Solid pseudopapillary carcinoma of the pancreas: differentiation from benign solid pseudopapillary tumour using CT and MRI

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AIM: To describe the computed tomography (CT) and magnetic resonance imaging (MRI) findings that differentiate solid pseudopapillary carcinomas (SPC) from benign solid pseudopapillary tumours (SPT) of the pancreas.

MATERIALS AND METHODS: Preoperative CT or MRI images for 26 patients (eight patients with SPC and 18 patients with SPT) were retrospectively reviewed. In addition to the general morphological features, the presence of pancreatic duct dilation, vascular invasion, and extrapancreatic metastases were comparatively assessed.

RESULTS: There were no significant differences between pancreatic SPC and benign SPT with respect to tumour size, location, capsule thickness, internal composition, and pattern of calcification, nor was there any correlation with the age and gender of the patients. Pancreatic duct dilation was present in four of the eight (50%) SPC patients, and was absent in all benign SPT patients (p = 0.005). Vascular encasement by the tumour (n = 2) and hepatic metastases (n = 2) were also exclusively demonstrated in SPC patients. Multivariate logistic regression analysis showed that pancreatic duct dilation (p = 0.001), vessel encasement (p = 0.027), and metastasis (p = 0.027) were the variables that can be used to differentiate SPC from benign SPT.

CONCLUSION: SPC of the pancreas may help to differentiate from benign SPT using the imaging features of aggressive behaviour of pancreatic duct dilation and vessel encasement with or without extrapancreatic metastases.

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Introduction

Solid pseudopapillary tumour (SPTs) of the pancreas are rare neoplasms with distinctive histological features and low-grade malignant potential, which mainly occur in women in the second to fourth decades of life.1e3 The characteristic histological features that distinguish SPT from other neoplasms of the pancreas include a combination of solid and cystic components with gradual degenerative changes culminating in pseudopapilla formation.1 Most reported cases of SPT are known to be benign; however, malignant behaviour does occur in 10—15% of cases.1,2,4e7 Unequivocal perineural invasion, angioinvasion, deep invasion into the surrounding tissue, or metastasis indicates malignant behaviour of SPTs.8 According to the 2000 World Health Organization (WHO) classification system, these lesions should be classified as solid pseudopapillary carcinomas (SPC) in order to differentiate them from benign SPT.8,9

Although most SPTs have an excellent prognosis after curative resection, local recurrence or metastases may occasionally develop with...
a latency of several years and rarely tumour-related death may occur.\textsuperscript{5–7} From a surgical standpoint, SPC should be treated by aggressive \textit{en bloc} resection of the primary tumour with proper margins, and careful long-term follow-up is needed.\textsuperscript{7} If non-metastatic SPC of the pancreas is suspected surgery should be undertaken without delay.

Therefore, it is clinically useful to recognize radiological findings that are preoperatively suggestive of SPC. The aim of the present study was to evaluate and define the CT and MRI features distinctive of SPC and benign SPT for the purpose of differential diagnosis.

**Materials and methods**

**Patient selection**

The institutional review boards approved this retrospective study and waived the need to obtain informed patient consent. Through a computerized search of medical records, we identified 29 patients who were diagnosed with SPC or benign SPT of the pancreas and who underwent surgery between January 2000 and December 2005. Preoperative CT or MRI images had been obtained for a total of 26 patients (three men and 23 women), with a mean age of 33 years (age range 13–59 years), who were diagnosed with SPC or benign SPT of the pancreas.

With the exception of one patient, all underwent complete pancreatic tumour resection by either distal pancreatectomy ($n=14$), pancreatoduodenectomy (the Whipple procedure; $n=7$), or excision ($n=4$) followed by definitive SPC or benign SPT diagnosis. The diagnosis of the remaining patient was confirmed by histopathological analysis of tissue obtained from a biopsy of the hepatic metastasis.

**Imaging acquisition**

Seven patients with SPC and 16 patients with benign SPT of the pancreas underwent CT examinations. Fifteen patients underwent CT examinations with a multidetector row CT system (MDCT; Somatom Sensation 16; Siemens, Forchheim, Germany or LightSpeed Plus; General Electric Medical Systems, Milwaukee, WI, USA or MX8000 IDT16; Philips Medical Systems, Cleveland, OH, USA). Seven patients underwent CT examinations with a single–detector row CT system (HiSpeed Advantage; General Electric Medical Systems, Milwaukee, WI, USA or Somatom Plus S; Siemens, Erlangen, Germany); and one patient underwent CT examinations with a conventional CT machine (HiLight Advantage; General Electric Medical Systems, Milwaukee, WI, USA). Each patient received 120–150 ml nonionic contrast material (iopromide, Ultravist 300; Schering, Berlin, Germany or iohexol, Omnipaque 300, Nycomed, Princeton, NJ, USA) through an 18 G angiographic catheter inserted into an antecubital vein. CT images were routinely obtained with the patient in the supine position during full inspiration. Using MDCT, acquisition of pancreatic phase images was initiated 18 s after reaching enhancement of the abdominal aorta up to 100 HU as measured using a bolus-tracking technique or SmartPrep (GE Medical Systems) with a power injector at a rate of 3 ml/s. Portal venous phase acquisition was obtained approximately 70 s after the initiation of the contrast medium injection. Arterial phase and the portal venous phase CT images were obtained using a section width of 2–5 mm and reconstruction increment of 2–5 mm. Using the single–detector row or conventional CT systems, CT images were obtained with section thicknesses ranging 3–7 mm.

A total of 14 patients with pancreatic SPC or benign SPT underwent MRI examinations performed using 1.5 T MRI systems (Signa MR; General Electric Medical Systems, Milwaukee, WI, USA or Gyroscan Intera; Philips Medical Systems, Best, the Netherlands or Magnetom Vision; Siemens, Erlangen, Germany). MRI included fat-suppressed, T1-weighted, spin-echo imaging or T1-weighted, spoiled gradient-echo images with/without fat suppression, and T2-weighted, fat-suppressed, fast spin-echo or spin-echo images. Dynamic MRI was also performed for 10 patients using fat-suppressed, breath-hold, spoiled gradient-echo sequences before and after an intravenous bolus injection of 0.1 mmol/kg gadopentetate dimeglumine (Magnevist; Schering, Berlin, Germany).

**Imaging analysis**

Two board-certified abdominal radiologists collectively and retrospectively reviewed the CT and MRI images by consensus on a picture archiving and communication system (PACS) workstation. Both observers were blinded to the nature of the lesions (either malignant or benign), but were aware that the patients were previously diagnosed with SPT of the pancreas.

The following morphological features of both SPC and benign SPT of the pancreas were evaluated: location of the tumour within the pancreas...
(head, neck, body, or tail), maximal transverse diameter of the tumour, shape (round, oval, or lobulate), thickness of the capsule [thin (less than 2 mm) or thick (more than 2 mm)], and morphology of calcifications (no calcification, central-stippled, peripheral-linear). The fraction of the tumour composed of cystic versus solid material was estimated and expressed as a percentage (100% solid, greater than 50% solid, less than 50% solid, 100% cystic). Images were also evaluated for pancreatic duct dilation, vascular invasion or vessel encasement, and metastasis to regional lymph nodes or adjacent solid organs. Measurement of the thickness of the capsule was done at the point of maximal thickness by carefully placing the cursor on the magnified images on a PACS monitor. The pancreatic duct was considered dilated when it measured more than 3 mm. Vascular invasion or vessel encasement was considered positive when vessel embedment in tumour or occlusion had occurred.

The internal density or signal intensity characteristics of the tumour were compared with those of the surrounding pancreas and were described as hypo-, iso-, or hyperdense or hyperintense. A round region of interest (ROI) cursor was placed over a tumour or surrounding pancreas while attempting to avoid including the tumour margin within the ROI. Areas found within the tumour corresponding to the density of water or, on T1- and T2-weighted images, as the approximate signal intensity of cerebrospinal fluid, were classified as cystic-composed material. Finally, the contrast-enhancement patterns (homogeneous or heterogeneous, peripheral or complete, and progressive fill-in patterns in multiphasic image) of the lesion and capsule were also determined for all contrast-enhanced CT and MRI images.

Statistical analysis

Each patient was assigned to either the malignant group (SPC) or the benign group (benign SPT) based on the histological criteria of the WHO classification of pancreatic neoplasm. Patient age and tumour size in the two groups were compared with each other using the Mann—Whitney U test. The location, shape, capsule thickness, morphology of calcifications, and proportion of solid to cystic composition of the tumours of the SPC and benign SPT groups, analysed from CT images, were compared using the Fisher’s exact test. The presence of pancreatic duct dilation, bile duct dilation, vessel invasion or encasement, and metastases to regional lymph nodes or adjacent solid organs were also compared using Fisher’s exact test. A multivariable logistic regression model was used to determine the best predictors of a differential diagnosis between the malignant group (SPC) and the benign group (benign SPT). Significant differences were defined as those with \( P \) values less than 0.05. All statistical analyses were performed with the SPSS software package (version 13.0; SPSS, Chicago, IL, USA).

Results

The different CT and MRI features observed in patients with SPC or benign SPT of the pancreas are summarized in Table 1. No significant differences were found between SPC and benign SPT of the pancreas with respect to gender or age of the patient, nor for tumour size, location, capsule thickness, composition, or shape of the intraleisonal calcifications.

SPC masses appeared lobulate in four cases and oval or round in two cases, respectively, whereas benign SPT appeared round in 10 cases, oval in five cases, and lobulate in three cases. The apparent lobulate configuration of the mass in four of eight patients with SPC was not significantly different (\( p = 0.228 \)) from the three of 18 patients with benign SPT that also exhibited a lobular shape.

MRI examinations were performed in five patients with SPC or benign SPT of the pancreas and oval or round in two cases, respectively, whereas benign SPT appeared round in 10 cases, oval in five cases, and lobulate in three cases. The apparent lobulate configuration of the mass in four of eight patients with SPC was not significantly different (\( p = 0.228 \)) from the three of 18 patients with benign SPT that also exhibited a lobular shape.

Histological analysis

Two gastrointestinal pathologists reviewed haematoxylin and eosin (H&E)-stained microscopic slides of pancreatic SPC and benign SPT in conference for this study. CT and MRI features were correlated with the histological findings in each case. In addition to the morphological characteristics of the mass, pathologists assessed biological characteristics, such as perineural invasion, angioinvasion, and invasion into the surrounding tissue for all SPC and benign SPT occurrences, except for one patient whose SPC diagnosis was made through biopsy of the hepatic metastasis.
After contrast-enhancement of the CT (n = 7 with SPC and n = 16 with benign SPT) or MRI (n = 4 with SPC and n = 6 with benign SPT) images, the lesions appeared to have mild peripheral heterogeneous enhancement (six of eight patients with SPC and 14 of 17 patients with benign SPT) or complete homogeneous enhancement (two of eight patients with SPC and three of 17 patients with benign SPT). Multiphasic dynamic CT (n = 5 with SPC and n = 11 with benign SPT) or MRI (n = 4 with SPC and n = 6 with benign SPT) analysis was performed, resulting in 3 of 6 SPC lesions and 9 of 14 benign SPT lesions being designated as having a progressive fill-in pattern (Fig. 2) during the portal venous and equilibrium phases. There was no statistical significance between SPC and benign SPT regarding the MRI signal intensity and contrast-enhancement patterns. CT tumour enhancement was concordant with the MRI tumour enhancement in those patients who received contrast for both imaging methods.

Pancreatic duct dilation upstream from the tumour was present in four of eight patients with pancreatic SPC (Figs. 1, 3), but was absent in patients with benign SPT (Fig. 4), demonstrating statistical significance in the difference between the tumours (p = 0.005). Vessel encasement and metastasis were present in two of eight patients with SPC (Fig. 5). These characteristics were absent in benign SPT of the pancreas; however, the data are not statistically significant (p = 0.086). Liver metastasis was detected in two patients with SPC at initial presentation. One patient with SPC had a single 4-cm liver lesion at initial presentation, which was proven to be a metastasis at surgery. One patient with SPC had multiple liver lesions with a large mass lesion located in the pancreas tail (Fig. 6).

Multivariate logistic regression analysis showed that pancreatic duct dilation (p = 0.001), vessel encasement (p = 0.027) and metastasis (p = 0.027) were the variables that can be used to differentiate SPC from benign SPT.

Correlation with histological features

Upon microscopic examination for the assessment of biologic characteristics, none of the benign SPT masses demonstrated angioinvasion, perineural invasion, or metastasis. Microscopic features of SPC of the pancreas are summarized in Table 2, and correlated with imaging features. Mild capsular invasion was visible in three of 18 patients (16.7%) with benign SPT; however, five of seven patients with pancreatic SPC showed deep parenchymal invasion into the capsule and the remaining two tumours showed mild parenchymal invasion. Four cases of pancreatic SPC with pancreatic duct dilation showed microscopic angioinvasion or perineural invasion, which is distinguishable from a benign lesion. Two cases of pancreatic SPC with splenic vein encasement showed microscopic angioinvasion.

Discussion

SPT of the pancreas was first described by Frantz in 1959, and the tumours have been variously designated as solid and cystic tumour, solid and papillary epithelial neoplasm, solid cystic papillary tumour, papillary cystic neoplasm, papillary cystic epithelial neoplasm, papillary cystic tumour, or Frantz’s tumour.2,4,10 In 1996, the WHO renamed this tumour SPT in the new classification of pancreatic neoplasms.6,9 In contrast to conventional ductal adenocarcinomas, most SPTs, although often large in size, are usually well circumscribed, and complete surgical resection has been reported to provide more than a 95% cure rate.1,8 According to the
WHO classification of tumours of the exocrine pancreas, SPT is usually defined as a benign neoplasm composed of monomorphic cells forming solid and pseudopapillary structures, frequently showing haemorrhagic-cystic changes, and variably expressing epithelial, mesenchymal, and endocrine markers. Although it is morphologically identical to SPT, SPC is defined as a low-grade carcinoma composed of monomorphic cells forming solid and pseudopapillary structures. Nishihara et al. compared the histological appearance of 19 non-metastasizing and three metastasizing SPTs, and noted that venous invasion, nuclear grade, and prominent necrobiotic nests were useful as histological parameters to detect the malignant potential of SPTs. Shimizu et al. reported a 34-year-old woman with SPC and liver metastasis having histological features of capsular invasion without signs of vascular or nerve sheath invasion. This group suggested that capsular invasion may also be an important histological indicator of malignant potential in SPT. According to the WHO classification scheme, unequivocal perineural invasion, angioinvasion, or deep invasion into the surrounding tissue are indicative of malignant behaviour, and such lesions should be classified as SPC. As determined by established WHO histological criteria, eight patients in the present study were regarded as having SPC of the pancreas.

There have been several reports identifying the CT and MRI features of SPT of the pancreas. CT usually demonstrates a well-encapsulated lesion with varying solid and cystic components due to haemorrhagic degeneration.
Calcifications have been described in up to 30% of SPT cases. MRI typically demonstrates a well-defined lesion and shows heterogeneous signal intensities, reflective of the complex nature of the mass on T1- and T2-weighted images. Areas of high signal intensity on T1-weighted images and low or inhomogeneous signal intensity on T2-weighted images can help identify blood products. In the present study, benign SPT of the pancreas demonstrates similar CT and MRI features to those just described. Imaging features of pancreatic SPC also demonstrate a well-encapsulated lesion with variable degrees of haemorrhagic degeneration ranging from solid
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to completely cystic components. Calcification was more frequently observed in SPC than in benign SPT, without statistical significance. Multivariate logistic regression analysis showed that pancreatic duct dilations, vessel encasement, and metastasis were the variables that could be used to differentiate SPC from benign SPT with statistical significance, whereas univariate analysis showed that pancreatic duct dilation was the only variable that could be used to differentiate SPC from benign SPT with statistical significance.

Distant metastases develop in up to 15% of cases and they are most commonly present at diagnosis. It is uncommon for metastases to develop later; however, they may occasionally develop with a latency of several years. Common sites for metastatic disease are the liver, omentum, peritoneum, and lymph nodes. Even in the event of metastasis, the lesions are slow-growing and are associated with long-term survival. Considering the favourable outcome, most current recommendations support aggressive management, targeting complete resection of both the primary tumour and the metastatic lesions whenever possible.

Pancreatic duct dilation was present in four of eight SPC patients in the present study. Furthermore, all four of these mass lesions, which were located in the pancreatic head, showed distal pancreatic ductal dilation. In spite of the large size of the masses, main pancreatic duct dilation and bile duct dilation were rare in SPT. Choi et al. reported that these findings confirm the

Figure 4  Benign solid pseudopapillary tumour without distal pancreatic duct dilation in a 48-year-old woman. Pancreatic phase axial CT image shows a mass in the tail of the pancreas without distal pancreatic duct dilation (arrow).

Figure 5  Solid pseudopapillary carcinoma of the pancreas with splenic vein encasement in a 15-year-old woman. (a) Contrast-enhanced CT image shows a multilocular cystic mass in the tail of the pancreas with peripheral curvilinear calcification. (b) CT image shows narrowing and flattening of the splenic vein (arrow) by the surrounding tumour located in the tail of the pancreas. Splenomegaly is also noted. (c) On a high-power photography (H&E stain, ×200), venous invasion of the uniform tumour cells (arrow) are seen.
slow-growing and noninvasive tendencies of SPT. Hassan et al.\(^5\) and Vargas-Serrano et al.\(^20\) reported cases of SPC located in the pancreas head with pancreatic or bile duct dilation. From the present study, pancreatic duct dilation was a more frequently observed imaging feature of SPC than of benign SPT, and these imaging features seem to reflect its invasive nature (microscopic angioinvasion or perineural invasion), which is distinguishable from a benign lesion (Table 2). However in the present study, bile duct dilation was absent in all cases, and this cannot be explained.

Occasionally, SPT can invade the surrounding pancreatic parenchyma and result in superior mesenteric vessel encasement.\(^5,11\) Venous invasion or angioinvasion is one of the microscopic characteristics of SPC of the pancreas. In the present study, vessel encasement was present in only two of eight patients with SPC; however, none of the 18 patients with benign SPT demonstrated this characteristic. Alexandrescu et al.\(^6\) reported a case of aggressive SPC resulting in vascular encasement of the superior mesenteric bundle and aorta, as well as local involvement of the mesenteric lymph nodes. Martin et al.\(^16\) and Cantisani et al.\(^10\) reported three cases of patients with SPT showing encasement of mesenteric vessels or invasion of the splenic hilum. In the present retrospective review of the microscopic features of pancreatic SPC, the two cases having splenic vein encasement also showed microscopic angioinvasion (Table 2). Therefore, vessel encasement is likely to be associated with microscopic angioinvasion, and may be a highly suggestive imaging feature of SPC.

There are limitations to the present study. First, due to the rare occurrence of SPC and benign SPT, the number of lesions is limited. However, despite the small sample size, pancreatic duct dilation, vessel encasement, and metastasis were the imaging features that could be used to differentiate SPC from benign SPT with statistical significance by multivariate analysis. Second, because the cases were retrospectively collected over 6 years from three different institutions, the CT and MRI protocols were inevitably not standardized. However, the different protocols did not influence the review process determining the subjective imaging features in the present study. Third, the present study had a relatively short period of patient follow-up, and a longer follow-up period would be important to confirm the malignant potential. Although it is uncommon for metastases to develop during the follow-up period, they may occasionally develop with a latency of several years.\(^5,16\)

In conclusion, even though SPC and benign SPT of the pancreas share the CT and MRI features of encapsulation with variable degrees of haemorrhagic degeneration with or without calcification, SPC could be differentiated from benign SPT by aggressive behaviour, such as pancreatic duct dilation and vessel encasement, either with or without metastases. If such imaging features are present, aggressive surgical approach is mandatory, and an intensive follow-up should be advised to the attending clinicians and radiologists.
Table 2 Microscopic features of solid pseudopapillary carcinoma (SPC) of the pancreas

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Size (cm)</th>
<th>Location</th>
<th>Solid:cystic ratio</th>
<th>Capsule invasion</th>
<th>Angioinvasion</th>
<th>Perineural invasion</th>
<th>Metastasis</th>
<th>Imaging features</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. F/30</td>
<td>9.3</td>
<td>Head</td>
<td>Less 50% solid</td>
<td>(+)</td>
<td>(+)</td>
<td>(−)</td>
<td>(−)</td>
<td>Pancreatic duct dilation</td>
</tr>
<tr>
<td>2. F/15</td>
<td>6.8</td>
<td>Tail</td>
<td>Less 50% solid</td>
<td>(++)</td>
<td>(−)</td>
<td>(+)</td>
<td>(−)</td>
<td>Splenic vein encasement</td>
</tr>
<tr>
<td>3. F/19</td>
<td>5.3</td>
<td>Head</td>
<td>Completely cystic</td>
<td>(+)</td>
<td>(+)</td>
<td>(+)</td>
<td>(−)</td>
<td>Pancreatic duct dilation</td>
</tr>
<tr>
<td>4. F/26</td>
<td>4.3</td>
<td>Tail</td>
<td>Less 50% solid</td>
<td>(+)</td>
<td>(+)</td>
<td>(+)</td>
<td>(−)</td>
<td>Liver metastasis</td>
</tr>
<tr>
<td>5. F/43</td>
<td>2.0</td>
<td>Head</td>
<td>Completely solid</td>
<td>(−)</td>
<td>(−)</td>
<td>(+)</td>
<td>(−)</td>
<td>Pancreatic duct dilation</td>
</tr>
<tr>
<td>6. F/46</td>
<td>7.2</td>
<td>Tail</td>
<td>Completely solid</td>
<td>(−)</td>
<td>(−)</td>
<td>(+)</td>
<td>(−)</td>
<td>Splenic vein encasement</td>
</tr>
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<td>7. F/56</td>
<td>6.6</td>
<td>Tail</td>
<td>Less 50% solid</td>
<td>(+)</td>
<td>(−)</td>
<td>(−)</td>
<td>(−)</td>
<td>Liver metastasis</td>
</tr>
<tr>
<td>8. F/24</td>
<td>3.2</td>
<td>Head</td>
<td>Completely cystic</td>
<td>(+)</td>
<td>(−)</td>
<td>(−)</td>
<td>(−)</td>
<td>Pancreatic duct dilation</td>
</tr>
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</table>

References


