Islet cell tumors (ICTs) are rare pancreatic neoplasms of neuroendocrine origin, posing a diagnostic challenge to radiologists. We illustrated a spectrum of features of pancreatic ICTs that could be found on multiphase dynamic CT or MRI, and elucidated the histopathologic characteristics by determining the contrast enhancement pattern of the lesions. Various enhancement patterns were dependant on the internal composition of the tumor, that is, the proportion of vascular densities for early enhancement and non-hypervascular interstitial tissue for late enhancement regardless of the size or functional behavior. This knowledge of the imaging-pathologic spectrum of ICTs could be helpful for the proper differential diagnosis from other pancreatic tumors.

Index words : Pancreatic Neoplasms
Tomography, X-ray Computed
Islet Cell Tumor

Imaging Protocol

All multiphase dynamic CT examinations were performed with a conventional helical CT scanner (HiSpeed Advantage; General Electric Medical Systems,
Milwaukee, WI, USA) or a multichannel unit (Somatom Sensation 16; Siemens, Erlangen, Germany). After the intravenous administration of 120–150 mL of nonionic contrast agent, iopamidol (Pamiray, Dongkook Pharmaceutical, Seoul, Korea) with an automatic injector at a rate of 3 mL/s, all patients underwent dynamic CT after pre-contrast imaging. In the multichannel unit, aortic enhancement was performed at the start of arterial phase imaging for 15 seconds at 100 Hounsfield units using the SmartPrep technique. Next, portal phase imaging was conducted 30 seconds after the start of arterial phase imaging. The delayed or equilibrium phase was conducted three minutes after the infusion of contrast media. All scans were acquired in the cephalocaudal direction with 3–5 mm thick image reconstruction.

MRI was performed in a 1.5 T system (Magnetom Vision; Siemens, Erlangen, Germany) using a protocol that includes fast spin-echo T2-weighted imaging (TR/TE = 4,060/138 ms, 8 mm section thickness, 1.4 intersection gap, 29 echo train length) followed by pre- and post-contrast dynamic (arterial, portal and 5-minute delayed phase) imaging using the 2D T1-weighted spoiled gradient echo sequences (TR/TE = 140/2.7 ms, flip angle 90°, 8 mm section thickness). The delay time for arterial and portal imaging was determined by a test bolus examination. Next, gadopentatate dimeglumine (0.1 mmol/kg) was administered with an automatic injector at a rate of 2 mL/s for dynamic imaging. Each imaging procedure was performed during a breath-holding period of 19 to 21 seconds.

Correlation of Histopathology with the Imaging Findings

Early-Enhancing Type

Pancreatic ICTs are usually demonstrated as small early enhancing lesions, so they are often difficult to distinguish from normal pancreatic parenchyma. With the advent of the recent multi-slice and multiphase imaging, there has been drastic improvement in the diagnostic accuracy of small ICTs. It was reported in one study that 71 to 82% of insulinomas could be visualized on dual phase imaging by thin slice multidetector CT (3). The main diagnostic clue comes from the hypervascular nature of ICTs. At least 83% of ICTs appear more hyperdense or partially hyperdense than the adjacent pancreatic parenchyma, whether they are functional or not (3). The exact timing of peak enhancement, however, sometimes appeared to lag, and the degree of contrast enhancement on delayed phases tended to vary.

Fig. 1. A 70-year-old man with a non-functioning islet cell tumor that was found incidentally.
A. A transverse contrast-enhanced CT scan obtained during the arterial phase shows a 3.8 cm, revealed a relatively homogeneous, strongly enhancing mass in the head portion of pancreas (arrowheads).
B. A delayed phase image at the same level as A, showed a markedly decreased attenuation density in the lesion (arrowheads), which is similar to or slightly lower than the intraluminal densities of adjacent vasculatures.
C. A photomicrograph (original magnification × 200, hematoxylin-eosin stain) showed tumor cells with abundant intervening vascular sinusoids (arrowheads).
D. A small vascular structure (arrowhead) in the irregular fibrotic capsule (arrows) was demonstrated. The lesion consists mostly of abundant tumor cells, intervening sinusoids, and scanty fibrotic interstitial space on the photomicrograph (original magnification × 100, hematoxylin-eosin stain).
Early Arterial Phase Enhancement

Regardless of tumor size, most pancreatic ICTs show strong early enhancement at the same time as abdominal aortic enhancement. This takes place before peak enhancement of the background pancreatic parenchyma related to the higher vascular densities in the lesion (Figs. 1, 2) (4). It is asserted that the optimal phase of detection for small hypervascular enhancing ICTs is the early arterial phase (5). A recent CT perfusion study has suggested that such a higher blood flow correlated with a high intratumoral microvascular density would be a histoprognostic factor for lower malignant potential compared with other pancreatic ICTs with smaller blood flow (6).

Lagged Peak Enhancement

In some cases, tumoral peak enhancement did not occur along with aortic enhancement, and peak enhancement was shown on the parenchymal or portal phase images (Fig. 3) (7). The cause of such lagged peak enhancement has not been well described. The recent perfusion CT study has illustrated a case of a pancreatic endocrine tumor with scanty vasculature and low intratumoral blood flow despite distinguishable contrast enhancement of the lesion (6). Therefore, a lag in the peak contrast enhancement of the tumor after peak arterial enhancement would not be related with high vascular density in pancreatic ICTs, and would ultimately reflect enhancement of the extravascular stroma of the tumor (Fig. 3).

As the inherently shorter time window for arterial enhancement resulted from a small amount of contrast material during the dynamic MRI, we should note that there is the possibility of improper image acquisition causing the missing peak tumoral enhancement.

Sustained Enhancement on Delayed Phase Images

Despite the many early-enhancing ICTs that became isodense or isosignal intensity during the delayed phase of dynamic CT or MRI, they cannot be distinguished from the remaining pancreatic parenchyma; this is especially true for small lesions (3). Regardless of the vascu-

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Fig. 2. A 64-year-old woman with functioning insulinoma.
A. Transverse contrast-enhanced CT scan obtained during the arterial phase showed a 1.5 cm homogeneously and strongly enhancing, lobulated mass in the body-tail portion of pancreas (arrowheads).
B. A delayed phase image at the same level as A, showed a sustained contrast enhancement in the lesion (arrowheads).
C. A photomicrograph (original magnification × 200, hematoxylin-eosin stain) showed tumor cells with abundant, variably-sized and intervening vascular sinusoids (arrowheads) in the lesion.
D. Numerous intratumoral thick-walled arterial vasculatures (arrows) were prominently demonstrated on the photomicrograph (original magnification × 200, hematoxylin-eosin stain). Many arterial tumor feeding vessels were also noted in the fibrotic capsule (not shown).
E. Tumoral parenchyma was also found to contain abundant irregular thick fibrous components with sclerotic hyalinized stroma (arrowheads) on the photomicrograph (original magnification × 100, hematoxylin-eosin stain).
lar densities of the tumor, pancreatic ICTs would have
variable degrees of interstitial space composed of hya-
line or amyloid materials intervening in the tumor cells
(8).

In the liver, prolonged enhancement occurs in a mass
with a large extent of interstitial space (9). Compared
with the normal washout of contrast materials from the
tumors without connective tissue stroma (Fig. 1), the
presence of connective tissue stroma could explain pro-
longed contrast enhancement in pancreatic ICTs (Figs.
2, 3).

**Hypovascular or Late-Enhancing Type**

In a minority of pancreatic ICTs, contrast enhance-
ment is not definitely demonstrated in the arterial or
portal phase images of dynamic imaging. Enhancement
of such tumors is gradual or considerably delayed. In
previous reports, abundant amyloid deposits or promi-
nent desmoplastic reactions with relatively smaller vas-
cular volume, were observed in early hypovascular and
rather delayed enhancing insulinomas (8). When a large
proportion of the tumoral component is replaced by hy-
povascular connective tissue stroma, there would be
minimal enhancement on the early phases of dynamic

[Fig. 3. A 48-year-old man with multiple, small, well enhancing insulinomas with
lagged peak enhancement.
A. On the transverse CT scan of the arterial phase, a 0.7 cm small nodular lesion on
the body portion showed slight enhancement (arrowhead).
B. The pancreatic body lesion was more prominently found with strong enhancement
(arrowhead) on the portal phase images of dynamic CT.
C. Prominent contrast enhancement was still present (arrowhead) during the equilib-
rium phase of the post-contrast CT.
D. A photomicrograph (original magnification × 200, hematoxylin-eosin stain) of the
solid lesion shows tumor cells with abundant intervening interstitial spaces of loose fi-
brotic connective tissue. Several small capillary vessels (arrowheads) were scattered in
the connective tissue stroma without prominent sinusoidal vascular spaces.
E. An early phase image of a post-contrast CT scan showed a 1.3 cm cystic lesion surrounded by a thin enhancing wall (arrowhead) in the tail of the pancreas.
F. The pancreatic tail lesion still showed a non-enhancing cystic component surrounded by an enhancing wall (arrowhead) on the equilibrium phase imaging (Reprinted with permission from Lippincott Williams & Wilkins).
G. A photomicrograph (original magnification × 20, hematoxylin-eosin stain) of the cystic lesion showed a cystic space lined by tu-
morous islet cells.]
Fig. 4. A 46-year-old man with an incidentally found nonfunctioning islet cell tumor showed gradual and delayed contrast enhancement during a dynamic CT examination.

A. A post-contrast CT scan obtained during the arterial dominant phase shows a 5 cm well-defined, marginally-enhancing and lobulated mass (arrowheads) in the tail of the pancreas. On the pre-contrast images, the mass demonstrated isoattenuation with the adjacent pancreatic tissue (not shown).

B. On three-minute-delayed-phase CT, markedly higher attenuation density of the mass (arrowheads) permitted the lesion to be well distinguished from the remaining pancreatic parenchyma.

C. The mass is mostly composed of amorphous sclerotic stroma with scanty tumor cells (arrow) on photomicrograph (original magnification × 200, hematoxylin-eosin stain). On Congo-red staining, the mass was hyalinized amyloid stroma (80%), showing birefringence (not shown).

Fig. 5. A 59-year-old man with abdominal pain and jaundice showed a malignant islet cell tumor mimicking a ductal cell adenocarcinoma in the tail of pancreas.

A. On the transverse arterial phase dynamic CT scan, the poorly defined hypovascular lesion (arrowheads) in the tail of pancreas was found to be associated with a retracted contour of pancreatic parenchyma and direct invasion of the splenic vein. Hepatic metastasis showed a relatively high attenuation density due to the low attenuation of background hepatic parenchyma with diffuse fatty infiltration (arrow).

B. Portal phase dynamic CT showed slight enhancement of the pancreatic lesion (arrowheads) with direct invasion of the splenic vein. Ring-like peripheral enhancement of the hepatic lesion (arrow) was also noted.

C. Three-minute-delayed post-contrast CT showed a greater attenuation density of the primary pancreatic lesion with marginal spiculations, suggesting invasive tumor growth (arrowheads).

D, E. A photomicrograph (original magnification × 200; D, hematoxylin-eosin stain; E, trichrome staining) of a sonography-guided liver biopsy specimen shows metastatic pancreatic endocrine tumor cells with abundant intervening thick collagenous bands (arrows).
imaging. However, gradual retention of contrast material in the extracellular interstitial tissue can explain delayed enhancement distinguished from background pancreatic parenchyma with a deficient interstitial volume (Fig. 4). In conjunction with rare invasive features of infiltrative ICTs which spread to adjacent organs and/or distant metastases [1], it is not always easy to differentiate such tumors from common pancreatic cancers of ductal cell origin (Fig. 5).

**Cystic or Hemorrhagic Type**

Nonfunctioning ICTs are typically heterogeneous tumors that are larger than functioning ICTs [3]. Regardless of functioning status, larger tumors are more likely to have cystic degeneration and central areas of necrosis. Cystic change in pancreatic ICTs has been found occasionally with only a 2–3% incidence among pancreatic ICTs [10]. Pathologically, this is explained by the presence of cystic cavities filled with clear fluid or hemorrhage. Moreover, the wall of the cavity is lined with islet cells without sound evidence of necrosis or infarction in most cases [Figs. 3, 6]. Despite the secondary features, contrast enhancement of the solid component depends on the tumoral vasculature and fibrotic stroma in the remaining parenchyma (Fig. 3). In the cases of young women, differentiating a cystic or hemorrhagic ICT from a solid pseudopapillary tumor (SPT) is not always easy. However, the more heterogeneous and less hypervascular nature of SPT could be helpful in differentiating them from ICTs on dynamic imaging studies.

**Conclusion**

In addition to aiding the detection of small lesions, multiphase dynamic CT or MRI can characterize pancreatic ICTs. Pancreatic ICTs have been known as rep-
representatives of hypervascular tumors. However, regard-
less of their size or functional behavior, imaging findings
on pancreatic ICTs vary depending on the internal com-
position. While early hypervascular ICTs show abun-
dant intratumoral vasculature, sustained or delayed en-
hancement is influenced by the amount of interstitial
connective tissue stroma that consists of variable de-
grees of maturity or degenerative changes. Cystic
change takes place during the process of intratumoral
hemorrhagic congestion and/or cystic degeneration,
which is also one of the representative features of pan-
creatic ICTs. The aforementioned pathological knowl-
edge on the various enhancement patterns of pancreatic
ICTs could help radiologists better understand these tu-
mors and perform a differential diagnosis.

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췌장 도세포종양: 다양한 다상역동영상소견과 병리소견과의
상호 관련성-비기능성 종양과 인슐린종을 중심으로

홍유진, 유정식, 박찬일, 권지은, 정재준, 김주희, 김기황

1연세대학교 의과대학 강남세브란스병원 영상의학과
2연세대학교 의과대학 강남세브란스병원 병리과

췌장도세포종양은 췌장의 내분비세포에서 발생하는 드문 종양으로 다양한 영상소견을 보이기 때문에 종종 진단에 어려움을 겪는다. 이 논문에서는 다양한 역동영상소견과 병리소견을 중심으로 한다. 다양한 조영증강패턴을 보이는 종양은 내부구성 요소에 따라 다르며 이를 규정하는 것으로 생각한다. 다양한 조영증강패턴은 다양한 영상소견의 연관성을 보이고, 이를 규정하는 것으로 생각한다.