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LETTER TO THE EDITOR

Letter to the Editor: Intrapancreatic Accessory Spleen Masquerading as a Pancreatic Neuroendocrine Tumor

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We read with interest the case study by Chan et al. entitled "Intrapancreatic Accessory Spleen Masquerading as a Pancreatic Neuroendocrine Tumor." The authors present a case of a 27-mm pancreatic tail lesion diagnosed as a functional pancreatic neuroendocrine tumor (pNET) that was determined on pathological analysis following resection to be an intrapancreatic splenule. The patient had normal blood tests. Pancreas magnetic resonance imaging (MRI) was suspicious for pNET, a DOTATATE PET scan suggested a well-differentiated pNET, and an endoscopic ultrasound revealed a well-circumscribed mass in the tail of the pancreas, which was not amenable to biopsy.

Cases such as the one the authors described present an important diagnostic problem. As the authors discuss, splenules are relatively common and can have an intrapancreatic location.[1] Differentiating pNETs from intrapancreatic splenules is particularly challenging as they both appear as arterial phase enhancing lesions on dynamic contrast-enhanced MRI and CT. Further, splenic tissue has normal physiologic uptake of octreotide analogues and is PET-avid.[2,3]

The authors elegantly reviewed the benefit of technetium-99 m heat-damaged red blood cell scan (Tc-99 m HDRBC) to assist in diagnostic differentiation of pNETs and intrapancreatic splenules. Unfortunately, the authors did not have this imaging method available at their institution. It should be noted, as the authors mentioned, that for small (< 20 mm) lesions, Tc-99 m HDRBC scans have been shown to have low sensitivity.[3,4] Importantly, a large proportion of intrapancreatic splenules and pNET lesions are smaller than this threshold.[5]

In order to address this clinical dilemma, we would like to describe our use of ferumoxytol enhanced MRI for the differentiation of intrapancreatic splenules from pNETs. Ferumoxytol (Feraheme, AMAG, Waltham, MA) is an ultrasmall superparamagnetic iron oxide particle (USPIO) that is currently approved by the US Food and Drug Administration as an intravenous treatment for iron deficiency anemia in patient with chronic kidney disease.[6] With a long half-life and accumulation in the blood pool, ferumoxytol has been recognized as a useful contrast agent, and there is revived interest in its off-label use as an MRI contrast agent.[7–10] Additionally, ferumoxytol is phagocytosed by macrophages over a 2–3 day time period, leading to its accumulation in the mononuclear phagocyte system (MPS) of the spleen, liver, and bone marrow with associated negative enhancement (i.e., hypointensity) on T2-weighted MRI.[3,7] Superparamagnetic iron oxide particle (SPIO) agents, ferumoxides, have specifically been reported to help differentiate splenules from other pancreatic lesions.[11] In a similar way, the behavior of ferumoxytol offers a unique opportunity to differentiate splenules from pNET with high spatial resolution compared to Tc-99 m scintigraphy.

At our institution, we have implemented a novel MR protocol with ferumoxytol administration and delayed imaging for detection of intrapancreatic splenules. Specifically, we administer 3 mg/kg of diluted ferumoxytol over 15 min[8] and obtain multiplanar T2-weighted single shot and conventional fast spin echo (FSE) imaging, axial 3D R2*mapping (IDEAL IQ, GE Healthcare, Waukesha, WI) and axial T1-weighted imaging with fat suppression. After 24–72 h, the MRI sequences are repeated, and T2 signal intensity is measured for the intrapancreatic lesion of interest and the spleen. Imaging can be performed at 1.5 T or 3 T. In our experience, the

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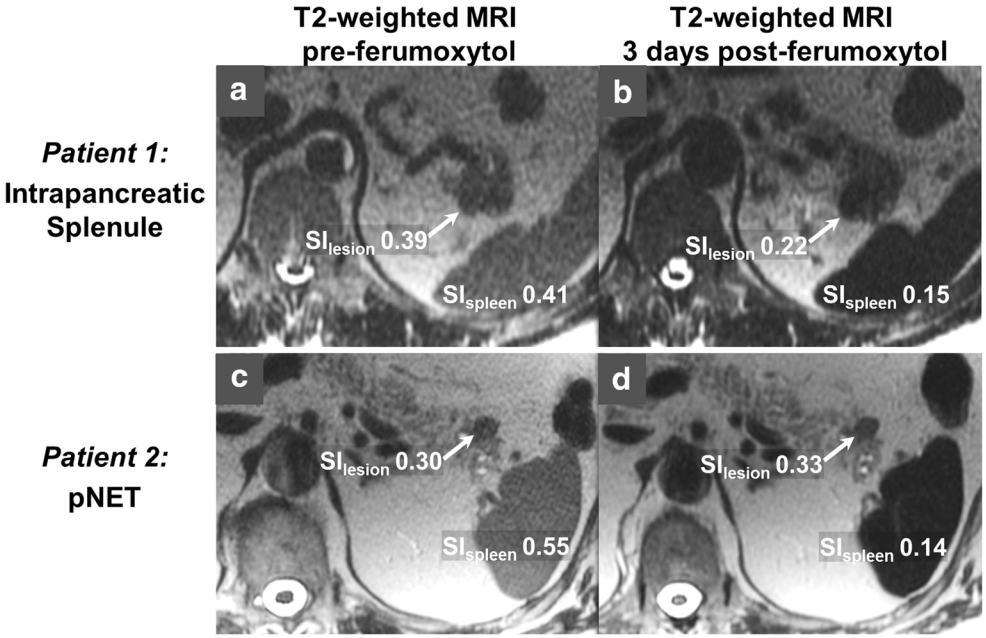

Fig. 1 Differentiation of intrapancreatic splenule from pancreatic neuroendocrine tumor (pNET) using delayed ferumoxytol-enhanced MRI. Both patients whose images are displayed here were found to have intrapancreatic hyperintense lesions on arterial phase contrast-enhanced CT imaging. An MRI was then performed on the day of ferumoxytol administration (**a**, **c**) and after 24–72 h as a delayed image (**b**, **d**). Due to the ferumoxytol uptake in the splenic mononuclear phagocyte system, splenules and the spleen display negative enhancement (i.e., decreased signal intensity (SI)) on delayed T2-weighted MRI (**b**). In contrast, pNETs will not demonstrate negative enhancement on delayed T2 imaging (**d**), enabling differentiation of these two lesions. In the figure above, the intrapancreatic lesion of interest in each study is denoted with a white arrow. The SI values of the lesion and spleen above were measured on axial T2 SSFSE and normalized by SI of fat

negative enhancement demonstrated on delayed T2-weighted imaging 24–72 h after ferumoxytol administration by the spleen and splenules is helpful to confirm the diagnosis of intrapancreatic splenule with superior spatial resolution compared to scintigraphy (Fig. 1).

In conclusion, fermuoxytol-enhanced MRI may be an alternative approach for characterization of intrapancreatic splenules, by exploiting the delayed uptake of ferumoxytol into splenic MPS that is not present in pNETs. Although the physiologic rationale for this strategy is strong, additional investigation into the clinical performance of this method is needed.

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Author's Contributions ERW and SBR conceived of this letter to the editor. VRR composed the letter and, along with MRM, acquired and synthesized contributing references and prepared the figure. All authors revised the manuscript and gave final approval of the version to be published.

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