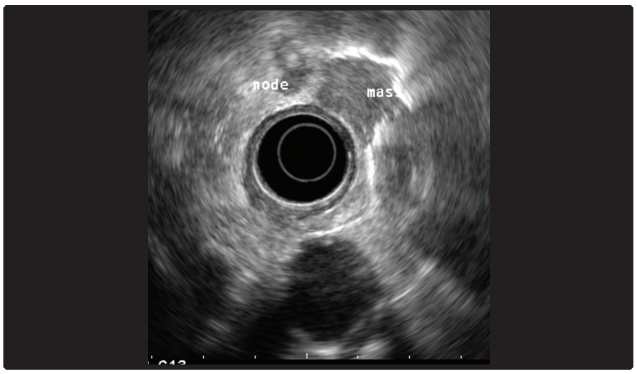

Figure 5. EUS was done to evaluate pancreatic cancer. Subsequent PET scan showed a tracer avid lesion in the mid esophagus; repeat EUS was required, which then identified a mediastinal periesophageal mass, which was overlooked on the previous EUS.

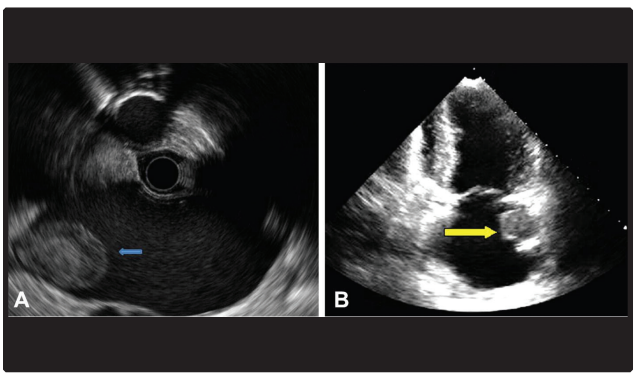

Figure 6. Incidental left atrial thrombus visualized on echoendoscope pull-out while doing EUS for pancreatic cystic lesion. Panel A: EUS image; Panel B: transesophageal echocardiographic (TEE) image.
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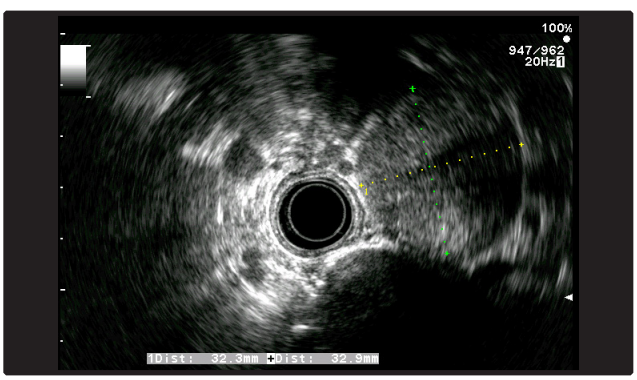

Figure 7. Incidental large thyroid mass visualized from the proximal esophagus while doing EUS staging of a small (T1b) esophageal cancer.

than just positioning the endoscope at a mass and then relinquishing the endoscope to the trainee so that he or she can perform the FNA. However, also according to the Dunning-Kruger effect, the expert who finds EUS "easy" may mistakenly assume that it must be "easy" for others and, in turn, may be a less effective teacher because of this.

Recognize When Imaging is Less Than Optimal

Document any limitations in your ability to conduct a complete examination. Some patients have gastric and/or duodenal anatomy makes it very challenging to position the echoendoscope properly in order to obtain adequate images. Obvious situations that can preclude complete EUS examination include gastric bypass surgery or anatomy after reconstructive surgery (Billroth I or II, pancreaticoduodenectomy, etc.). An asymptomatic mild post-bulbar stenosis may make it impossible to safely advance the echoendoscope to the deep duodenum. Gentle dilation of a post-bulbar duodenal stricture with a 14mm or 15mm TTS balloon can frequently make the difference in obtaining complete pancreatic imaging. We have also encountered cases in which initial deep duodenal intubation was achieved early in the examination, but subsequently could not be achieved. The reason for this phenomenon is unclear, but we suspect insufflated air in the stomach and proximal small bowel changes the orientation of the patient's anatomy in a dynamic way that makes repeated deep intubation difficult.

It is good to get into the habit of adequately documenting the EUS anatomy with endosonographic images, although no standard of care exists as to how many images should be obtained and exactly what structures must be photographed, and individual practice varies widely. Of note, some sites performing EUS do not have the ability to record EUS images and this should not be considered a violation of the standard of care either. With newer EUS consoles, there is the capability of transferring DICOM (digital imaging and communications in medicine) images to the hospital-wide PACS (picture archiving and communication system), and this has proven invaluable, for example, at multidisciplinary tumor board meetings.

Annotated photos illustrate what the endosonographer was seeing, because almost no one else is likely to be able to make definitive sense of the EUS images after the fact. Insufficient visualization is a reality of EUS, and should be appropriately documented.

Figure 8a. Pyloric channel ulcer; biopsy negative for malignancy.

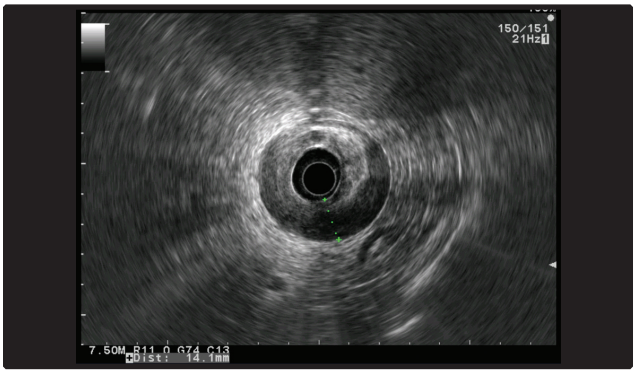

Figure 8b. EUS imaging shows concentric wall thickening. FNA of the wall not done.

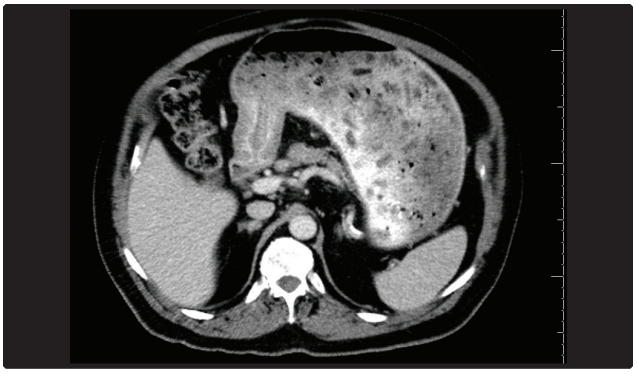

Figure 8c. CT appearance of pyloric channel showing wall thickening extending to antrum, and retained gastric contents, consistent with gastric outlet obstruction.

Recognize When Repeat or Complementary Imaging is Required

Further imaging may be necessary if adequate endosonographic imaging is impossible, felt to be incomplete or inadequate for any reason, or for any of the other reasons mentioned above (Figure 9). In some

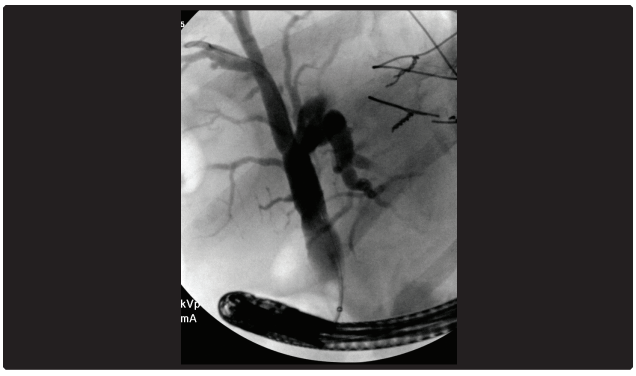

Figure 9a. A jaundiced patient underwent ERCP for CBD and gallbladder stones noted on MRI. Biliary dilation but no distinct stricture was noted. Stones extracted from CBD after biliary sphincterotomy.

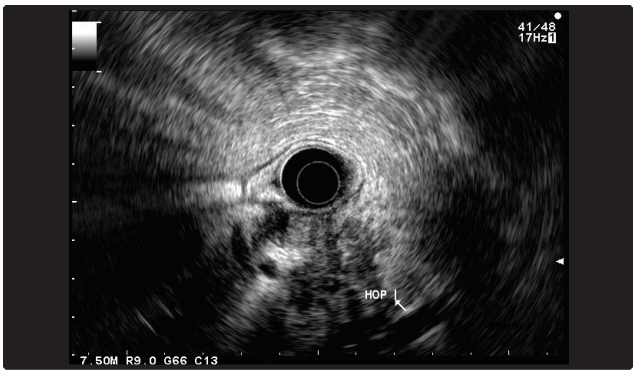

Figure 9b. Increase in LFTs 3 months later prompted EUS, revealing an uncinate mass, FNA positive for cancer.

cases, a repeat EUS will prove useful, for example, if initial FNA is negative but the index of suspicion is high for malignancy, repeat EUS FNA is generally warranted.[12] Complementary imaging with CT or MRI may also be a good option in some cases. A "cancer until proven otherwise" approach is prudent when one is an EUS specialist. One must realize that the patients referred for pancreatic EUS imaging will be part of a pool "enriched" for patients harboring pancreatic neoplasia, so a high index of suspicion is the best approach. This can apply to patients referred for a CT read simply as "fullness of the head of the pancreas", a slightly elevated CA 19-9, or even idiopathic acute pancreatitis. It is better to expect to find cancer than to be surprised by it.

CONCLUSION

Practitioners of endoscopic ultrasound never cease to be amazed at the ability of this modality to visualize and access structures in the chest, abdomen, and pelvis, and have a good sense as to when it will be helpful. One of our roles is to educate our colleagues on how EUS is an indispensable diagnostic modality, and is having a larger role in therapeutics as well. However, we must honestly confront the limitations of EUS in any given patient or anatomical situation, and recognize how to handle this. Those who understand the art of EUS realize that we have arrived here by "standing on the shoulders of giants", and we must lend a shoulder for those that follow us who want to learn endoscopic ultrasound. ■

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