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Intrapancreatic Accessory Spleen: Possibilities of Computed Tomography in Differentiation From Nonfunctioning Pancreatic Neuroendocrine Tumor

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Abstract

Objective—The aim of this study was to evaluate the ability of computed tomography (CT) in differentiating between intrapancreatic accessory spleen (IPAS) from pancreatic neuroendocrine tumor (PanNET).

Methods—Eight IPASs and 12 PanNETs in the pancreatic tail were retrospectively evaluated by 2 radiologists. Readers assigned a diagnosis to each examination and evaluated for the presence or absence of 9 CT findings that may aid in the diagnosis.

Results—Reader 1 had a sensitivity of 0.83 and a specificity of 1; reader 2 had a sensitivity of 0.78 and a specificity of 0.86. Three of the 9 CT findings were found to be statistically significant in IPASs: the lesion present along the pancreatic dorsal surface, the lesion demonstrating the same enhancement as the spleen on venous phase, and heterogeneous enhancement during arterial phase.

Conclusions—CT can be used to differentiate between IPAS and PanNET with good specificity and sensitivity. The IPAS mirrors the spleen's enhancement and is usually located along the dorsal surface of the pancreas.

Keywords

intrapancreatic accessory spleen; pancreatic neuroendocrine tumor; pancreatic mass

Differentiating an intrapancreatic accessory spleens (IPASs) from a pancreatic neuroendocrine tumors (PanNETs) in the tail of the pancreas can prove to be quite a diagnostic dilemma on computed tomography (CT). The management of these 2 entities is

quite different: most neuroendocrine tumors are treated with surgery and/or chemotherapy, whereas the IPAS does not require treatment.

With increasing use of CT, IPASs are more commonly being detected on imaging studies. Furthermore, recent studies have shown that, because of advances in CT, increasing numbers of nonfunctioning PanNETs are being detected when they are small.¹ As many of these lesions are found incidentally on CT, correct diagnosis between these 2 entities is important. Although other modalities are helpful in making this distinction such as magnetic resonance imaging (MRI) or nuclear medicine imaging, as CT is usually the first modality that identifies these lesions, the purposes of this study are to evaluate the usefulness of CT in differentiating these 2 lesions and to define possible criteria for CT diagnosis of IPAS.

MATERIALS AND METHODS

Subjects

This retrospective study was approved by our institutional review board with waiver of informed consent and Health Insurance Portability and Accountability Act authorization.

The CT examinations from 8 patients with an IPAS were used. These cases were encountered during clinical evaluation of suspected pancreatic mass from December 2005 to December 2010. All but 2 cases were pathologically proven. The other two were confirmed by liver spleen nuclear imaging.

The PanNET control cohort consisted of 12 consecutive patients who had nonfunctioning neuroendocrine tumors diagnosed at our institution during the same period and confirmed by pathologic examination (distal/partial pancreatectomy). All patients had preoperative CT reports describing the lesion as a solid mass within the tail of the pancreas. On the basis of the findings of the preoperative CT, controls were matched to patients with IPASs by the size of the tumor on CT (please refer to Table 1 for the summary of subjects).

CT Technique

The CT examinations were performed on multidetector CT scanners including a Siemens Sensation 16 scanner and 64 scanner (Siemens Medical Solutions, Malvern, PA). Detector collimation settings of 16×0.75 mm or 64×0.6 mm were used. The data were reconstructed at 0.75-mm slice thickness at 0.5-mm intervals for multiplanar reformation imaging. For diagnostic reading, 3- or 5-mm slice thickness and 3- or 5-mm reconstruction intervals were used. Parameters of above scanning included 120 kV and 150 to 200 mAs.

For dedicated evaluation of the pancreas, after fasting for 2 to 3 hours, each patient ingested 750 to 1000 mL of water. Typically, 500 to 750 mL of water was administered 20 to 30 minutes before the study, and an additional 250 mL of water was administered immediately before the study. One hundred to 120 mL of iohexol (Omnipaque 350; GE Healthcare, Princeton, NJ) was injected through a peripheral venous line at 3 to 4 mL/s. Dual-phase imaging at 25 seconds for arterial phase and 55 to 60 seconds for early portal venous phase from the start of injection of intravenous contrast material was obtained.

All but two of the CTs provided for interpretation were 2 phase examinations (arterial and venous phase imaging), as described above. One patient with IPAS and 1 patient with neuroendocrine tumor had CTs that were performed with a single phase (venous phase).

Image Interpretation

On the basis of review of other published articles regarding IPASs,²⁻⁸ a list of 9 CT findings that have the potential of differentiating an IPAS from PanNET were compiled into a questionnaire (Table 2).

The CT readers were provided with a set of anonymized cases from the 20 total patients (both cohorts). The CT readers were 2 attending abdominal imaging radiologists with fellowship training in body imaging. One had been a faculty member for 4 years; the other, 7 years. The readers were blinded to the patient demographics as well as the clinical and histopathologic findings.

Each reader was instructed to provide a diagnosis on a 1-to-5 scale, with 5 as most likely PanNET and 1 as most likely IPAS, with the numbers in between denoting varying degrees of reader confidence in their chosen diagnosis. A diagnosis of 3 was equivalent to an indeterminate diagnosis. In addition, the readers were given the 9-item questionnaire regarding the presence or absence of a particular CT finding within the case (Table 2). Each reader was aware that these CT findings were suggestive of an IPAS based on published articles.

Statistical Analysis

The sensitivity and specificity of each reader's assessments were calculated using the true pathological result as the gold standard. Reader scores of 1 to 2 were grouped together as a "negative" result, and 4 to 5 were grouped together as "positive." A diagnosis of 3 on the 1-to-5 scale represented an indeterminate reading of the CT, so sensitivity and specificity were calculated twice: once excluding these scores and once including them with the 4 to 5 scores as "positive" assessments. Then, 95% confidence intervals for sensitivity and specificity were calculated using an exact binomial distribution. To compare the agreement of the 2 readers' assessments of the same CT, a Cohen kappa statistic was calculated. For each item on the 9-item questionnaire, the proportion of patients for whom the readers denoted the presence of a CT finding was compared between those with an IPAS versus a PanNET using Fisher's exact test.

Two patients contributed data from single phase examinations. To ensure that these 2 observations did not contribute uncertainty to the main results, a sensitivity analysis was performed.

RESULTS

The IPAS cohort consisted of 6 men and 2 women, with a mean age of 66 years and an age range of 27 to 81 years. The mean size of the lesions on CT was 2.7 cm, with a range of 1.1 to 4.3 cm. The PanNET cohort consisted of 6 men and 6 women with a mean age of 64 years

and an age range of 52 to 75 years. The mean size of the lesions on CT was 2.1 cm, with a range of 0.9 to 4.8 cm.

Five (13%) of the 40 diagnoses were indeterminate; of those, 3 or 60% were ultimately PanNETs.

Table 3 summarizes the sensitivity and specificity of each reader's assessment, first excluding indeterminate responses and then including indeterminate responses in the pathological group.

Excluding indeterminate diagnoses, the 2 readers agreed on 93% of the CT determinations (Cohen kappa = 0.87). When indeterminate diagnoses were included in the calculation, percent agreement dropped to 85% (Cohen kappa = 0.69).

Table 4 summarizes the answers to the 9 questionnaire items for each reader. All IPASs in our series were located at the tip or within 3 cm in the tip of the tail of the pancreas. Interestingly, all our cases of, not in IPAS were not completely embedded in the pancreatic parenchyma and therefore were exposed to the peripancreatic fat, often located along the dorsal surface of the pancreas. Heterogeneous enhancement of the lesion during arterial phase was seen in approximately 60% of IPASs but was also seen in a small number of neuroendocrine tumors. The lesion was considered homogeneously enhancing during venous phase in all cases of IPAS by 1 reader and 88% by the second reader, but this finding was also observed in most neuroendocrine tumors. The same degree of enhancement as the spleen during the arterial and venous phases was seen in most of the IPASs but was also observed in some of the neuroendocrine tumors. Splenic vein involvement was seen in 1 case of neuroendocrine tumor by 1 reader, but this finding was not observed in any of the IPASs.

Among the 9 findings listed in the questionnaire, 3 findings were found to be significantly different when the IPASs were compared with neuroendocrine tumors: when not completely embedded in the pancreatic parenchyma, the lesion is located along the dorsal surface of the pancreas (reader 1), the lesion shows heterogeneous enhancement at arterial phase (reader 1), and the lesion shows the same degree of enhancement as the spleen at venous phase (reader 2).

To determine the effect of the 2 single phase examinations on the study's sensitivity and specificity, sensitivity analysis was performed, which showed no significant change in the results. Therefore, the results discussed in this article included these 2 examinations.

DISCUSSION

In combination with the 9-point questionnaire included in this study, CT can be used to differentiate between IPASs and PanNETs with high specificity and sensitivity. In our study, in cases where the reader was unsure of the diagnosis, most of the cases deemed indeterminate were ultimately proven to be PanNETs. Placing indeterminate diagnoses in the more likely to be PanNET category slightly improved sensitivity while slightly decreasing specificity in reader 2 and decreased specificity in reader 1. Given that treating

indeterminate diagnoses as malignant decreased specificity in both readers, further imaging with nuclear medicine imaging or MRI should be performed in these cases. Two specific MR imaging techniques have been shown to be helpful in making this distinction. A specific type of MRI contrast media, in the form of superparamagnetic iron oxide particles, is taken up by the reticuloendothelial system structures (liver, spleen, lymph nodes, etc.), and uptake will be seen in the IPAS.⁹ Diffusion weighted imaging has also been shown to differentiate between IPAS and small solid pancreatic tumors,¹⁰ with the IPAS demonstrating lower signal intensity values on diffusion weighted imaging compared with solid pancreatic tumors. When further imaging is unable to provide a diagnosis, pathologic confirmation can be performed with fine needle aspiration via endoscopic ultrasound.¹¹

Among the 8 cases of IPAS in this study, diagnosis was made by distal/partial pancreatectomy, and histological examination by surgical specimen was done in 6 cases. Most of these surgical cases were performed early in our experience with this entity. Although IPAS was considered as a differential diagnosis in most cases based on CT, we were unable to confirm preoperative diagnosis, and further evaluation was not confirmatory: false negative nuclear medicine scintigraphy or nondiagnostic endoscopic ultrasound biopsy. One IPAS was excised because of its size (4.1 cm) and associated small bowel intussusception, which suggested a more malignant pathology.

The 9-point questionnaire included CT findings that radiologists may associate with IPASs. The criteria that were found to be of highest association were those that used the unique enhancement pattern of the spleen during the arterial and venous phases applied to the lesion in question. Figure 1 shows the typical appearance of an IPAS on the arterial and venous phases, matching the enhancement of spleen. The location of the lesion along the dorsal surface of the pancreas when not completely embedded in the pancreatic parenchyma was also found to be associated with IPASs.

Although not statistically significant, several other findings are also helpful to differentiate IPASs from neuroendocrine tumors. All IPASs in this study were located at the tip or within 3 cm of the tip of the tail of the pancreas. Therefore, if an enhancing mass is seen more than several centimeters from the tip of the tail of the pancreas, it is less likely to represent IPAS and more likely a neuroendocrine tumor. Others have also reported on the typical location of an IPAS near the tip of the tail of the pancreas.^{9,12–16} Involvement of the splenic vein has been seen with neuroendocrine tumor, but not with IPAS. Balachandran et al⁸ in 2012 reported venous narrowing or occlusion in 31 of 88 patients with neuroendocrine tumor, 21 of those involving the splenic vein. In our series, one of the PanNETs had splenic vein occlusion, which was recognized by one of the readers. This case is shown in Figure 2. This lack of recognition in addition to the small percentage of cases involved showing this pathology most likely contributed to the lack of statistical significance that was found for this particular finding.

Limitations in the study included a small pool of cases evaluated, which ultimately affected the precision with which sensitivity and specificity could be estimated. The CT reader questionnaire was created based on published articles and may have influenced the reader when making their diagnosis for each case. Although including the questionnaire into the

decision-making process may have introduced bias into the study and affected the true sensitivity and specificity of CT in differentiating between IPASs and PanNETs, it should be noted that many radiologists routinely use internal checklists during their image interpretation.

The observation that an IPAS tends to be incompletely embedded in the pancreatic parenchyma, often exposed to peripancreatic fat and located along the dorsal surface of the pancreas, has been observed previously although not adequately studied.² The statistical significance of this finding based on our small number of cases suggests that it should be confirmed in a larger cohort. According to a study by Mortelet et al,¹⁷ where accessory spleens on CT were evaluated in 1000 patients, accessory spleens were found most commonly at the inferior third of the posteromedial portion of the splenic hilum, which is adjacent (lateral, posterior, and superior) to the tail of the pancreas; this observation may simply reflect the common location of an accessory spleen. It is also possible that an IPAS that is completely embedded by the pancreatic parenchyma is likely small in size and may be difficult to detect by CT. Further accumulation of cases is necessary to determine the adequacy of this criterion for the diagnosis of IPAS.

In conclusion, CT can be used to differentiate between IPASs and PanNETs with a high degree of sensitivity and specificity. Specific findings on CT are more prevalent with IPASs and can help increase diagnostic confidence. These findings include a lesion that is not completely embedded in the pancreatic parenchyma, a lesion that is located along the dorsal surface of the pancreas, a lesion that shows heterogeneous enhancement at the arterial phase, and a lesion that has the same degree of enhancement of the spleen at the venous phase. The reader should look for enhancement of the IPAS matching the enhancement pattern of the spleen on multiphase CT examination. Furthermore, routine evaluation of the splenic vein should be performed with each lesion as occlusion of the vein has been associated with nonfunctioning PanNETs. In cases where the reader finds the lesion as indeterminate, although most were ultimately PanNETs in our study, given the associated decline in overall reader specificity seen in our study, the CT reader should recommend confirmatory testing such as 99mTc-labeled heat-damaged red blood cell scintigraphy or MRI rather than an observation with fine needle aspiration as needed for confirmation.

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FIGURE 1.

An 81-year-old woman with IPAS (arrow) showing heterogeneous enhancement similar to the spleen on arterial phase (A) and then more homogeneous enhancement similar to the spleen on venous phase (B). Note that the lesion enhances the same as the spleen on the arterial and venous phases.

FIGURE 2.

A 62-year-old woman with PanNET. Homogeneously enhancing lesion within the tail of the pancreas on venous phase (A). Note the associated gastric varices present, related to splenic vein occlusion (B). Both readers gave a diagnosis of IPAS, but this was a pathologically proven nonhyperfunctioning neuroendocrine tumor. Splenic vein occlusion can be seen with PanNET.

TABLE 1

Descriptive Summary of Patients

	IPAS	PanNET
No. (%) cases	8 (40)	12 (60)
Mean age (range) in years	66 (27–81)	64 (52–75)
Gender	6 males, 2 females	6 males, 6 females
Mean size (range) in cm	2.7 (1.1–4.3)	2.1 (0.9–4.8)

TABLE 2

Nine-Item Questionnaire Answered by Readers During the Evaluation of Each Case

Q1: Lesion at the tip or within 3 cm of the tip of the pancreatic tail? ³
Q2: Lesion not completely embedded/exposed to peripancreatic fat? ^{2,7}
Q3: If exposed to fat, located along the dorsal surface of the pancreas? ²
Q4: Lesion enhances heterogeneously during arterial phase? ^{4,5}
Q5: Lesion enhances homogeneously during venous phase? ⁴⁻⁶
Q6: Same degree of enhancement as the spleen during arterial phase? ⁴⁻⁶
Q7: Same degree of enhancement as the spleen during venous phase? ⁴⁻⁶
Q8: Does the lesion have a well-defined border? ³
Q9: Absence of involvement of the splenic vein? ⁸

TABLE 3

Sensitivity and Specificity of the CT Reader Assessments, Excluding and Including Indeterminate Responses

	Reader 1		Reader 2	
	1-2 vs 4-5	1-2 vs 3-5	1-2 vs 4-5	1-2 vs 3-5
Sensitivity [95% CI]	0.83 [0.52, 0.98]	0.83 [0.52, 0.98]	0.78 [0.40, 0.97]	0.83 [0.52, 0.98]
Specificity [95% CI]	1 [0.59, 1]	0.88 [0.47, 1]	0.86 [0.42, 1]	0.75 [0.35, 0.97]

1-2, IPAS given as diagnosis; 3, indeterminate given as diagnosis; 4-5, PanNET given as diagnosis.

TABLE 4

List of 9 Questionnaire Items, With Description of Answers by Reader

Questions	Reader 1			Reader 2		
	IPAS (N = 8), Yes, n (%)	PanNET (N = 12), Yes, n (%)	P	IPAS (N = 8), Yes, n (%)	PanNET (N = 12), Yes, n (%)	P
Q1	8 (100)	9 (75)	0.242	8 (100)	9 (75)	0.242
Q2	8 (100)	9 (75)	0.242	8 (100)	11 (92)	>0.99
Q3	7 (88)	1 (8)	<0.001	6 (75)	3 (25)	0.065
Q4	4 (57)	1 (9)	0.047	4 (57)	4 (36)	0.63
Q5	8 (100)	9 (75)	0.242	7 (88)	10 (83)	>0.99
Q6	7 (100)	6 (55)	0.101	6 (86)	4 (36)	0.066
Q7	8 (100)	7 (58)	0.055	7 (88)	3 (25)	0.02
Q8	8 (100)	11 (92)	>0.99	7 (88)	7 (58)	0.325
Q9	8 (100)	11 (92)	>0.99	8 (100)	12 (100)	

Values are the number and proportion of patients for whom the reader answered yes, stratified by the true path diagnosis (IPAS or PanNET). *P* values for Fisher's exact test for differences in the proportion of positive responses by the true diagnosis.