대한영상의학회지

Imaging Findings of Pancreatic Solid Pseudopapillary Neoplasm with High-Grade Malignant Transformation: Focusing on Diffusion-Weighted Imaging and Normalized Apparent Diffusion Coefficient Values

고등급 악성전환을 보인 고형 가유두상 종양의 영상소견: 확산강조영상 및 표준화 현성확산계수값

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Solid pseudopapillary neoplasm (SPN) of the pancreas is an uncommon neoplasm characterized by low-grade malignant potential and uncertain histogenesis, and usually afflicts relatively young women. The tumors typically manifest as well-marginated, mixed density lesions consisting of a solid peripheral and central cystic component in conjunction with hemorrhagic foci. SPN with apparent high-grade malignant transformation is a rare histologic variant. Herein, we report a rare case of SPN with high-grade malignant transformation diagnosed in a 75-year-old female, with emphasis on differential diagnoses and role of normalized ADC values. SPN with malignant transformation should be included in the differential diagnosis in cases of mixed solid and cystic masses with hemorrhagic components, irregular margin and lower normalized apparent diffusion coefficient (ADC) values in an elderly female patient, as was the case discussed below.

Index terms
Diffusion Magnetic Resonance Imaging
Magnetic Resonance Imaging
Pancreatic Neoplasms

INTRODUCTION

Solid pseudopapillary neoplasm (SPN) of the pancreas, first reported by Frantz in 1956, is an uncommon but distinct pancreatic neoplasm with a low malignant potential, accounting for 1−3% of all pancreatic tumors (1). Most SPNs have a tendency to affect young women and have excellent prognoses following complete surgical resection (2). Although the majority of SPNs have an indolent clinical course and low malignant potential, 10% to 15% of cases exhibit aggressive clinical and pathologic features (2). Histologically, most SPNs are composed of uniform polygonal cells with hemorrhage, necrosis, and characteristically prominent cystic portions, but there is a high-grade malignant histologic variant that is composed of numerous nuclear atypia and mitosis, causing a diagnostic dilemma (3). Although there are comprehensive several reports regarding imaging features of SPN in literature, there have been few reports specifying detailed description of diffusion weighted MR imaging findings, including mean apparent diffusion coefficient (ADC) values and normalized ADC values with respect to differentiating SPN with malignant transformation from benign SPN. We herein report a rare case of pancreatic SPN with

high-grade malignant transformation in an older woman focusing on diffusion weighted MR imaging including normalized ADC values.

CASE REPORT

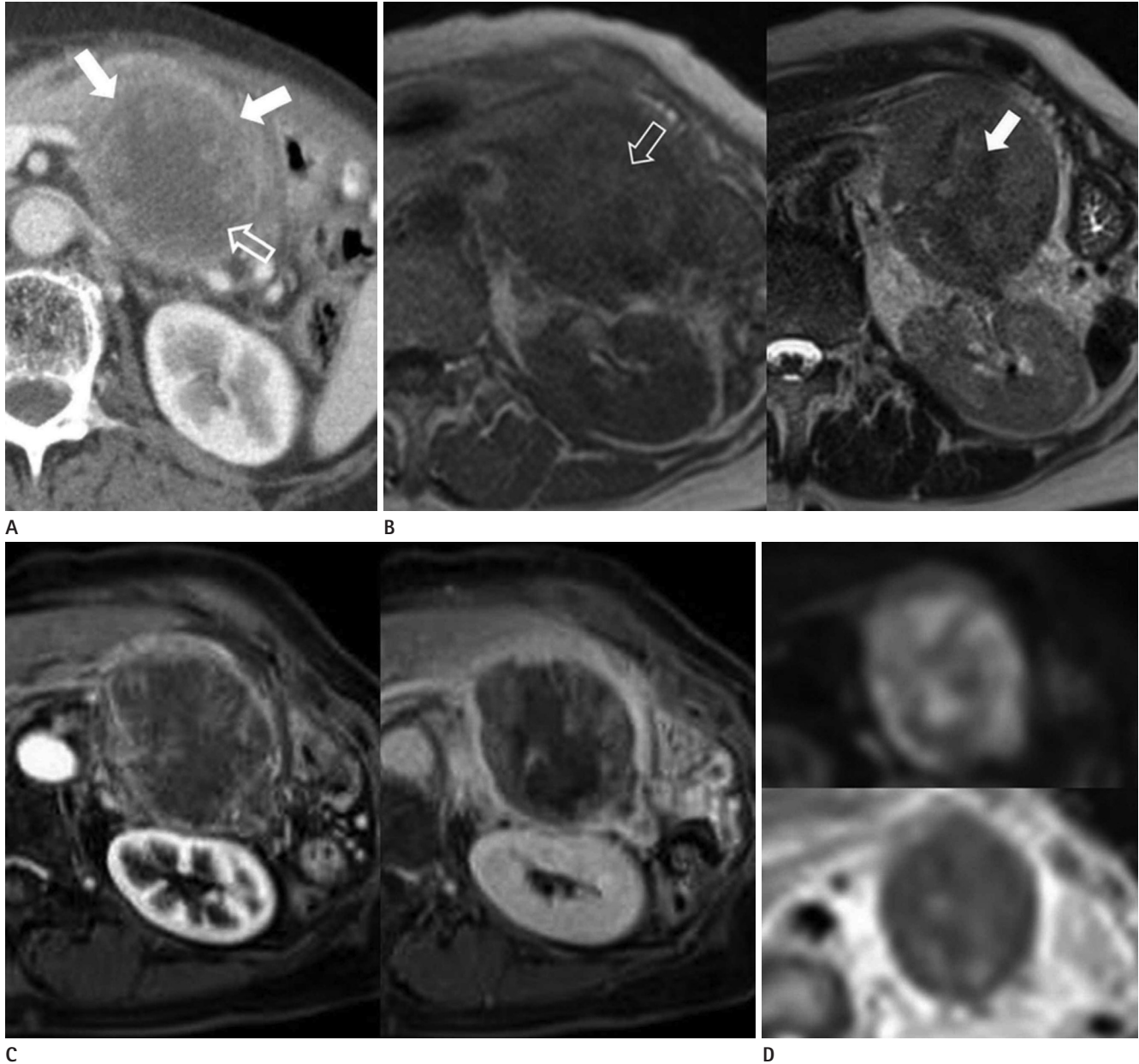A 75-year-old female patient presented to our internal medi-

Fig. 1. A 75-year-old female patient presented a pancreatic solid pseudopapillary neoplasm with high-grade malignant transformation.
A. Contrast-enhanced axial computed tomography image demonstrates about 9.2 × 6.6 × 7.0 cm sized relatively well-demarcated lobulated mixed density mass in the tail of the pancreas, composed of enhancing solid component peripherally (solid arrows) and non-enhancing cystic component centrally (open arrow).
B. The MRI shows heterogeneous low to intermediate signal intensity with some central high signal intensity foci (open arrow) on T1-weighted image (left column), heterogeneous intermediate to high signal intensity with internal low signal intensity areas (solid arrow) on T2-weighted images (right column).
C. On the dynamic MRI, the mass shows heterogeneous peripheral enhancement in the arterial phase (left column), and heterogeneous peripheral gradual enhancement with internal non-enhancing cystic portion in the delayed phase (right column).
D. On diffusion-weighted imaging, the intensity is high, with a high b value (800 sec/mm^2) (upper row) and low signal intensity on apparent diffusion coefficient mapping (lower row).
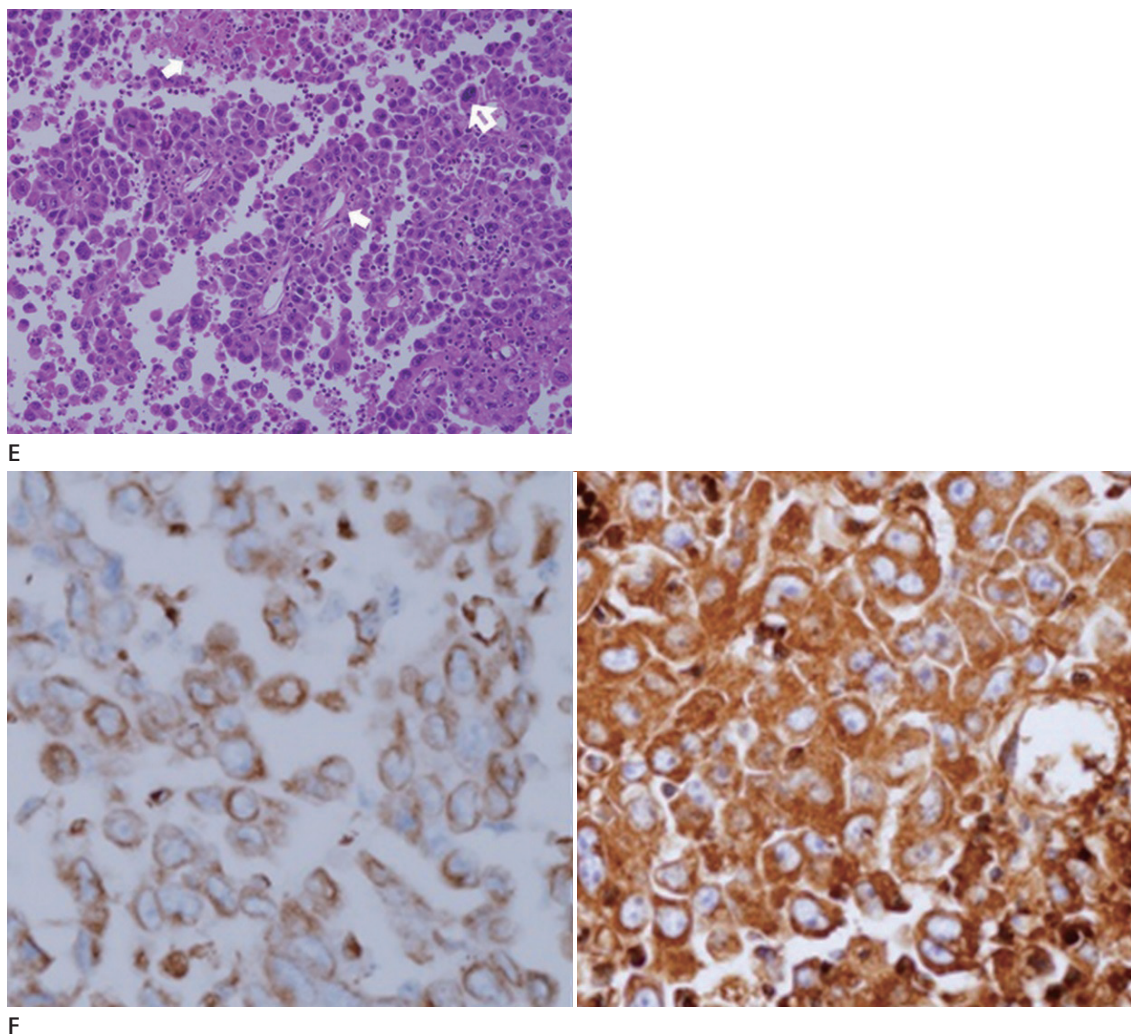MRI = magnetic resonance image

Fig. 1. A 75-year-old female patient presented a pancreatic solid pseudopapillary neoplasm with high-grade malignant transformation.
E. Microscopic findings shows that the tumor cells are radially arranged with papillary configurations composed of delicate and somewhat hyalinized fibrovascular core on the necrotic background (solid arrows) with cellular pleomorphic and numerous mitosis (open arrow) (hematoxylin and eosin stain, × 40).
F. Immunohistochemical staining shows that the tumor cells are positive for alpha-1-antitrypsin (left column) and vimentin (right column) (immunohistochemical stain, × 200).

cine department with the chief complaint of worsening upper abdominal discomfort that had persisted for 7 months and weight loss of 10 kg over 3 months. She had a 30-year medical history of diabetes mellitus and two surgical episodes for peritonitis 40 years prior.

On admission, physical examination revealed normal body temperature and stable hemodynamics. The lower abdomen was distended with rebound tenderness on palpation. Initial laboratory tests revealed a raised white blood cell count, 15.2 × 10⁹/L, and a high C-reactive protein level of 2.8 mg/dL, consistent with an inflammatory reaction. Other biochemical values were normal.

The initial abdominal radiograph revealed normal findings. Subsequent contrast-enhanced abdominal computed tomography (CT) examination using a 128-detector-row CT scanner (Definition AS+; Siemens Medical Solutions, Forchheim, Germany) was performed to evaluate the cause of abdominal discomfort. We obtained axial, coronal, and sagittal reformatted images that were 5 mm in thickness. The CT scan showed an approximately $9.2 \times 6.6 \times 7.0$ cm sized relatively well-demarcated lobulated mixed density lesion with suspicious direct invasion to the splenic vessel and gastric lesser curvature, composed of a peripheral solid component and a central cystic component with some high density foci in the pancreatic tail, suggestive of

a pancreatic tumor (Fig. 1A). Subsequently, we performed dynamic magnetic resonance image (MRI) using a 3.0T system (Magnetom Verio; Siemens Medical Solutions, Erlangen, Germany) with a body phased-array coil. The MRI showed an encapsulated mass with heterogeneous low to intermediate signal intensity with some central high signal intensity foci on T1-weighted images and heterogeneous intermediate to high signal intensity with internal low signal intensity areas on T2-weighted images (Fig. 1B). This internal high signal intensity on T1-weighted MR images and low signal intensity on T2-weighted MR images were considered as hemorrhagic component within the mass. Dynamic study of the tumor revealed peripheral gradual filling of contrast material with internal a non-enhancing cystic portion (Fig. 1C). On diffusion-weighted imaging, the intensity was high, with a high b value (800 sec/mm^2) and low signal intensity on apparent diffusion coefficient mapping (Fig. 1D). By applying the copy and paste function of the picture archiving and communication system (PACS) system (Maroview 5.4; Marotech, Seoul, Korea), region of interests (ROIs) were identically positioned at peripheral solid portion of the pancreatic mass, normal pancreas and spleen. For the pancreas, 2 ROIs were obtained from the head of the pancreas. For the spleen, 2 ROIs from 3 contiguous slices were measured with a central section obtained through the level of the splenic hilum. The mean and normalized ADC values were calculated using b values of 0, 50, 400, and 800 sec/mm^2 from 3 contiguous slices. The mean ADC values of the solid portion, normal pancreas and spleen in our case are 0.932×10^{-3} mm^2/sec, 1.406×10^{-3} mm^2/sec and 0.780×10^{-3} mm^2/sec, respectively. The patient was taken for a distal pancreatectomy with splenectomy. Intraoperatively, the resected mass was measured as 8.0×6.0 cm in size. The mass showed central hemorrhagic necrosis, but a whitish glistening nature in the cortical area. Morphologically, the tumor cells were arranged radially around delicate and somewhat hyalinized fibrovascular stalks on a necrotic background, with a few hyaline globules, and had pleomorphism and numerous mitosis, along with deep invasion of the pancreatic parenchyma and capsule, consistent with the histologically malignant features (Fig. 1E). Moreover, the positive rate of Ki-67, a predictive factor for malignancy, was more than 90%. On immune-histochemical staining, the tumor cells were positive for vimentin, Alpha 1 antitrypsin (AAT), and CD10 and negative for CD56 and chro-

mogranin-A (Fig. 1F). The patient recovered well and was discharged on the 6th postoperative day.

DISCUSSION

SPN is an uncommon exocrine tumor, accounting for 6% of all exocrine tumors in the pancreas (1). The World Health Organization (WHO) classified these tumors as solid pseudopapillary tumors in 1996 and reclassified them as solid pseudopapillary neoplasms (SPNs) in 2010 (1). After the WHO reclassification in 2010, SPN is now classified as an epithelial tumor under the borderline subcategory and is pathologically characterized as a rare cystic pancreatic neoplasm (1). The cellular lineage of the tumors is unknown; general theories of histogenesis can be divided into three main groups: pancreatic duct cell origin, acinar cell origin, and primitive cell origin (4). Moreover, some assume that SPNs may originate from genital ridge related cells that are incorporated into the pancreas during organogenesis on the basis of some similarities between SPN and ovarian surface cells and the proximity between genital ridges and the pancreas anlage during early embryogenesis (4). Others have speculated that sex hormones may play a role in the pathogenesis or growth of SPNs because the tumors have a tendency to affect young women and the growth of an SPN in the pancreas seems to be enhanced by pregnancy. Patients with malignant transformation of SPN are often older at presentation and have a male predilection (4).

SPN has distinctive pathologic features. The smaller tumors are organized in solid sheets and nests of cells. However, large tumors contain a mixture of solid, cystic, and pseudopapillary patterns. Solid areas are contain of necrosis, foamy macrophages, cholesterol granulomas, and calcifications and pseudopapillae are supported by hyalinized fibrovascular stalks (2).

Immunohistochemically, SPNs are typically positive for vimentin, neuron-specific enolase (NSE), α-1-antitrypsin, CD10, CD56, progesterone receptors, and β-catenin and negative for chromogranin, epithelial membrane antigen, and cytokeratin (4). Most SPNs have an indolent clinical course, but some of these have malignant potentials, include vascular or perineural invasion, Ki-67 positive, significant cellular pleomorphism, nuclear atypia, increased mitotic activity and increased β-catenin.

According to the WHO classification scheme, SPNs with clear

criteria for malignancy (vascular and nerve sheath invasion or lymph node and liver metastasis) are designated as solid pseudopapillary carcinomas (SPCs) (3). There have been attempts to identify imaging characteristics that aid in differentiating benign SPN from malignant SPC. Recent studies demonstrate that hepatic or peritoneal involvement, main pancreatic duct obstruction, infiltration of pancreatic parenchyma, vascular encasement, focal discontinuity of the capsule, large tumor size (> 6.0 cm) and pancreatic tail location may suggest malignancy of SPN (5, 6). The case reported in our study is consistent with aforementioned findings.

Typical, classic imaging characteristics are a well-encapsulated heterogenous mass with peripheral capsule containing varying amounts of internal hemorrhagic and cystic degeneration, and necrosis (1). Although imaging features of SPN overlap with those of other pancreatic neoplasms, misdiagnosis is common. Internal hemorrhagic and cystic degeneration is the hallmark of SPN owing to the fragile vascular network of the tumor. Therefore the radiologic differential consideration in cases of mixed solid and cystic masses with hemorrhagic components in the pancreas, as in our case, should include cystic neuroendocrine tumor, acinar cell carcinoma (ACC), and mucinous cystadenocarcinoma. First, areas of high signal intensity on T1-weighted images and low or inhomogeneous signal intensity on T2-weighted images, signatures of a hemorrhagic component, may help differentiate SPNs from neuroendocrine tumors, whose cystic components have increased signal intensity on T1- and T2-weighted images (4). Second, ACC of the pancreas typically appears as a well-marginated, exophytic, hypovascular mass which shows less homogenous enhancement than the surrounding pancreas when small, but contains cystic areas owing to necrosis when large. In agreement with clinical manifestations, ACCs can also cause hyperlipasemia, which may lead to diffuse subcutaneous nodules and, interestingly, polyarthropathy (7). Third, mucinous cystadenocarcinoma is typically seen as a predominant cystic pancreatic lesion with intracystic enhancing solid components. However, the signal intensity in the cystic portion of the mass in our case is not as high as that of the mucin component on T1- and T2-weighted MR images. Therefore, our case's lesions favor a diagnosis of SPN owing to a peripheral gradual enhancement pattern within the tumor and internal hemorrhagic components. In other words, despite the

fact that our patient was an older female and the imaging findings were aggressive, SPN should be included in the differential diagnosis in cases of mixed solid and cystic mass with hemorrhagic components in the pancreas.

In general, the diffusion restriction that is seen primarily in malignant tumors is related to the high degree of cellularity and increased amount of macromolecules. Although there is substantial overlap, the mean ADC value of malignant tumors is significant lower than that of benign lesion. Barral et al. (8) reported that SPNs have a lower ADC compared with normal pancreatic parenchyma with a mean ADC of 1.208×10^{-3} mm^2/sec (range: 1.05×10^{-3} mm^2/sec to 2.793×10^{-3} mm^2/sec) at 1.5 T using b values of 0, 500 and 0, 400, 800 sec/mm^2. The mean ADC value of the solid portion in our case (0.932×10^{-3} mm^2/sec) is lower than previously reported data (1.208×10^{-3} mm^2/sec). However ADC values are influenced by a number of factors including the patient, hardware, acquisition related parameters and artifacts related to the susceptibility effect (9). To overcome these matters, standardized diffusion-weighted imaging MR imaging protocols have been made including normalization of ADC values using the normal pancreas and spleen (9, 10). Previous report revealed that normalized ADC using the normal pancreas as a reference organ helps characterize focal pancreatic lesions and further discriminate between pancreatic malignant tumor, benign tumor and mass-forming pancreatitis, measuring in 0.933, 1.807, 0.839 in median, respectively (10). In our case, normalized ADC values using the pancreas as a reference organ was 0.662, which is much lower than that of the malignant tumor (0.933) and mass forming pancreatitis (0.893). The reason for decreased ADC value is probably because the mass has histologically high cellularity, pleomorphism and increased mitosis.

According a recent study, the spleen is an ideal reference organ for normalization of ADC value, and is usually used for quantitative analysis (9). In our case, normalized ADC value using the spleen as reference organ was calculated to be 1.194, lower than that of reported normalized ADC values of the pancreas (1.208). Our report suggests that normalized ADC value may have a potential role in discriminating between benign and malignant SPN.

However, because we only have a single case review, there is limitation for characterization of benign and malignant pancre-

atic pathologies. Thus, further studies are needed.

In summary, SPN with malignant transformation should be included in the differential diagnosis in cases of mixed solid and cystic masses with hemorrhagic components, irregular margin and lower normalized ADC values in old female patients.

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고등급 악성전환을 보인 고형 가유두상 종양의 영상소견 : 확산강조영상 및 표준화 현성확산계수값

강가람[1] · 신옥란[2] · 이수림[1] · 구영미[1]*

췌장의 고형 가유두상 종양은 그 조직 발생에 대해서는 명확히 알려져 있지 않지만, 비교적 낮은 악성도를 보이는 종양으로 주로 젊은 여성에서 호발한다. 일반적으로 경계가 좋고 주변부는 고형 성분으로, 중심부는 출혈성 병소를 포함하는 낭성 성분으로 구성된 비균일한 음영을 가지는 병변으로 보인다. 고등급 악성전환을 보이는 고형 가유두상 종양은 흔하지 않은 변이 형태이다. 저자들은 75세 여성에서 고등급 악성전환을 보인 고형 가유두상 종양의 증례를 보고하고, 감별진단을 하는 데에 있어서 표준화 현성확산계수값의 유용성에 대해 알리고자 한다. 본 증례처럼 고령의 여성에서 명확하지 않은 경계를 보이며, 주위 조직으로의 침범소견을 보이고 출혈성 병소를 포함하며 낮은 표준화 현성확산계수값을 보이는 고형성분이 혼합된 경우, 고형 가유두상 종양의 악성전환을 감별에 포함해야 한다.

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