Use of quantitative endoscopic ultrasound elastography for diagnosis of pancreatic neuroendocrine tumors

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A 63-year-old man with a history of chronic hepatitis C and lung cancer presented for further evaluation of a pancreatic mass found during imaging surveillance of a complex hepatic cyst. Magnetic resonance imaging (MRI) of the abdomen showed a 16 mm × 13 mm T2-weighted hypointense, arterially enhancing lesion within the distal pancreatic body [Figure 1]. Endoscopic ultrasound (EUS), using Pentax EG-3630U endoscope (Montvale, NJ, USA), illustrated a 14 mm × 16 mm well-circumscribed, hypoechoic, and homogeneous mass at the distal body of the pancreas with no communication to the main pancreatic duct or abutment of the surrounding vasculature [Figure 2]. Using EUS elastography, the mass demonstrated a diffuse homogenous blue pattern with an elastography color score of 5 [range: 1 (soft) to 5 (hard/solid)] [Figure 3]. Quantitative EUS elastography revealed a strain ratio (SR) of 16.17 [Figure 4]. Under EUS-guided fine-needle aspiration (EUS-FNA), four samples of the mass were obtained using a 25-gauge needle. Cytopathology identified a well-differentiated neuroendocrine tumor [Figure 5], with Ki-67 proliferative index <2% [Figure 6]. Immunohistochemistry identified positive CAM5.2, synaptophysin [Figure 7], chromogranin A [Figure 8], and was focally positive cytokeratin 7 (CK7). Stains were negative for Caudal Type Homeobox 2, CK20, and thyroid transcription factor-1 (TTF-1). Cytopathology and immunohistochemistry were diagnostic of pancreatic neuroendocrine tumor (PNET). Distal pancreatectomy was recommended as a treatment option.

PNETs are rare pancreatic neoplasms comprising 1%-2% of all pancreatic tumors with an annual incidence rate of 1-5 cases per million in the United States. They have indolent clinical course and better overall prognosis.[1] EUS provides high-resolution images of the entire pancreatic parenchyma and the ductal system. Compared to computed tomography (CT), MRI, and somatostatin receptor scintigraphy (SRS), EUS is considered the most accurate modality for the diagnosis and staging of solid and cystic pancreatic lesions as small as 2-5 mm.[2] However, differential diagnosis of pancreatic lesions remain a challenge without the use of FNA. A recent meta-analysis of 13 studies (N = 456) showed a high pooled sensitivity (87.2%) and specificity (98.0%) using EUS to detect

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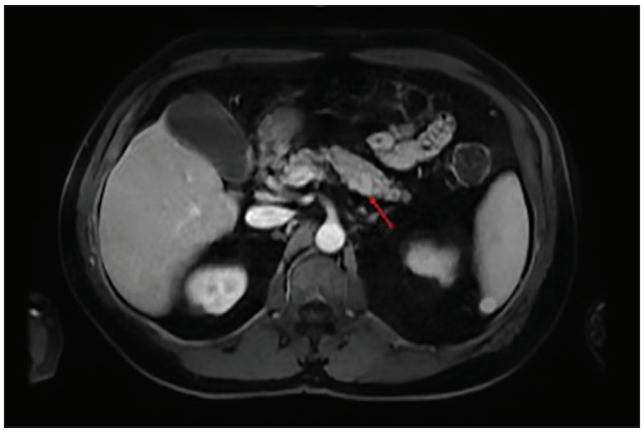

Figure 1. MRI (cross-sectional view) (arrow) showing T2-weighted hypointense lesion within the pancreatic body

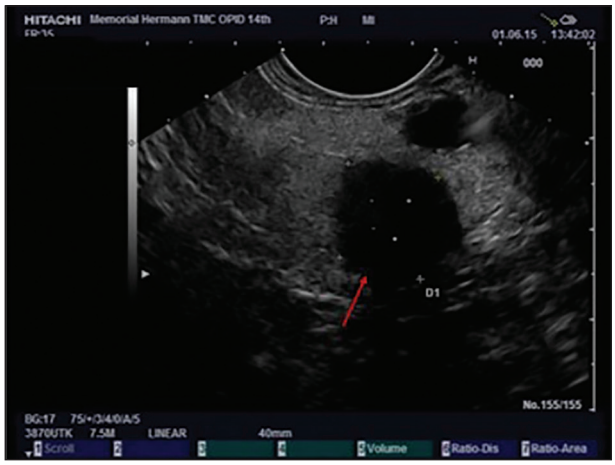

Figure 2. EUS (arrow) showing well-circumscribed, hypoechoic, and homogeneous pancreatic body mass

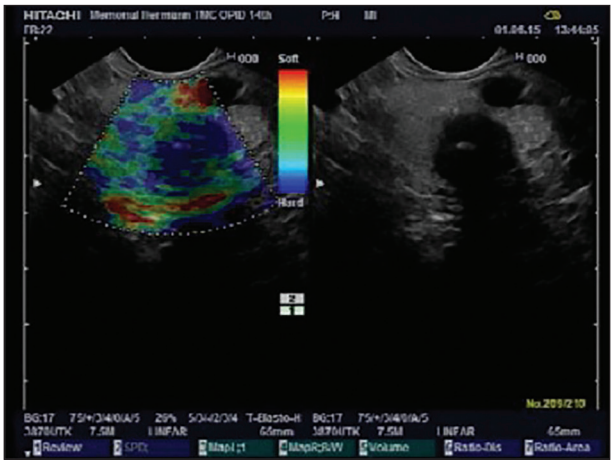

Figure 3. Qualitative EUS elastography showing blue hue (hard), with an elastography color score of 5

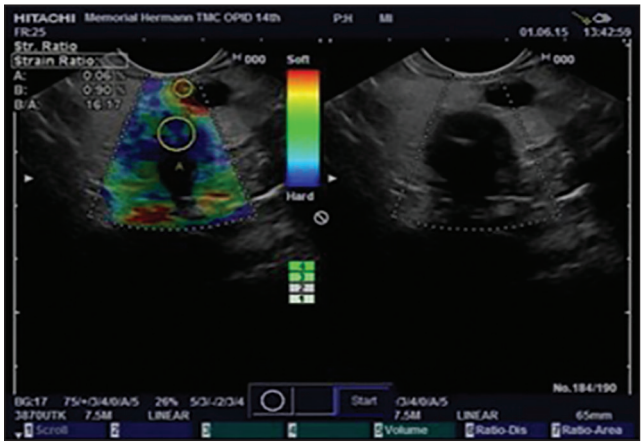

Figure 4. Quantitative EUS elastography showing a strain ratio of 16.17

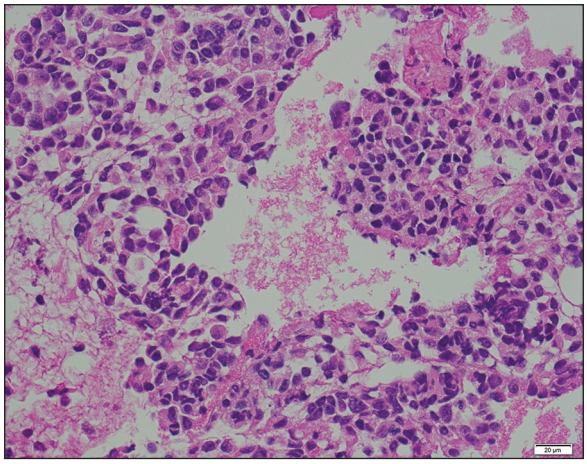

Figure 5. H&E staining showing well-differentiated neuroendocrine tumor

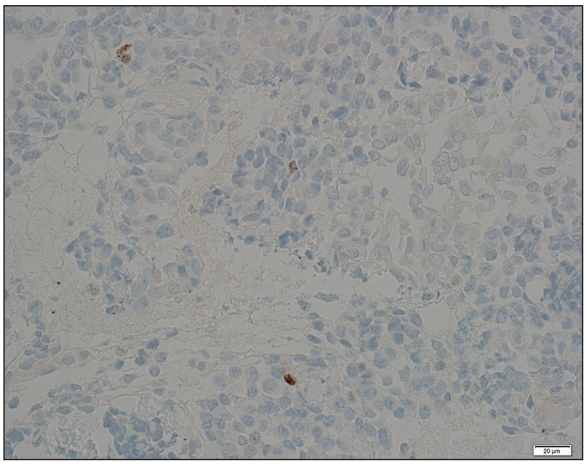

Figure 6. Immunohistochemistry showing low Ki-67 proliferative index

PNETs.[3] EUS can guide FNA of pancreatic lesions for cytological evaluation. However, EUS-FNA is a time-consuming and technically demanding procedure that requires several needle passes to obtain adequate tissue for histopathological evaluation. Also, the sensitivity of cytology for malignancy is limited with false negative results seen in up to 20%-40% of the cases.[4] Real-time differentiation of benign from malignant pancreatic lesions can be aided with the use of EUS elastography.

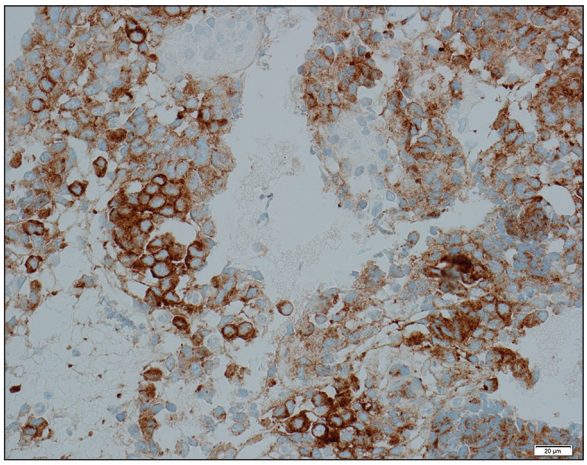

Figure 7. Immunohistochemistry showing positivity for synaptophysin

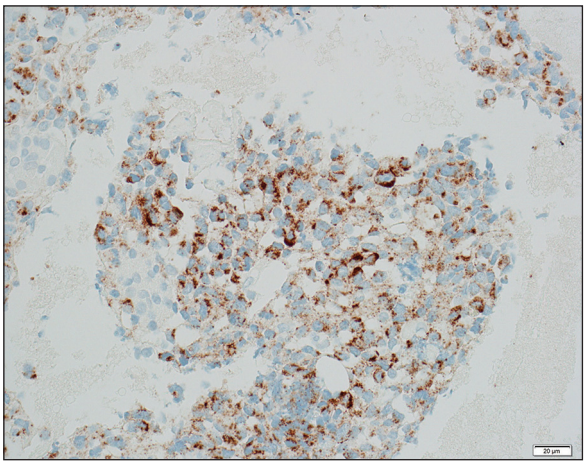

Figure 8. Immunohistochemistry showing positivity for chromogranin A

This novel technology evaluates elasticity or firmness of a given tissue relative to that of adjacent normal tissue. Elastographic assessment of the tissue can be performed either qualitatively or quantitatively. Qualitative elastographic assessment is mainly based on the predominant color seen (red: Soft; green to yellow: Intermediate; and blue: Hard) and on the homogeneity or heterogeneity of color distribution. The major limitation of qualitative assessment is the subjective analysis of elastographic pattern. A meta-analysis of qualitative EUS elastography for the diagnosis of solid pancreatic masses, by Mei *et al.*[5] involving 1,044 patients, showed a high sensitivity of 95% and an acceptable low specificity of 67%.

In contrast, quantitative elastography provides an objective measurement of tissue hardness by calculating the SR, with higher SR representing less elasticity. In a number of studies, the utility of quantitative EUS elastography has been studied not only for differentiation of benign and malignant pancreatic lesions but also for its differential diagnosis.[6,7] A study by Iglesias García *et al.*[7] reported a sensitivity of 100% and specificity of 88% for the use of quantitative elastography in differentiating pancreatic adenocarcinoma from PNETs when the cutoff value of SR was 26.6. Overall, the sensitivity and specificity to differentiate benign from malignant lesions was 93% and 86%, respectively, when the cutoff for SR was 6.0. In comparison, a study by Havre *et al.*[8] showed a sensitivity of 67% and specificity of 71%, when using a SR of 4.4 as a cutoff for malignancy. In our case both qualitative and quantitative elastography data were suggestive of PNETs; however, the SR value was relatively low (16.17) compared to a cutoff value of 26.6 was noted earlier.

In conclusion, qualitative and quantitative EUS elastography can be a valuable supplement of real-time analysis to differentiate benign from malignant tissue in adjunct to performing EUS-FNA. Quantitative EUS elastography not only help to differentiate benign and malignant pancreatic lesions but can also be helpful to differentiate different pancreatic lesions. Guidelines by the European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB)[9] state that at the present time EUS elastography cannot replace cytopathological diagnosis of pancreatic lesions; however suspicious findings on elastography can guide further clinical decisions if FNA is negative. Further studies using quantitative EUS elastography are needed to better define its utilization in the diagnostic workup of PNETs.

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Conflicts of interest

There are no conflicts of interest.

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