



Differential Diagnosis of Pancreatic Cancer and its Mimicking Lesions

췌장암 및 췌장암으로 오인할 수 있는 병변의 감별진단

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Pancreatic cancer is usually detected through contrast-enhanced CT and MRI. However, pancreatic cancer is occasionally overlooked because of its small size or is misdiagnosed as other conditions due to atypical imaging features that present diagnostic challenges. Considering the rapid growth and poor prognosis associated with pancreatic cancer, the ability to accurately detect and differentiate pancreatic lesions is crucial for appropriate surgical intervention. Reviewing diverse challenging cases of pancreatic cancer at an early stage and other mimicking lesions may help us accurately interpret the imaging features of pancreatic cancer on CT and MRI scans. Therefore, we aimed to illustrate various imaging features of pancreatic cancer and its mimicking lesions and provide valuable insights for differential diagnosis.

Index terms Pancreas; Carcinoma; Computed Tomography; Magnetic Resonance Imaging

INTRODUCTION

Pancreatic ductal adenocarcinoma (i.e., pancreatic cancer) is a catastrophic disease with a 5-year overall survival rate of <10%, and its incidence is increasing by approximately 0.5% per year (1, 2). Despite recent developments in its detection, management, and treatment, <30% of patients with pancreatic cancer undergo curative resection (2), and their prognosis is grim (3). Most patients with pancreatic cancer show symptoms in the late stages of the disease and are asymptomatic in the early stages (4).

Although pancreatic ductal adenocarcinoma is the most common malignancy of the pancreas, diagnosing pancreatic cancer and mimicking lesions is sometimes challenging owing to the complicated anatomical relationships between the variable structures. These anatomical structures often mimic pancreatic cancer (5) and various diseases, including pancreatic neuroendocrine tumors, lymphoma, metastasis,

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and inflammatory lesions, can overlap with the imaging findings of pancreatic cancer (4, 6).

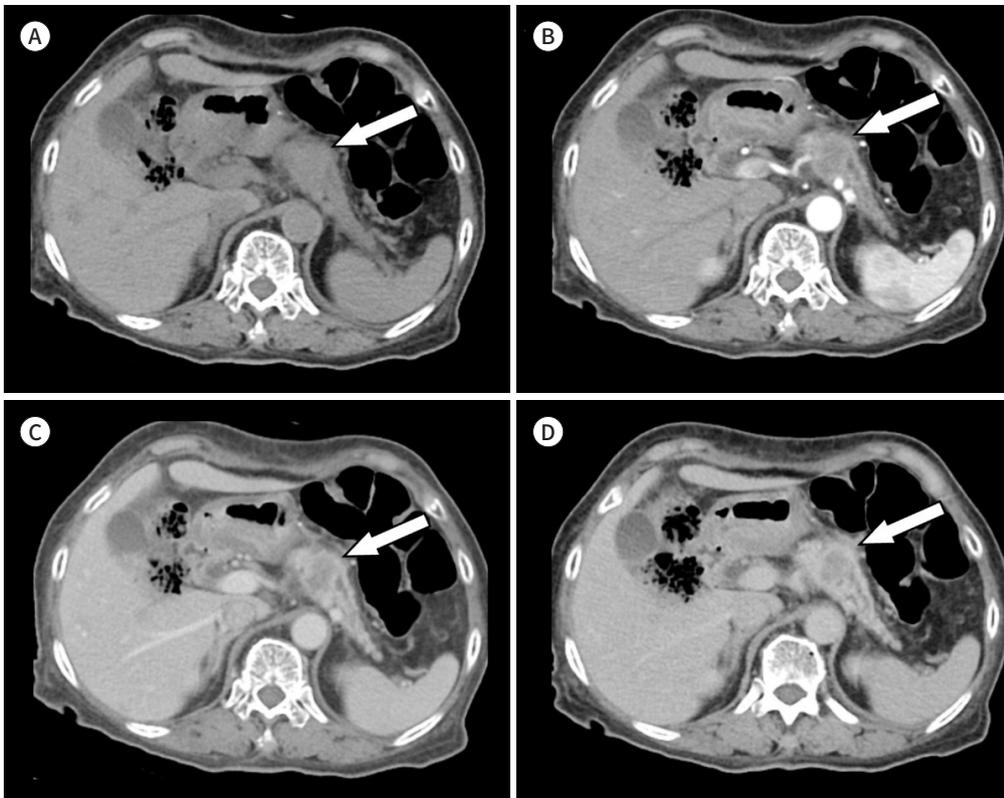
A multimodal imaging approach, including CT, MRI, and endoscopic ultrasonography, may be helpful in diagnosing pancreatic cancer (7). Awareness of the various imaging findings of pancreatic cancer is important for differentiating it from other pancreatic lesions, enabling accurate diagnosis and treatment. Therefore, we reviewed various pancreatic cancers and their associated lesions.

PANCREATIC CANCER WITH TYPICAL IMAGING FEATURES

Typical imaging features of pancreatic cancer on dynamic CT include a hypoattenuating mass compared with the adjacent pancreatic parenchyma in the late arterial and portal venous phases due to decreased vascularity within the tumoral tissue and desmoplastic stroma (Fig. 1) (8). Pancreatic cancer exhibits a desmoplastic reaction, reflecting its dense fibrous stroma, disorganized growth pattern, and obstructive features (9, 10). Upstream pancreatic duct dilatation, pancreatic atrophy, and perilesional infiltration are common (Fig. 1) (8). An abrupt pancreatic duct cut-off sign is associated with an increased incidence of pancreatic cancer (11). However, if the lesion is located in the tail, uncinate process, or outside the path-

Fig. 1. Typical imaging features of pancreatic cancer in a 79-year-old female patient with uncontrolled diabetes mellitus and elevated CA19-9 levels (3009.95 U/mL).

A-D. Axial pre- (A), arterial- (B), portal- (C), and delayed (D) phase images of multiphase CT show a 3.0-cm ill-defined low-attenuating mass (arrows) in the pancreatic body with upstream pancreatic duct dilatation, pancreatic tail atrophy, and peripancreatic infiltration suggestive of pancreatic cancer. The lesion was confirmed to be a pancreatic cancer (ductal adenocarcinoma) after fine-needle aspiration.



way of the pancreatic duct, pancreatic cancer may not show ductal dilatation.

PANCREATIC CANCER WITH ATYPICAL IMAGING FEATURES

Some pancreatic cancers present with atypical imaging features that can lead to misdiagnosis. Atypical imaging features include isoattenuating mass (Fig. 2), cystic change, multifo-

Fig. 2. Isoattenuating pancreatic cancer in a 66-year-old male patient with icteric sclera and elevated direct bilirubin (14.91 mg/dL) and CA 19-9 levels (111.97 U/mL).

A-D. Axial pre- (**A**), arterial- (**B**), portal- (**C**), and delayed-phase (**D**) CT images show interruption of the pancreatic duct in the head and neck portion (arrows) with upstream pancreatic duct dilatation without a visible obstructive mass, possible iso-attenuating pancreatic cancer.

E. Axial fat suppression T1-weighted image on portal venous phase shows a about 3.0 cm sized focal low signal intensity lesion (arrow) in the pancreatic head with duct dilatation.

F. The diffusion-weighted image and apparent diffusion coefficient map (not shown) reveal a about 3.0 cm sized mass (arrow) with diffusion restriction, suggesting pancreatic cancer. The patient underwent pancreaticoduodenectomy (Whipple operation) and was diagnosed with pancreatic cancer (ductal adenocarcinoma).

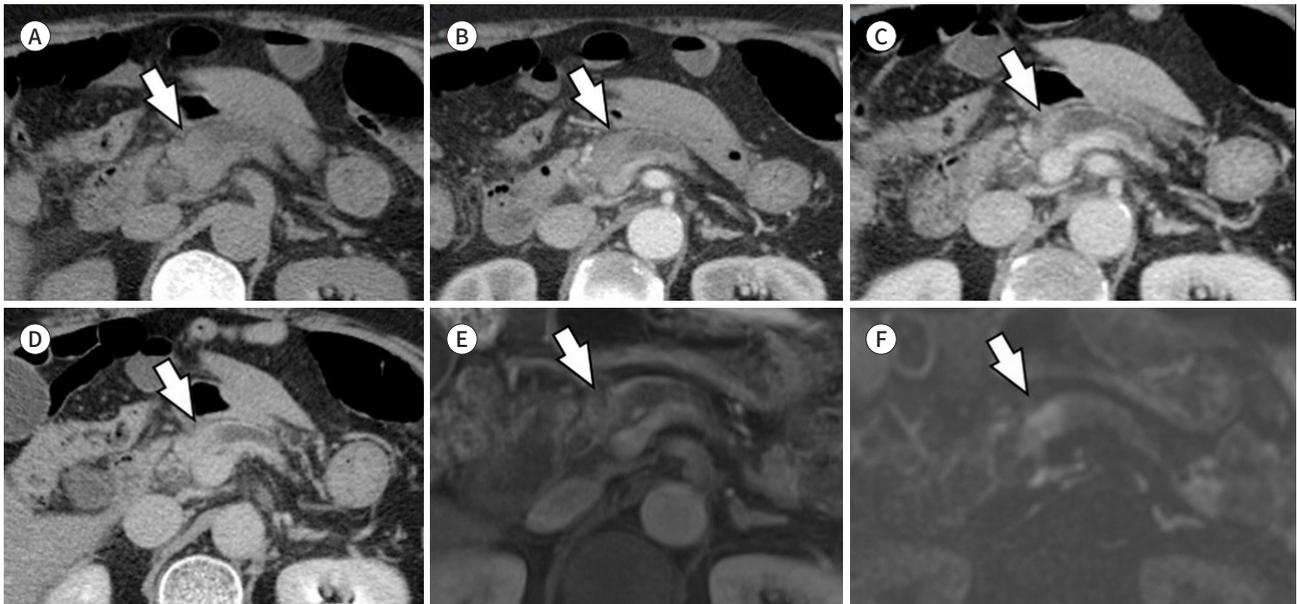
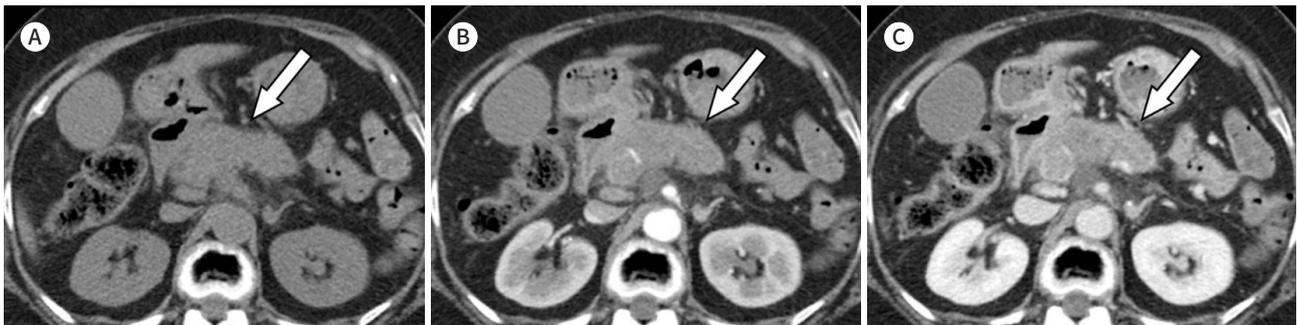


Fig. 3. Diffuse infiltrative pancreatic cancer in a 79-year-old female patient with epigastric pain and elevated CA 19-9 levels (> 7000.00 U/mL).

A-C. Axial pre- (**A**), arterial- (**B**), and portal- (**C**) phase multiphase CT images show a diffuse infiltrative, heterogeneous density lesion in the pancreatic head and body (arrows). Invasion of the celiac axis, common hepatic artery, distal main portal vein, portomesenteric junction, and superior mesenteric vein are also shown, suggesting an unresectable pancreatic cancer. The lesion was confirmed as pancreatic cancer (ductal adenocarcinoma) after fine-needle aspiration.



cal masses, diffuse infiltrative lesion (Fig. 3), and associated with pancreatitis (Fig. 4) (12, 13). Pancreatic cancer in patients with chronic pancreatitis and multiple pseudocysts can be misdiagnosed as inflammatory nodules (Fig. 4). Small pancreatic cancers do not exhibit pancreatic duct dilatation (Figs. 5-8).

Isoattenuating pancreatic cancer, with attenuation similar to that of the surrounding normal parenchyma (within 10 Hounsfield units) on late arterial- and portal venous-phase imaging, can be challenging. These cancers account for an incidence of approximately 5.4%–14% in cases of pancreatic duct adenocarcinoma (14, 15). Isoattenuating pancreatic cancer is a mass that is not visible on dynamic CT and is detectable only on ancillary imaging (14, 16). Ancillary imaging findings include dilatation of the pancreatic duct with abrupt luminal narrowing, narrowing of the distal common bile duct with upstream dilatation of the bile duct, disruption of the pancreatic duct with atrophy, and mild infiltration of the upstream pancreas (14). If isoattenuating pancreatic cancer is suspected based on the CT images, pancreatic MRI may be useful as a subsequent examination to diagnose pancreatic cancer. Dynamic MRI is superior to dynamic CT in the detection of isoattenuating pancreatic cancer (16). Visually isoattenuating pancreatic cancers show low signal intensity (SI) on non-enhanced T1-weighted image (T1WI) and variable SI on T2 weighted image (T2WI), depending on their desmoplastic

Fig. 4. Pancreatic cancer in an 88-year-old female patient with chronic pancreatitis, obstructive jaundice, and elevated CA19-9 levels (174.50 U/mL).

A-C. Axial arterial- (**A**), portal- (**B**), and coronal portal- (**C**) phase images of multiphasic CT show a 1.8-cm low attenuating nodule (arrows) in the pancreatic head with an upstream pancreatic duct, bile duct dilatation, and gall bladder distension.

D. The axial portal phase image of multiphasic CT reveals diffuse calcifications and atrophic changes in the whole pancreas, suggestive of underlying chronic pancreatitis. Both pancreatic head cancer and inflammatory nodules could possibly be associated with chronic pancreatitis. The lesion was confirmed to be a pancreatic cancer (ductal adenocarcinoma) after fine-needle aspiration.

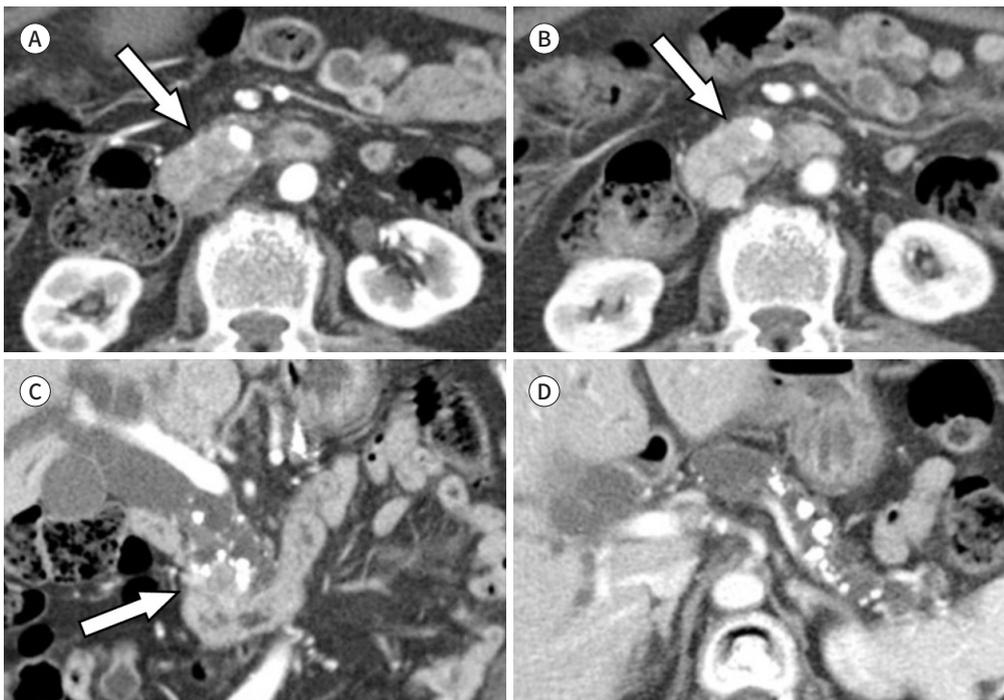


Fig. 5. Small pancreatic cancer in a 79-year-old female patient with gross hematuria, weight loss (13 kg/1 year), and diabetes mellitus. **A-C.** Axial pre- (**A**), portal (**B**), and coronal portal (**C**) phase CT images show a 0.9-cm low-attenuation lesion (arrows) in the pancreatic body without pancreatic duct dilatation and with distal parenchymal atrophy. Although the radiologist initially interpreted pancreatic cancer, the clinician did not evaluate pancreatic lesions at that time. **D-F.** After 5 months, axial pre- (**D**), arterial- (**E**), and coronal portal- (**F**) phase CT images show an interval increased size (0.9-cm to 2.5-cm) of the low-density lesion (arrows) in the pancreatic body with aggravation of distal parenchymal atrophy (gray arrow), suggesting probable pancreatic cancer. The patient underwent a distal pancreatectomy and was diagnosed with pancreatic cancer (ductal adenocarcinoma).

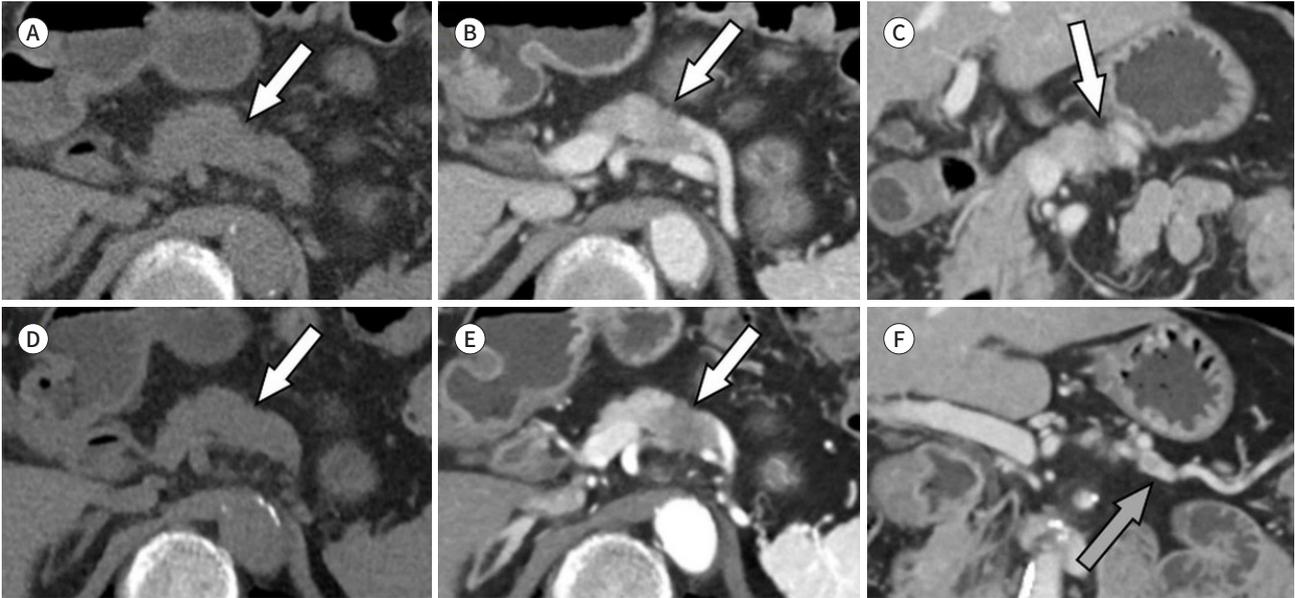


Fig. 6. Small pancreatic cancer in a 68-year-old male patient with history of early gastric cancer with endoscopic submucosal dissection in 2017, weight loss (7 kg/1 month), and elevated CEA levels (6.76 ng/mL).

A-F. The patient underwent regular CT examinations for early gastric cancer. Follow-up axial arterial (**A**), portal (**B**), and coronal portal (**C**) phase CT images show a 1-cm low-attenuation lesion (arrow) in the arterial phase (**A**), but not in the portal venous phase (**B, C**). The radiologist had not detected the lesion at that time. However, after 9 months, the axial arterial (**D**), portal (**E**), and coronal portal (**F**) phase CT images show a low-attenuation lesion (arrows) with an interval increased in size (1-cm to 3-cm) and invasion of the celiac axis, intact gastroduodenal artery, and proper hepatic artery, suggestive of borderline resectable pancreatic cancer. The patient underwent distal pancreatectomy with celiac artery resection (AppleBy Operation) and was diagnosed with pancreatic cancer (ductal adenocarcinoma).

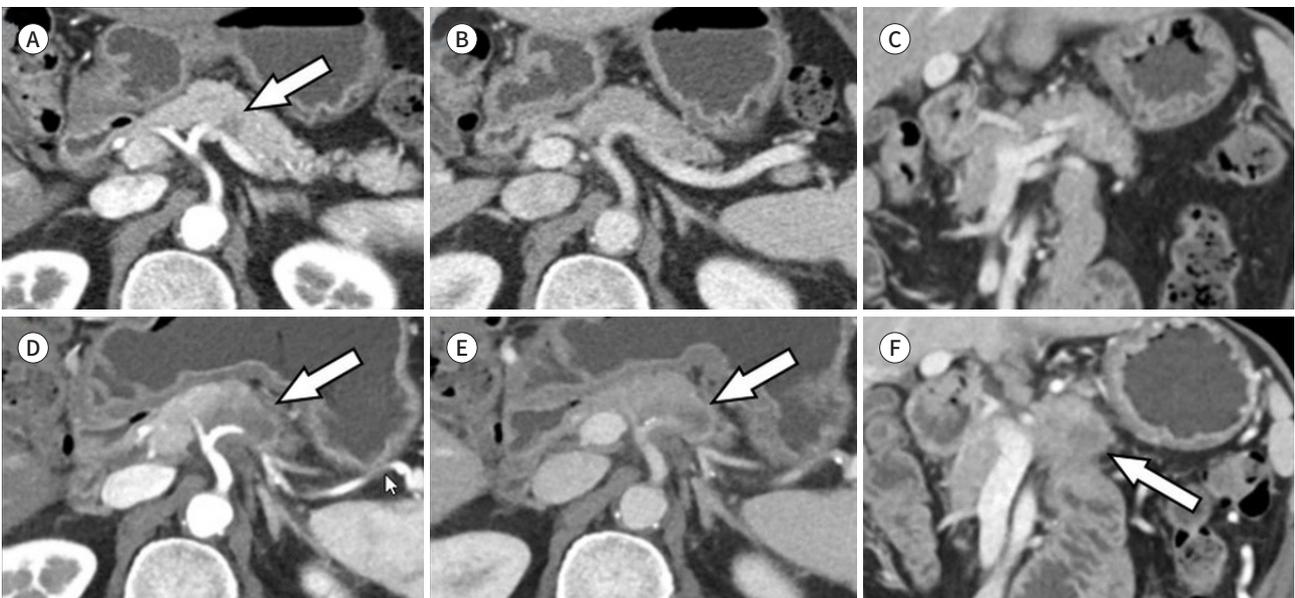
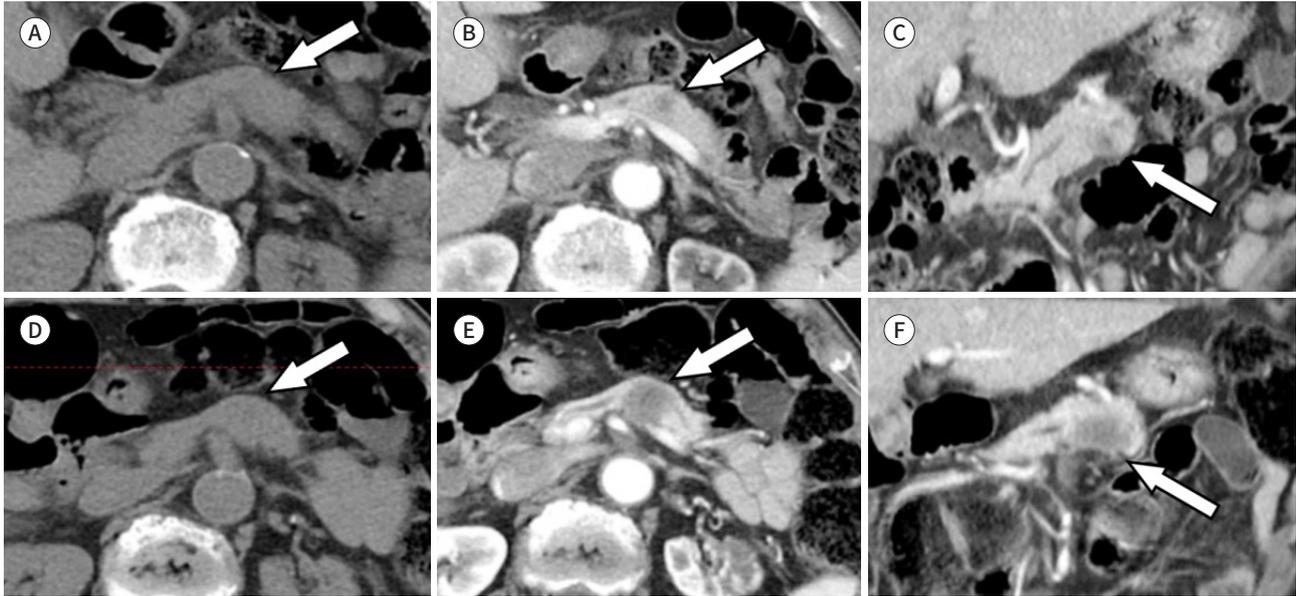


Fig. 7. Small pancreatic cancer in an 85-year-old male patient with abdominal pain and a history of superior mesentery artery and left renal artery occlusion.

A-C. Initial axial pre- (A), portal (B), and coronal portal (C) CT images show a 1-cm low-attenuation lesion (arrows) with mild pancreatic duct dilatation in the pancreatic body in the portal venous phase (B, C). However, the radiologist initially missed a small pancreatic lesion. **D-F.** Five-month follow-up axial pre- (D), portal- (E), and coronal portal-phase (F) CT images reveal an interval increase in the size (1-cm–2.2-cm) of a low-attenuation mass (arrows) in the pancreatic body with mild pancreatic duct dilatation, suggestive of pancreatic cancer. The lesion was confirmed to be a pancreatic cancer (adenocarcinoma) after fine-needle aspiration.



components. Diffusion-weighted imaging and apparent diffusion coefficient maps are helpful for increasing the sensitivity of visually isoattenuating pancreatic cancer detection (Fig. 2) (17).

Diffuse infiltration of pancreatic cancer involves more than half of the longest axis of the pancreatic parenchyma, with a normal or minimally dilated pancreatic duct (Fig. 3) (13). Diffuse infiltrative masses usually suggest malignancy or inflammatory processes, including pancreatic cancer or metastasis, lymphoma, autoimmune pancreatitis (AIP), or pancreatitis (18). When older patients exhibit first-time pancreatitis with diffuse infiltration, pancreatic cancer cannot be ruled out.

Small pancreatic cancer (<1 cm) without pancreatic duct dilatation can either be missed or found incidentally during regular surveillance CT examinations. It presents with ill-defined margins and a hypoattenuating nodule, without pancreatic duct dilatation (Figs. 5-8) (19). Usually, these tumors are smaller than typical pancreatic cancers and are difficult to distinguish from the surrounding parenchyma (20). Radiologists often miss pancreatic cancer on CT when the lesion is small or shows enhancement similar to that of the adjacent normal pancreas in the portal venous phase, with a visible lesion only in the late arterial phase without ancillary features. Small pancreatic cancers can show focal distal atrophy, focal duct cut-off, and vascular encasement or narrowing. These missed cancers detected after several follow-up CT scans are larger in size (Fig. 9) (21). MRI revealed low-SI lesions on T1WI with diffusion restriction and hypoenhancement on gadoteric acid-enhanced images, whereas the pancreatic parenchyma exhibited high SI on T1WI (Fig. 8).

Fig. 8. Small pancreatic cancer in a 62-year-old female patient with history of non-small cell lung cancer (adenocarcinoma) and breast cancer (invasive ductal carcinoma).

A, B. The patient underwent regular CT for lung cancer. Follow-up CT, axial arterial- (**A**) and portal-phase (**B**) CT images show minimal focal pancreatic duct dilatation in the pancreatic portion.

C, D. Axial arterial (**C**) and portal (**D**) phase CT images after 1 month show a 1.7-cm ill-defined nodule (arrows) in the pancreatic tail portion with persistent pancreatic duct dilatation, raising suspicion of pancreatic tail cancer or neuroendocrine tumor.

E. Pre-contrast T1 weighted image shows a focal low signal intensity lesion in pancreatic tail portion.

F. Fat suppression T1-weighted image on late arterial phase shows a 1.4-cm focal nodular lesion (arrow) with distal duct dilatation.

G. T2-weighted image shows focal pancreatic duct dilatation in the tail portion.

H. The diffusion-weighted image and apparent diffusion coefficient map (not shown) show a nodule with diffusion restriction, suggestive of pancreatic cancer with obstructive pancreatitis. The patient underwent a distal pancreatectomy, and the lesion was confirmed to be an invasive micropapillary carcinoma.

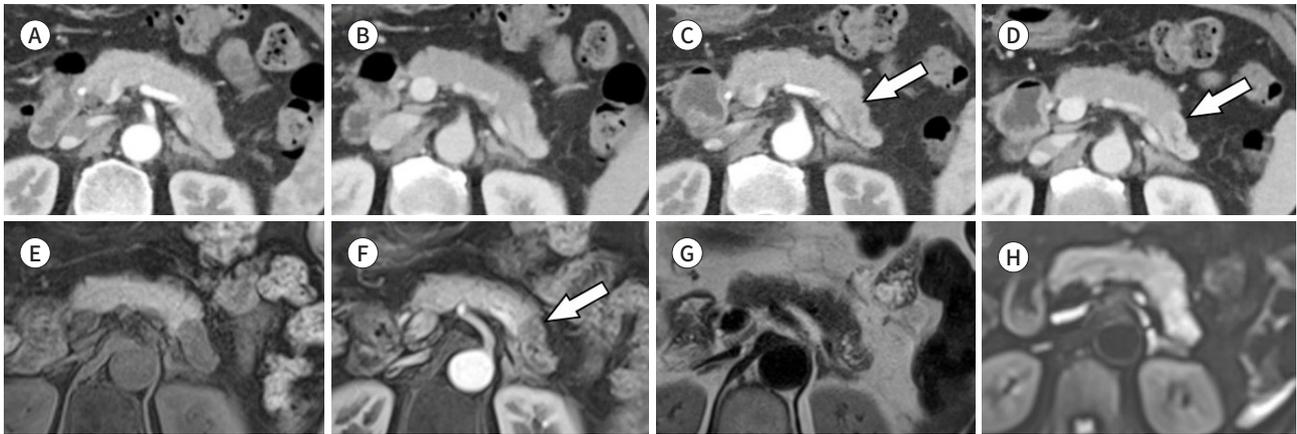
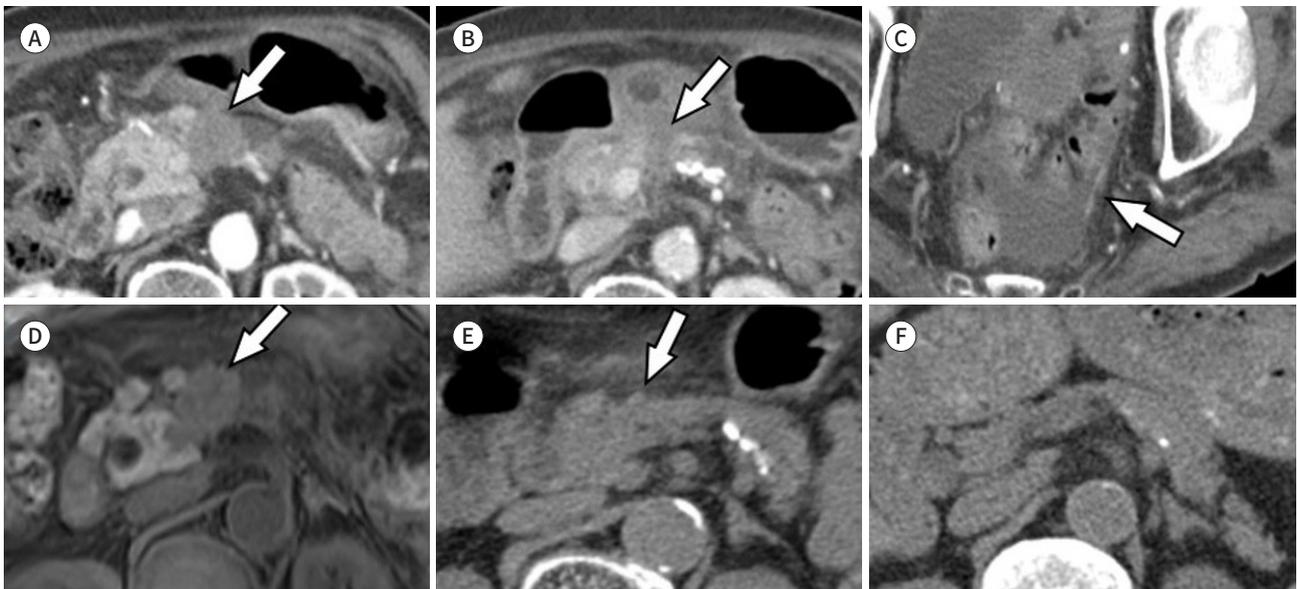


Fig. 9. Pancreatic cancer in an 83-year-old female patient with abdominal discomfort, uncontrolled diabetes mellitus, and elevated CA19-9 levels (6877.95 U/mL).

A-C. Axial arterial (**A**) and portal venous (**B, C**) phase CT images show a 2-cm ill-defined low attenuating mass (arrows) with pancreatic duct dilatation and parenchymal atrophy in the pancreatic body (**A, B**), and peritoneal seeding lesions and malignant ascites (arrow) can be seen (**C**).

D-F. T1-weighted Dixon water-only image (**D**) also shows a 2-cm pancreatic body cancer (arrow). The lesion was confirmed to be a pancreatic cancer (ductal adenocarcinoma) after fine-needle aspiration. After reviewing previous CT images, including chest CT, an increase in pancreatic volume was observed on chest CT obtained 1 year prior (arrow) (**E**) compared with a CT scan from 3 years prior (**F**). The patient developed uncontrolled diabetes mellitus a year prior. Pancreatic cancer was suspected because an abnormal volume increase was observed a year prior based on the history of imaging features.



CONDITIONS MIMICKING PANCREATIC CANCER

AUTOIMMUNE PANCREATITIS

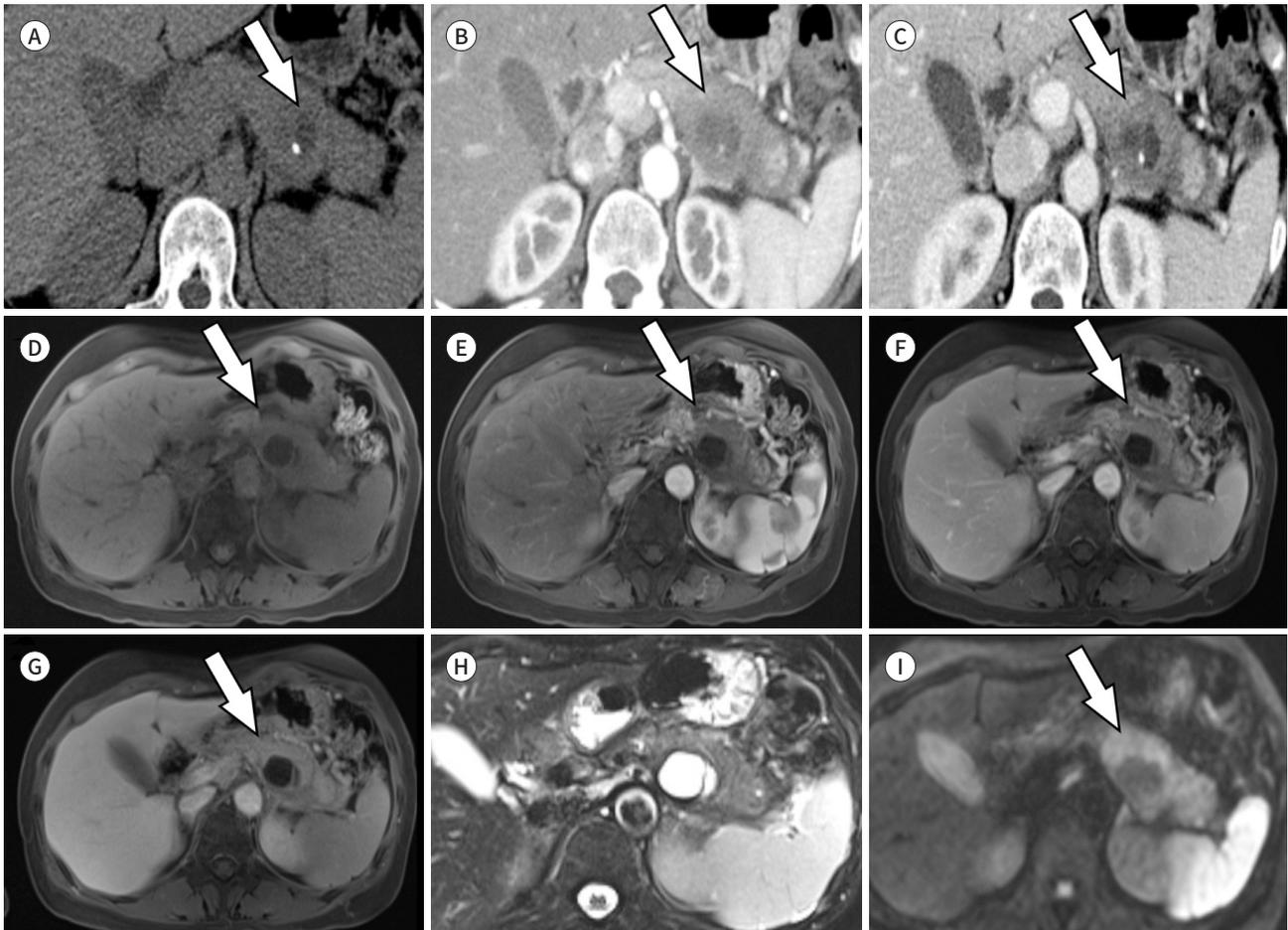
AIP is a rare type of chronic pancreatitis and benign fibroinflammatory disease (22) with two different morphological imaging patterns (23). One is the diffuse form, where CT imaging revealed an enlarged sausage-like appearance of the pancreas with delayed enhancement of the pancreatic parenchyma and a low-density capsule-like rim with gradual enhancement (24, 25), characteristics typically not confused with pancreatic cancer. The second pattern is a focal form presenting as a well-circumscribed focal mass, retraction of the pancreatic tail, and irregular narrowing of the pancreatic duct, mimicking pancreatic cancer (Fig. 10) (22, 25). Indicative of AIP are imaging findings such as irregular narrowing of the pancreatic duct with minimal upstream pancreatic duct dilatation (i.e., duct-penetrating sign), multiple pan-

Fig. 10. Autoimmune pancreatitis in a 53-year-old female patient with left flank pain.

A-C. Axial pre- (**A**), arterial- (**B**), and portal- (**C**) phase images of multiphasic CT show a 6.7-cm oval-shaped low-attenuating mass (arrows) with solid and cystic components and internal calcification in the pancreatic tail, suspected to be either pancreatic cancer or a solid pseudopapillary tumor with hemorrhagic degeneration.

D-H. Gadoxetic acid-enhanced pre- (**D**), arterial- (**E**), portal- (**F**), transitional- (**G**) and T2-weighted image with fat suppression (**H**) phase MR images show a 6.7-cm mass with a thick peripheral rim with progressive enhancement (arrows), solid and cystic components, and internal calcification in the pancreatic tail.

I. The diffusion-weighted image and apparent diffusion coefficient map (not shown) reveal a mass with partial diffusion restriction (arrow).



creatic lesions, and a fibrotic component of chronic pancreatitis showing progressive and persistent delayed enhancement (24, 25).

PANCREATIC NEUROENDOCRINE TUMOR

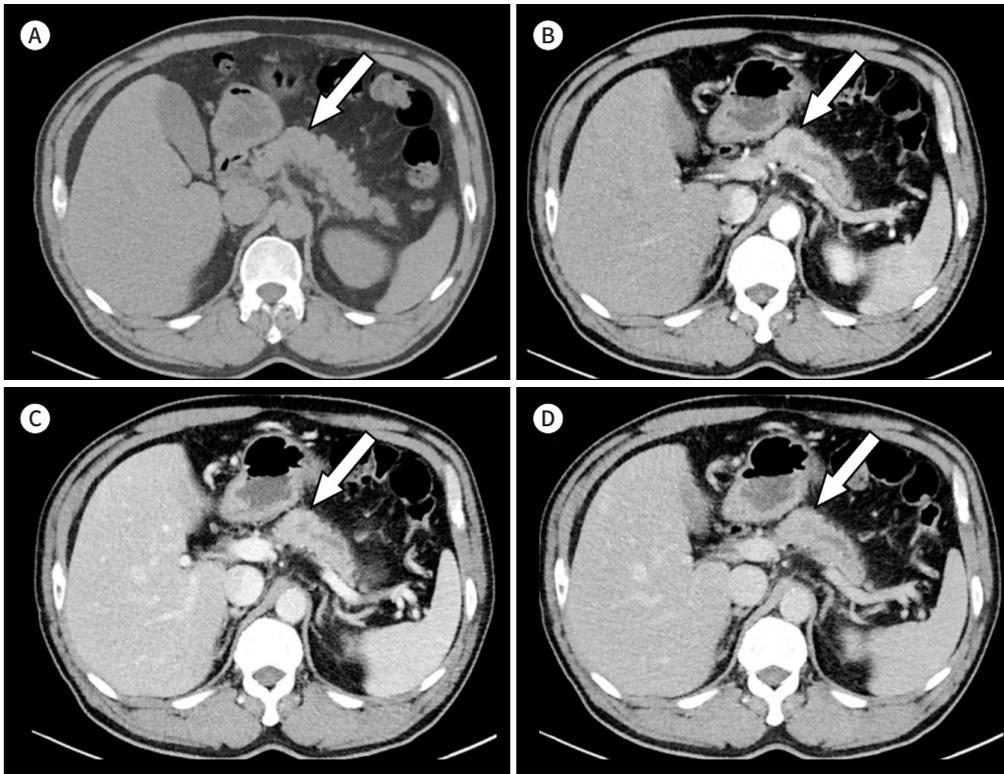
Pancreatic neuroendocrine tumors account for approximately 2% of detected pancreatic tumors (26). Although the typical imaging features of pancreatic neuroendocrine tumors include small (<3 cm) hypervascular lesions with avidly solid enhancement in the arterial phase and persistent enhancement in the portal venous phase, atypical pancreatic neuroendocrine tumors show hypovascular lesions with pancreatic or bile duct dilatation, making them difficult to distinguish from pancreatic cancer (7, 26, 27) (Fig. 11).

LYMPHOMA

Primary pancreatic lymphoma is an extremely rare disease, accounting for 0.1% of all malignant lymphomas and 0.2% of all pancreatic tumors (28). A lymphoma involving the splenic hilum abutting the pancreatic tail can mimic pancreatic malignancy. CT findings of pancreatic lymphoma reveal localized or well-defined hypovascular mass-like lesions with or without minimal ductal dilatation (29). Imaging features include large mass lesions with delayed homogeneous enhancement patterns, peripancreatic fat infiltration, and surrounding ves-

Fig. 11. Atypical pancreatic neuroendocrine tumor mimicking pancreatic cancer in a 50-year-old male patient who was transferred from a local clinic for suspected pancreatic cancer.

A-D. Axial pre- (A), arterial- (B), portal- (C), and delayed- (D) phase images of multiphasic CT show a 1.0-cm ill-defined low-attenuating nodule (arrows) in the pancreatic body with upstream pancreatic duct dilatation suggestive of pancreatic cancer. However, fine-needle aspiration confirmed that the lesion was a pancreatic neuroendocrine tumor.



sels without obliteration (Fig. 12) (30). Pancreatic lymphoma rarely presents with dilatation of the common bile duct or pancreatic duct, posing a challenge in differentiation from pancreatic cancer (29). However, the presence of multiple enlargements of lymph nodes in other abdominal areas and splenomegaly supports the evidence of lymphoma (29, 30). A rare form of lymphoma involves diffuse infiltration with enlargement or replacement of almost the entire pancreas, which can easily be mistaken for acute pancreatitis (29).

UNEVEN FATTY CHANGE IN THE PANCREAS

Focal, uneven fatty changes typically occur in the anterior part of the pancreatic head, sparing the uncinate process (31). Some less experienced radiologists may misinterpret the

Fig. 12. Lymphoma mimicking pancreatic cancer in a 60-year-old female patient with obstructive jaundice, abdominal pain, and elevated CA-125 levels (76.2 U/dL).

A-C. Axial pre- (**A**) and portal (**B**) phase images of multiphase CT show peripancreatic soft tissue infiltration (arrow), and coronal portal (**C**) phase image reveals a 3.5 cm ill-defined low-density lesion (gray arrow) in the pancreatic tail abutting the spleen and stomach, suggesting a possible diagnosis of metastatic cancer infiltration or pancreatic tail cancer. The patient underwent laparoscopic exploration with tissue biopsy, partial omentectomy, and appendectomy and was diagnosed with grade 1 follicular lymphoma.

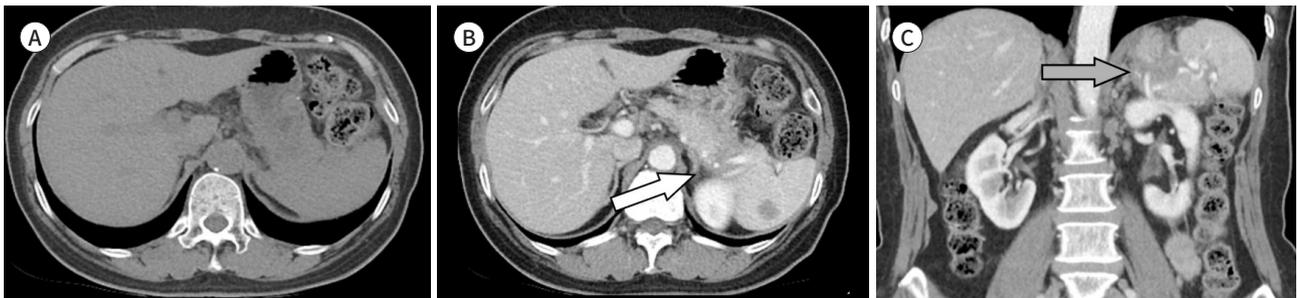
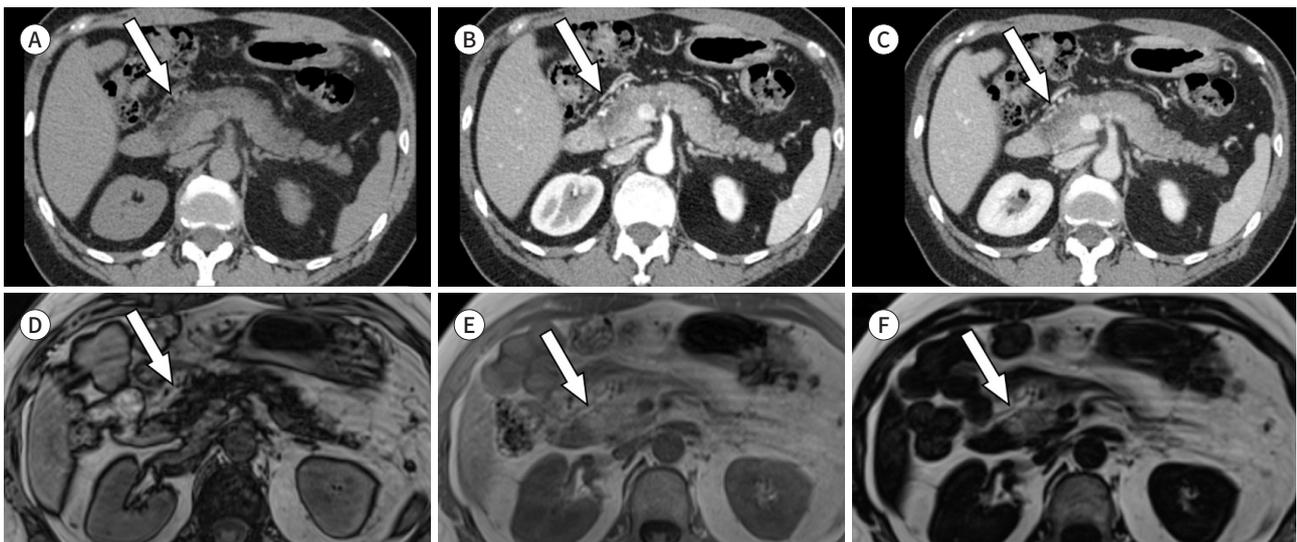


Fig. 13. Focal uneven fatty change in the pancreas of a 51-year-old female patient who was transferred from a local clinic for suspected pancreatic cancer.

A-C. Pre- (**A**), arterial- (**B**), and portal-phase (**C**) CT images show a 3-cm low-attenuation lesion (arrows) in the pancreatic head without pancreatic duct dilatation or abnormal enhancement in the portal venous phase.

D-F. Pancreatic MR images of the chemical shift-opposed phase (**D**), chemical shift-in phase (**E**), and Dixon fat only (**F**) reveal the mass (arrows) harboring fat-containing lesions with a signal decrease in the opposite phase (**D**).



low-density uneven fatty changes observed on CT as pancreatic cancer and refer patients to tertiary hospitals (Fig. 13). Focal fatty changes in the pancreatic head on CT reveal a low-density mass penetrating the main pancreatic duct without pancreatic duct dilatation and with a normal contour of the pancreatic parenchyma (32). However, when the lesion is small (<1 cm) with low density in the pancreas on CT, it may be challenging to differentiate focal uneven fatty changes from pancreatic cancer or small cystic lesions. Pancreatic MRI, including fat-suppressed and non-fat-suppressed T2WI and Dixon-type sequences, can help detect fat components and exclude pancreatic cancer (5).

SMALL CYSTIC LESION IN THE PANCREAS

Advancements in imaging techniques, such as high-spatial-resolution CT scans, have increased the detection rates of various pancreatic cystic lesions (33). However, small (<0.5 cm) pancreatic cysts presenting as low-density lesions on CT can be difficult to differentiate from focal uneven fatty changes or pancreatic cancers. Pancreatic cystic lesions range from benign entities to malignant tumors and are differentiated by imaging features, including cyst morphology, communication with the pancreatic duct, and location, size, and number (6, 33). Pancreatic MRI is useful for evaluating whether a lesion is a cyst and determining its characteristics (Fig. 14) (6).

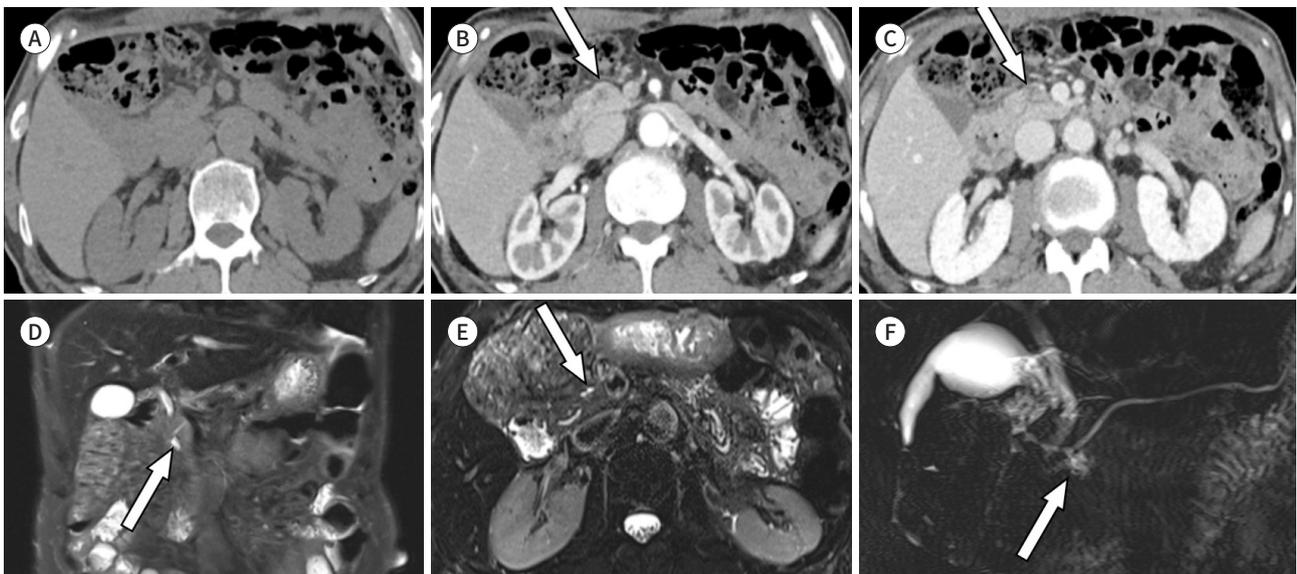
CONCLUSION

Reviewing various challenges, including cases of pancreatic cancer and mimicking diseases-

Fig. 14. Small cystic lesion in the pancreas of an 82-year-old male patient who was transferred from a local clinic for suspected pancreatic cancer.

A-C. Pre- (A), arterial- (B), and portal-phase (C) CT images show a 1-cm ill-defined low-attenuation lesion (arrows) without pancreatic duct dilatation in the pancreatic head. The lesion could not be evaluated by CT because of its small size. Therefore, the patient underwent pancreatic MRI for further evaluation.

D-F. Coronal T2-weighted image with fat suppression (D), axial fat suppression T2-weighted image (E), and MR cholangiopancreatography (F) show a well-defined high signal intensity lesion (arrows) with a connection to the main pancreatic duct, suggestive of a benign cystic lesion, such as a branch-duct type intraductal papillary mucinous neoplasm or pseudocyst.



es may assist us in accurately interpreting diagnoses on CT and MRI.

Author Contributions

Conceptualization, P.S.H.; data curation, Y.D.H., Y.S.; visualization, P.S.H.; writing—original draft, Y.D.H.; and writing—review & editing, P.S.H.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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췌장암 및 췌장암으로 오인할 수 있는 병변의 감별진단

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췌장암은 일반적으로 조영증강 컴퓨터단층촬영이나 자기공명영상에서 발견된다. 그러나 췌장암은 작은 크기 때문에 종종 놓치거나 비 특이적인 영상 소견으로 인해 진단이 어려워지면 서 다른 질환으로 오인하게 된다. 급격히 커지고 예후가 좋지 않은 췌장암의 특성을 고려했 을 때, 췌장 병변을 정확하게 발견하고 해석하는 것은 적절한 관리 및 수술을 위해 중요하다. 다양한 까다로운 췌장암 초기 소견과 췌장암으로 오인하기 쉬운 병변에 대한 사례들을 살펴 보는 것은 컴퓨터단층촬영이나 자기공명영상에서 췌장암을 정확하게 진단하는데 도움이 될 것이다. 따라서, 본 임상화보에서는 다양한 췌장암 및 췌장암으로 오인할 수 있는 병변의 영 상 소견과 감별진단에 도움이 되는 유용한 정보를 소개하고자 한다.

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