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High F-18 fluorodeoxyglucose accumulation in solid pseudo-papillary tumors of the pancreas

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We report two cases of young women with a solid pseudo-papillary tumor of the pancreas which having cystic and hemorrhagic components with marked calcification on computed tomography and magnetic resonance imaging. F-18 fluorodeoxyglucose positron emission tomography revealed abnormally increased accumulation of F-18 fluorodeoxyglucose in the pancreas tail tumors, especially in the non-calcified solid portion of the tumors. These patients underwent elective resection of the masses and distal pancreatectomy and were diagnosed with solid pseudo-papillary tumors by histopathological analysis. There was no evidence of distant metastasis on follow-up after surgery and they showed no histopathological findings suggesting malignancy. These cases suggest that solid pseudo-papillary tumor may show high uptake of F-18 fluorodeoxyglucose.

Key words: solid pseudo-papillary tumor, pancreas, F-18 fluorodeoxyglucose (F-18 FDG), positron emission tomography (PET)

INTRODUCTION

SOLID PSEUDO-PAPILLARY TUMOR (SPT) of the pancreas is a rare benign or low-grade malignant neoplasm that is seen mostly in young female patients. Surgical excision means cure in cases before malignant degeneration develops. Regarding the pathology, SPT is usually large and encapsulated and is composed of a mixture of cystic, solid, and hemorrhagic components. The capsule and intratumoral hemorrhage are important clues to its diagnosis because they are rarely found in other pancreatic neoplasms.[1–4]

Computed tomography (CT) usually reveals a well encapsulated lesion with varying solid and cystic components owing to hemorrhaging.[5] Also, magnetic resonance imaging (MRI) typically shows a well-defined lesion with heterogeneous signal intensity on T1- and T2-weighted images, which reflects the complex nature of the tumor. An area of high signal intensity on T1-weighted images can help identify blood products.[5,6] These findings are sufficient for a preoperative diagnosis that may lead to early surgery and cure.

The F-18 fluorodeoxyglucose (FDG) uptake of SPT on positron emission tomography (PET) is largely unknown. To our knowledge, FDG-PET features of only two cases have been reported in the literature.[7,8] Here, we present two cases of SPT of the pancreas which showed high uptake of FDG on PET.

CASE REPORT

Case 1

A 31-year-old woman was admitted to our hospital because she had a left upper abdominal calcified tumor which was incidentally found by chest CT examination during a medical check up. Physical examination revealed no abnormal findings. There were no abnormalities in clinical laboratory tests such as serum amylase level or pancreatic cancer markers, such as CA19-9, CEA, DUPAN-2, and SPAN-1.

Abdominal CT examination showed a large (5.6 × 5.8 cm) whirl-like calcified tumor of the pancreas tail. The non-calcified solid portion of the tumor showed moderate

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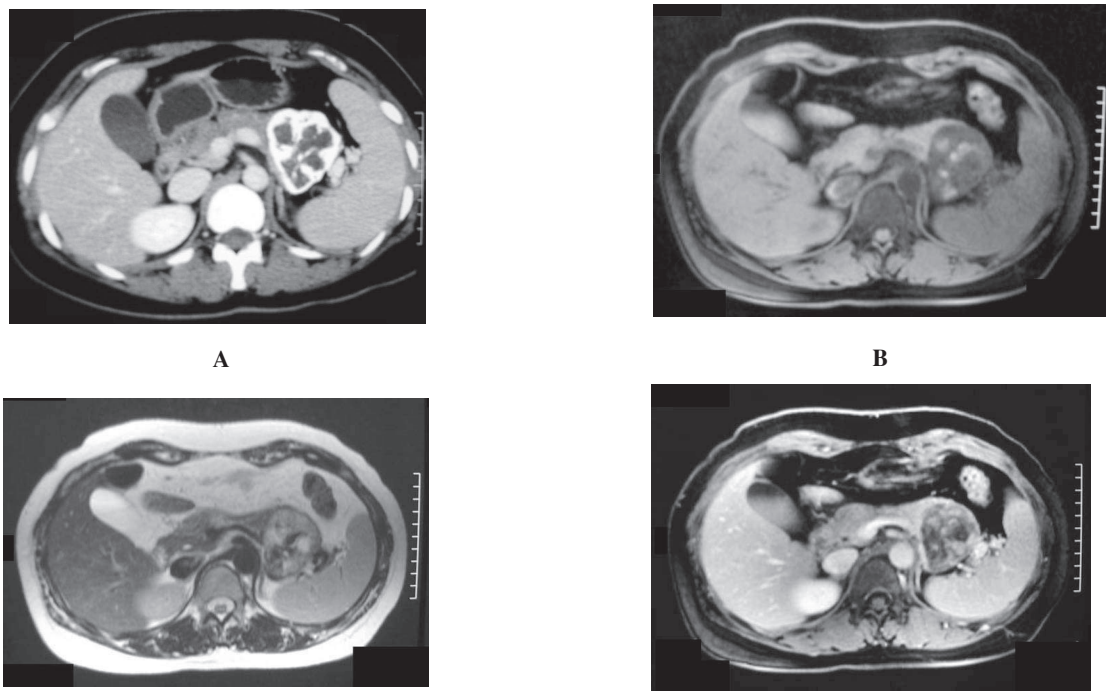


A B C D

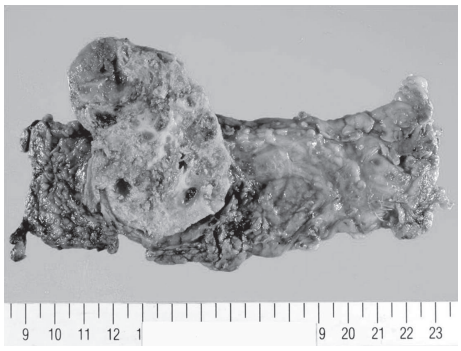
Fig. 1 Abdominal CT examination showed a large whirl-like calcified tumor of the pancreas tail. The non-calcified solid portion of the tumor showed moderate enhancement (A). T1-weighted MR imaging showed a round, well-circumscribed, hypointense mass in the pancreas tail (B). The mass was slightly hyperintense on T2-weighted imaging (C), and contained cystic and hemorrhagic components which were hyperintense on T1- and T2-weighted imaging. Gd-enhanced T1-weighted imaging showed moderate enhancement in the solid component (D).

A B

Fig. 2 Abnormally increased accumulation of FDG was observed in the pancreas tail tumor, especially the non-hemorrhagic portion, 60 (A) and 120 (B) minutes after FDG administration. The mean standard uptake values of the tumor 60 and 120 minutes were 4.2 and 3.9, respectively.

enhancement after contrast material administration (Fig. 1A). Unenhanced T1-weighted imaging revealed a round, well-circumscribed, hypointense mass in the pancreas tail (Fig. 1B). The mass was slightly hyperintense on T2-weighted imaging (Fig. 1C), and contained cystic components which showed hyperintense on T1- and T2-weighted imaging, suggesting the presence of hemorrhagic components. Gadolinium (Gd)-enhanced dynamic scans showed progressive filling in of the solid component of the tumor (Fig. 1D). These radiological findings suggested a SPT of the pancreas.

FDG-PET was performed as a systemic search of this pancreas tumor. The patient fasted for more than five hours before receiving an intravenous injection of 250 MBq of F-18 FDG. Then, 60 and 120 minutes after the injection, transmission and emission scans were obtained



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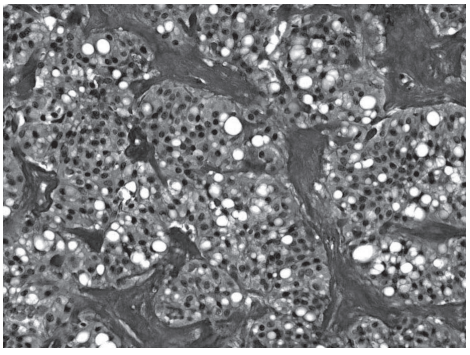

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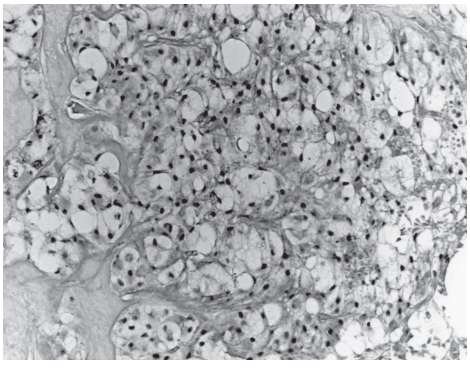
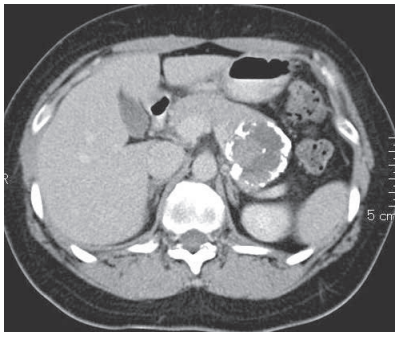


C

Fig. 3 On gross pathological examination, a soft, round, well-circumscribed 5.6 cm mass was identified in the pancreas tail (A). On histologic analysis, the tumor was found to be composed of uniform polygonal cells with moderate to abundant amphophilic cytoplasm, which were arranged into solid nests with areas of degeneration (B). Immunohistochemical staining of Glut-1 and HK-II showed poor expression of Glut-1 and moderate expression of HK-II (C).

from the upper thigh to the neck with a high-resolution dedicated system (Allergro; Philips/ADAC, Cleveland, USA) with 56 cm axial field of views and resolution of 4 mm (axial) × 4 mm (in-plane) in full width at half maximum and 3-dimensional acquisition mode. The acquisition data were reconstructed using a segmented attenuation correction and a 3-Dimension Raw Action Maximum Likelihood Algorithm (3D-RAMLA) method. Abnormally increased accumulation of FDG was



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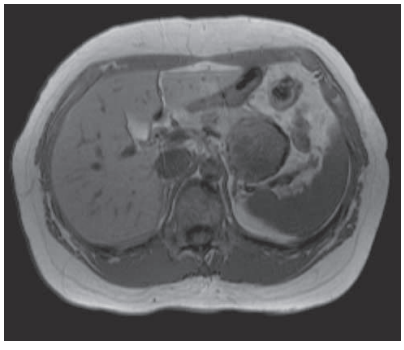

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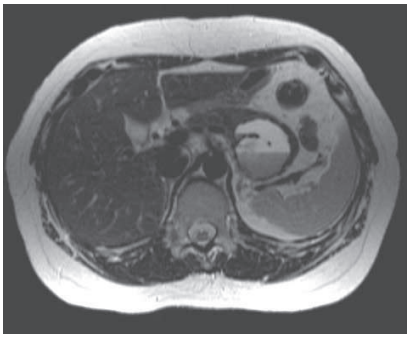

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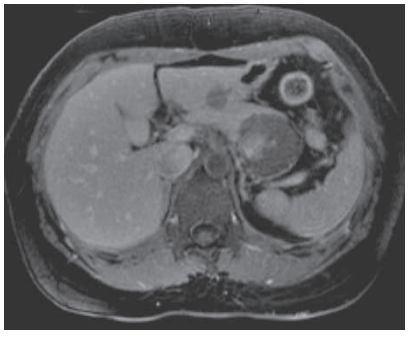
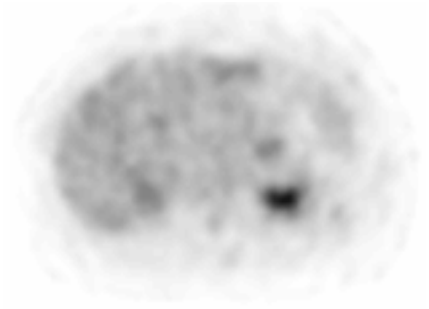


D

Fig. 4 Abdominal CT examination showed a large marginal calcified tumor of the pancreas tail. The non-calcified solid portion of the tumor showed moderate enhancement (A). Unenhanced T1- and T2-weighted imaging revealed a round, well-circumscribed mass in the pancreas tail. The mass contained cystic components which showed hyperintense and fluid-fluid level formation on T1- and T2-weighted imaging, suggesting the presence of hemorrhagic components (B and C). Gd-enhanced dynamic scans showed progressive filling of the small solid component (D).



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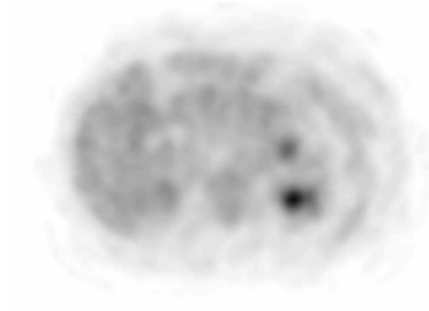

B

Fig. 5 Abnormal increased accumulation of FDG was observed in the solid part of the tumor 60 (A) and 120 (B) minutes after FDG administration. The SUVmax of the tumor 60 and 120 minutes were 3.0 and 3.2, respectively.

observed in the pancreatic tail tumor on both 60- and 120-minute images. This accumulation showed a doughnut-like appearance corresponding to the solid and non-hemorrhagic portion of the tumor (Fig. 2A, B). The maximum standard uptake values (SUVmax) of the tumor at 60 and 120 minutes were 4.2 and 3.9, respectively. Tc-99m methylene diphosphate (MDP) bone scan showed increased accumulation in the calcified portion of the tumor.

The patient underwent elective resection of the mass and distal pancreatectomy. On gross pathological examination, a soft, round, well-circumscribed 5.6 cm mass was identified in the pancreas tail (Fig. 3A). On histologic analysis, the tumor was found to be composed of uniform polygonal cells with moderate to abundant amphophilic cytoplasm, which were arranged into solid nests with areas of degeneration (Fig. 3B). For immunohistochemical analysis, the tumor cells were diffusely positive for α-1-antitrypsin and α-1-antichimotrypsin and mitochondria-rich by anti-mitochondria antibody staining. Immunohistochemical staining of glucose transporter-1 (Glut-1) and hexokinase-II (HK-II) showed poor expression of Glut-1 and moderate expression of HK-II (Fig. 3C).

Case 2

A 37-year-old woman was admitted to our hospital because she had a left upper abdominal calcified tumor

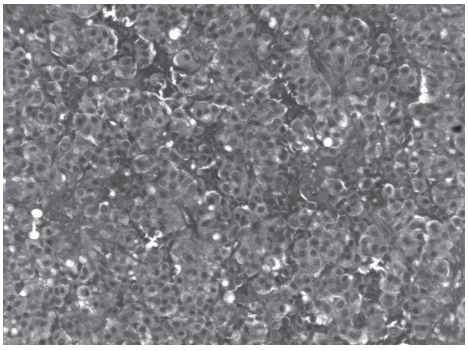

Fig. 6 On histologic analysis, the tumor was found to be composed of uniform polygonal cells with moderate to abundant amphophilic cytoplasm, which were arranged into solid nests with areas of degeneration.

which was incidentally found by abdominal CT examination during evaluation after a traffic accident. Her physical examination revealed no abnormal findings, and there were no abnormalities in her clinical laboratory test results, or pancreatic cancer markers.

Abdominal CT examination showed a large 5.3 × 5.0 cm marginal calcified tumor of the pancreas tail. The non-calcified solid portion of the tumor showed moderate enhancement after contrast material administration (Fig. 4A). Unenhanced T1- and T2-weighted imaging revealed a round, well-circumscribed mass in the pancreas tail. The mass contained cystic components which showed hyperintense and fluid-fluid level formation on T1- and T2-weighted imaging, suggesting the presence of hemorrhagic components (Fig. 4B, C). Gd-enhanced dynamic scans showed progressive filling of the small solid component. Abnormally increased accumulation of FDG was observed on both 60- and 120-minute images. This accumulation corresponded to the small solid portion, which showed moderate enhancement on Gd-enhanced dynamic scans. The accumulation pattern was slightly different between the 60- and 120-minute images (Fig. 5 A, B). The SUV max of the tumor at 60 and 120 minutes were 3.0 and 3.2, respectively.

The patient underwent elective resection of the mass and distal pancreatectomy. On histologic analysis, the tumor was found to be composed of uniform polygonal cells with moderate to abundant amphophilic cytoplasm, which were arranged into solid nests with areas of degeneration (Fig. 6). Poor expression of Glut-1 and moderate expression of HK-II on immunohistochemical staining of Glut-1 and HK-II were also noted.

DISCUSSION

Solid pseudo-papillary tumors (SPT) of the pancreas are rare and found mainly in young women in the second and third decades of life.[1–3] SPT can occur anywhere in the pancreas but is most frequently found in the head or tail.

On gross histological examination, the mass is usually large and well encapsulated and exhibits varying degrees of necrosis, hemorrhage, and cystic changes. Although most SPT exhibit benign behavior, malignant degeneration does occur. Lam, et al. found that 66 of 452 reported tumors (15%) were malignant with evidence of metastases or invasion of adjacent structures.[1] The malignant SPT were often older on presentation and had a male predilection.[1–3] Even in the presence of disseminated disease, the clinical course is usually protracted, and the overall 5-year survival rate is 97%.[3] Nishihara et al. reported that these metastatic cases tend to show venous invasion, higher nuclear grade, and more prominent necrobiotic cell nests characterized by aggregates of cells with pyknotic nuclei and eosinophilic cytoplasm.[4] However, SPT, like neuroendocrine tumors of the pancreas, are difficult to differentiate between benign and malignant cases, even histopathologically.

A variety of imaging techniques may help the differentiation of SPT from other cystic neoplasms such as serous cystoadenoma, mucinous cystic tumors, and neuroendocrine tumors of the pancreas. CT usually shows a well encapsulated lesion with varying solid and cystic components owing to hemorrhaging. Following contrast material administration, enhanced solid areas are typically noted peripherally, whereas cystic areas are usually more centrally located.[5] MR imaging typically reveals a well-defined lesion with heterogeneous signal intensity on T1- and T2-weighted images, which reflects the complex nature of the tumor. An area of high signal intensity on T1-weighted images and low or inhomogeneous signal intensity on T2-weighted images can help identify blood products and may also help to differentiate SPT from neuroendocrine tumors of the pancreas. Moreover, Gd-enhanced dynamic studies show early heterogeneous peripheral enhancement with progressive fill-in.[5,6] Our two cases showed typical CT and MRI findings with hemorrhagic change. Marked calcification is another characteristic finding in these patients, and these findings may be sufficient for the diagnosis of SPT. However, it is impossible to determine if the tumor is benign or malignant, despite the absence of findings suggesting distant metastasis, peritoneal dissemination, and lymph node swelling.

The FDG accumulation of SPT seen by PET studies is largely unknown. To our knowledge, high FDG accumulation seen by PET studies of only two cases has been reported in the literature.[7,8] Okaizumi et al. reported 39 cases of abdominal benign disease which showed high accumulation on the examination for FDG-PET, and one of these was a case of SPT of the pancreas.[7] However, its detailed characteristics were unknown. Lee et al. reported on a SPT with a diameter of 3.2 cm which showed increased accumulation of FDG and its SUVmax 60 min after FDG administration was 2.6.[8] However, its detailed histopathological findings and clinical outcome were not mentioned. Our case had a larger tumor compared with the case of Lee and the SUVmax 60 and 120 minutes after FDG administration were higher at 4.2 and 3.9, and 3.0 and 3.2 respectively. The accumulation of these few cases including ours suggests that it would be important to investigate whether SPT consistently shows high FDG accumulation using a larger series. In addition, it would also be important to investigate the difference in FDG accumulation between clinically benign and malignant SPT because it is difficult to differentiate between these forms by other radiological and histopathological procedures. Nakamoto reported that the diagnostic accuracy in differentiating between malignant and benign pancreatic lesions was 83% and 87.2%, respectively, when applying the cut-off SUV of 2.5 and 2.8 at 1 hour post injection.[9] Rasmussen demonstrated a sensitivity of 91.7% and a specificity of 75% using a cut-off SUV of 3.5.[10] According to these results, SUVs in our cases are relatively high, which highly suggested malignant pancreatic neoplasm. However, there were no histopathological signs of malignancy, such as venous invasion, mitotic figures, nuclear atypica, or necrobiotic cell nests. In addition, there was no evidence of recurrence or metastasis after a one-year follow-up period in these patients. Nakamoto also reported that improved accuracy can be achieved using an additional delayed scan to differentiate malignant from benign lesions, because many malignant lesions showed a constantly increasing FDG uptake, while many benign lesions showed a decrease in FDG uptake.[9] However, there are a number of malignant pancreatic tumors that showed decreased FDG uptake, as well as a number of benign lesions that showed increased FDG uptake.[10] The usefulness of delayed scan in differentiating benign and malignant SCT can not be determined based solely on our two cases, because one of our cases showed increased FDG uptake on delayed scan, whereas the other case showed slightly decreased FDG uptake. These observations indicate that SUVmax of early and delayed scan may have limited usefulness in differentiating benign and malignant SPT.

From the view point of differential diagnosis of FDG accumulated pancreatic tumors, we must consider SPT, in addition to pancreatic cancers, neuroendocrine tumors, autoimmune pancreatitis, etc.[12–14] Nakamoto reported on the limited detectability of islet cell tumors by FDG-PET. However, 53% of their cases showed FDG accumulation and their SUV were higher than 2.3.[12] They also reported a high accumulation of FDG in autoimmune pancreatitis in six cases, one of which showed localized uptake, which is necessary to differentiate pancreatic tumors.[14] SPT showed relatively characteristic CT and MRI features with a mixture of cystic, solid, and hemorrhagic components. However, some cases lack cystic and hemorrhagic components, for which it is difficult to differentiate from other pancreatic tumors using CT and MRI. FDG-PET may also have limited value regarding differentiated

pancreatic duct cancer compared to other pancreatic tumors, especially neuroendocrine tumors and SPT, which show relatively benign courses. From our results, SUV and additional delayed scanning may have limited value in terms of differentiating pancreatic cancer and SPT. Therefore, it is important to judge pancreas tumor which showed high FDG accumulation by use of clinical, laboratory, and other radiological findings.

Furthermore, FDG-PET seems to have value for detecting distant metastatic foci if malignant SPT shows high FDG accumulation. The preoperative identification of metastatic disease is of considerable importance because SPT is a low grade type of malignant tumor that is associated with an excellent prognosis on complete resection. In fact, disease-free intervals of up to 21 years after surgery of metastatic foci have been reported.

Concerning the mechanism of FDG accumulation in SPT, our cases showed relatively high tumor cell density and tumor cells that were rich in mitochondria. Moreover, CT and MRI showed moderate enhancement of the solid portions, which denoted the hypervascular nature of this tumor. These histopathological and radiological findings may contribute to the high FDG accumulation of SPT; however the relationship between mitochondria and high FDG accumulation is uncertain. On the other hand, these cases showed poor expression of Glut-1 and moderate expression of HK-II on immunohistochemical staining. It is difficult to discuss this based only on our two cases but SPT may not show overexpression of Glut-1 and HK-II like various other malignant tumors including pancreatic cancer.[15,16]

In conclusion, from our limited experience, solid pseudopapillary tumors seem to show high uptake of F-18 FDG. Further investigation using a larger number of subjects is necessary to assess whether this tumor consistently shows high accumulation of FDG and to compare the degree of FDG accumulation between clinically benign and malignant tumors.

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