Review Article

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Basic pancreatic lesions: Radiologic-pathologic correlation

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ABSTRACT

The basic pancreatic lesions include location, size, shape, number, capsule, calcification/calculi, hemorrhage, cystic degeneration, fibrosis, pancreatic duct alterations, and microvessel. One or more basic lesions form a kind of pancreatic disease. As recognizing the characteristic imaging features of pancreatic basic lesions and their relationships with pathology aids in differentiating the variety of pancreatic diseases. The purpose of this study is to review the pathological and imaging features of the basic pancreatic lesions.

Key words: pancreatic diseases, pancreatic neoplasms, pancreatitis, pancreatic ducts, magnetic resonance imaging, computed tomography, radiology, pathology

INTRODUCTION

The pancreas is an important organ in the human body, consisting of two organs in one: an exocrine gland and an endocrine gland.[1] Pathological characteristics of basic pancreatic lesions include location, size, shape, number, capsule, calcification/calculi, cystic degeneration, fibrosis, duct alterations, and microvessel.[2,3] These pathological characteristics are reflected in radiological images. The spectrum of pancreatic diseases is extensive, including pancreatitis and neoplasm. Chronic pancreatitis (CP) and serous cystic neoplasm (SCN) are characterized by calcification. Pancreatic calcification/calculi in CP are mostly found in the main ducts, side branches, or parenchyma.[4,5] SCN is characterized by the typical central stellate scar that calcium is frequently shown.[6] Hemorrhage mainly occurs in solid-pseudopapillary neoplasm (SPN).[7] CP and pancreatic ductal adenocarcinoma (PDAC) are characterized by pancreatic duct alterations.[8,9] "String of pearls" appearance of main duct is found in CP.[10] "Double-duct sign" or "cutoff sign" is found in PDAC.[11] In pancreatic cystic neoplasms, SCN was mainly multilocular and multiseptal,[12] while mucinous cystic neoplasm (MCN) was mainly large and unilocular,[13] and Intraductal papillary mucinous tumors (IPMN) is communicated with the main duct.[14] The blood supply of the lesion is also a key clue to our diagnosis. Most pancreatic neuroendocrine tumors (pNETs) are significantly enhanced in late arterial or portal phase,[15] while most PDAC shows no significant enhancement or the mild progressive enhancement.

However, radiologists start to analyzes the imaging findings of various basic pancreatic lesions and then combine these imaging findings with the relevant pathological characteristics to give the final diagnosis. So, it is very important to understand the pathological mechanism and imaging findings of the basic pancreatic lesions for the accurate diagnosis of pancreatic diseases. However, previous literatures have focused on the imaging findings of a pancreatic disease. Therefore, the main purpose of this paper is to comprehensively review the pathologic and radiologic characteristics of the basic pancreatic lesions and improve the understanding of these common pancreatic diseases.

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LOCATION

The pancreas is divided into the head, neck, body, and tail.[16] The pancreatic head is located at the right margin of the superior mesenteric vein-portal vein (SMV-PV) confluence; the pancreatic body is located between the SMV-PV confluence and the left margin of the abdominal aorta; the pancreatic tail is located between the left margin of the abdominal aorta and splenic hilum.[17] PDAC, mass-forming pancreatitis (MFP), and serous SCN occur predominantly in the head of the pancreas. Branch duct-IPMN (BD-IPMN) is commonly found in the uncinate process,[18] while SPN and MCN are more frequently found in the body and tail of the pancreas.

SIZE

The size of a mass depends on its location, nature (benign or malignant), and functionality. Masses in the pancreatic head are often smaller at diagnosis than those in the pancreatic body and tail due to narrow growth spaces and their tendency to cause pancreaticobiliary obstruction. Masses with higher degrees of malignancy (such as PDAC) often cause abdominal pain, lower back pain, weight loss, and elevation of tumor markers (such as carbohydrate antigen 19-9); they are also usually smaller at diagnosis than benign or low-grade malignant tumors (such as SCN, SPN, and MCN). Functional pancreatic tumors, such as functional pNET, are often smaller at diagnosis because of their unique clinical symptoms resulting from hormone releases.[19]

SHAPE AND NUMBER

Pancreatic masses may be circular, circle-like, or lobulated. Most are unifocal; multifocal masses are relatively rare and mainly develop in cases involving pNET-associated syndromes, BD-IPMN or mixed-IPMN, von Hippel-Lindau (VHL) syndrome,[20] SPN, and pancreatic metastases.[21]

CAPSULE

Tumor capsules, a fibrous membrane surrounding the tumor, can be categorized as either true capsules or pseudocapsules. The former is inherent, while the latter are fibroplasia as a result of slow tumor growth and compression of the surrounding tissues. Most true capsules are observed in rare pancreatic tumors such as pancreatic schwannoma, lipoma, leiomyosarcoma, solitary fibrous tumor, hamartoma, and perivascular epithelioid cell tumor. Pseudocapsules, on the other hand, are frequently found in cases of pNET and SPN. The majority of highly invasive masses, such as PDAC and adenosquamous carcinoma, lack capsules. Generally, a tumor with an intact capsule shows a clear separation from the peripheral pancreatic tissues, whereas a tumor without a capsule shows invasive growth and unclear separation from its peripheral pancreatic tissues. Capsular changes also reflect the pathological process of disease progression. For instance, the disruption of an initially intact capsule indicates that the tumor tends to become malignant, as it has penetrated the capsule and shows an invasive growth pattern.

Despite differences in the mechanisms of formation, both true capsules and pseudocapsules are fibrous capsules and thus show low attenuation on unenhanced multislice computed tomography (MSCT), hypointense signals on T1WI, and iso-hyperintense signals on T2WI with delayed postcontrast enhancement.

PANCREATIC CALCIFICATION/ CALCULI

Calcification caused by pancreatic diseases is considered dystrophic calcification; it implies the abnormal deposition of calcium salts in degenerated, necrotic tissues or foreign body granulomas.[22] Pancreatic calcification/calculi are mostly located in the side branches, main ducts, or parenchyma in the cases of CP.[23] Pancreatic stone protein (PSP) plays a vital role in the formation of calcification. Reduced PSP leads to supersaturation of calcium carbonate in the pancreatic juice.[24] Calcification is also often found in cases of MFP and pancreatic pseudocyst (PPC). Calcification with MFP results from CP. PPC consists mainly of mature granulation and fibrous connective tissues. In contrast, calcification in PPCs is more frequently observed in patients with a longer history of CP and may lead to calcium deposition on cystic walls. In colloid carcinomas, the thick jelly-like mucus inside is prone to calcification. Calcium deposition due to hemorrhage and poor absorption by necrotic tissues may lead to calcification in the SPN. Calcification in pNETs is similar to that in the SPN and may be associated with hormone secretion. Calcification in the MCN is commonly found on cyst walls and in the intercapsular septa, and it is characterized by lamellar calcification.[25] Calcification in the SCN is often found in polycystic lesions and is characterized by the typical central stellate scar with calcium deposits (Figure 1).[12,26,27]

Unenhanced CT is the most sensitive imaging modality for detecting calcification/calculi, which are characterized by "hyper attenuation."

HEMORRHAGE

The disruption of blood vessels by inflammation and tumors and the fragility of blood vessels may lead to

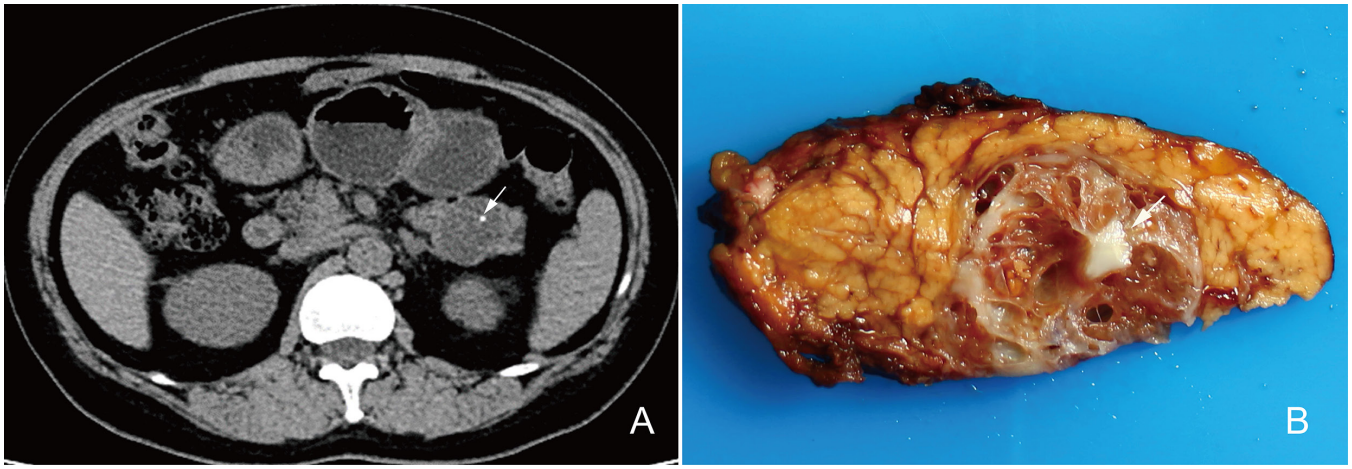

Figure 1: Serous cystic neoplasm of the pancreas in a 38-year-old woman. (A) Surgical specimen (distal pancreatectomy): serous cystic neoplasm with typical microcystic appearance and central scar (arrow). (B) Axial nonenhanced computed tomography image shows a cystic mass with central calcification, known as the "sunburst" sign (arrow).

hemorrhage. Massive infiltration of inflammatory cells during acute pancreatitis (AP) may result in the rupture of blood vessels and hemorrhage.[28] The SPN is most prone to hemorrhage, as it mainly contains fragile blood vessels, which is the stalks of the pseudopapillae.[29–31] The fragile, thin-walled blood vessels lack a strong support structure and rupture when tumor cells detach (Figure 2A, B). The majority of pNETs consist of well-differentiated tumor cells and abundant stromal blood vessels, which form a dense network of capillaries that may lead to intratumoral hemorrhage following rupture of blood vessels destroyed by tumor cells. In the solid mass, there are large of cells, separated by thin stroma and small blood vessels in an acinar cell carcinoma of the pancreas (ACCP).[32,33] ACCP is thus prone to hemorrhage.[34] Inflammation caused by PDAC disrupts surrounding blood vessels and may also lead to intratumoral hemorrhage (Figure 2C, D). The SCN is characterized by the secretion of a clear, serous fluid, but secretion of blood-stained fluids can also be observed within the cystic cavities. MR T1WI is the most sensitive imaging modality for detecting hemorrhage, which is characterized by a "hyperintense signal."

CYSTIC DEGENERATION/VARIANTS

Cystic degeneration is found in the SPN, pancreatic undifferentiated carcinoma with osteoclast-like giant cells (UC-OGC), and solid pNET, which are associated with hemorrhage. Cystic pNET might occur as the initial manifestation, which is not related to hemorrhage or necrosis and represents an uncommon variant of pNET.[35–37]

Cystic degeneration may also be caused by intratumoral necrosis. Pancreatic adenosquamous carcinoma (PASC), which is a variant of PDAC, shows the central necrosis.[38,39] PASC is composed of two distinct components of adenocarcinoma and squamous carcinoma in which the squamous component should be at least 30%[40]; its imaging characteristics are determined by the proportions and distributions of both components. Most PASCs consist of cells arranged in solid nests and are prone to degeneration, necrosis, and, consequently, cystic lesions due to the lack of blood supply in the central region of the solid nests.[41] Cystic degeneration exhibits low attenuation on CT scans, hypointense signals on T1WI, and hyperintense signals on T2WI (Figure 3).[42]

FIBROSIS

The formation of fibers is an important step in tissue repair in the human body and is significant in the reconstruction of tissue structures and functions. Any deviation that develops during the physiological process may lead to abnormal or pathological fibrosis that will seriously affect relevant organs and tissues. There are two types of pancreatic lesions, CP and PDAC, with extraordinarily significant fibrosis as their histological characteristic. Pancreatic stellate cells (PSCs) are distributed in pancreatic interlobular spaces, accounting for 4% of pancreatic tissues. When PSCs are activated, collagen deposition occurs, leading to fibrosis of the organ.[43]

The histopathological components of fibers include fibroblasts and fibrocytes, collagen fibers, and inflammatory cells (mainly lymphocytes and histiocytes). Based on the proportions of the above three components, the fibers can be categorized into cell-rich, intermediate, and fiber-rich stroma.

In the early stages of CP, fibrosis is rich in cellular and

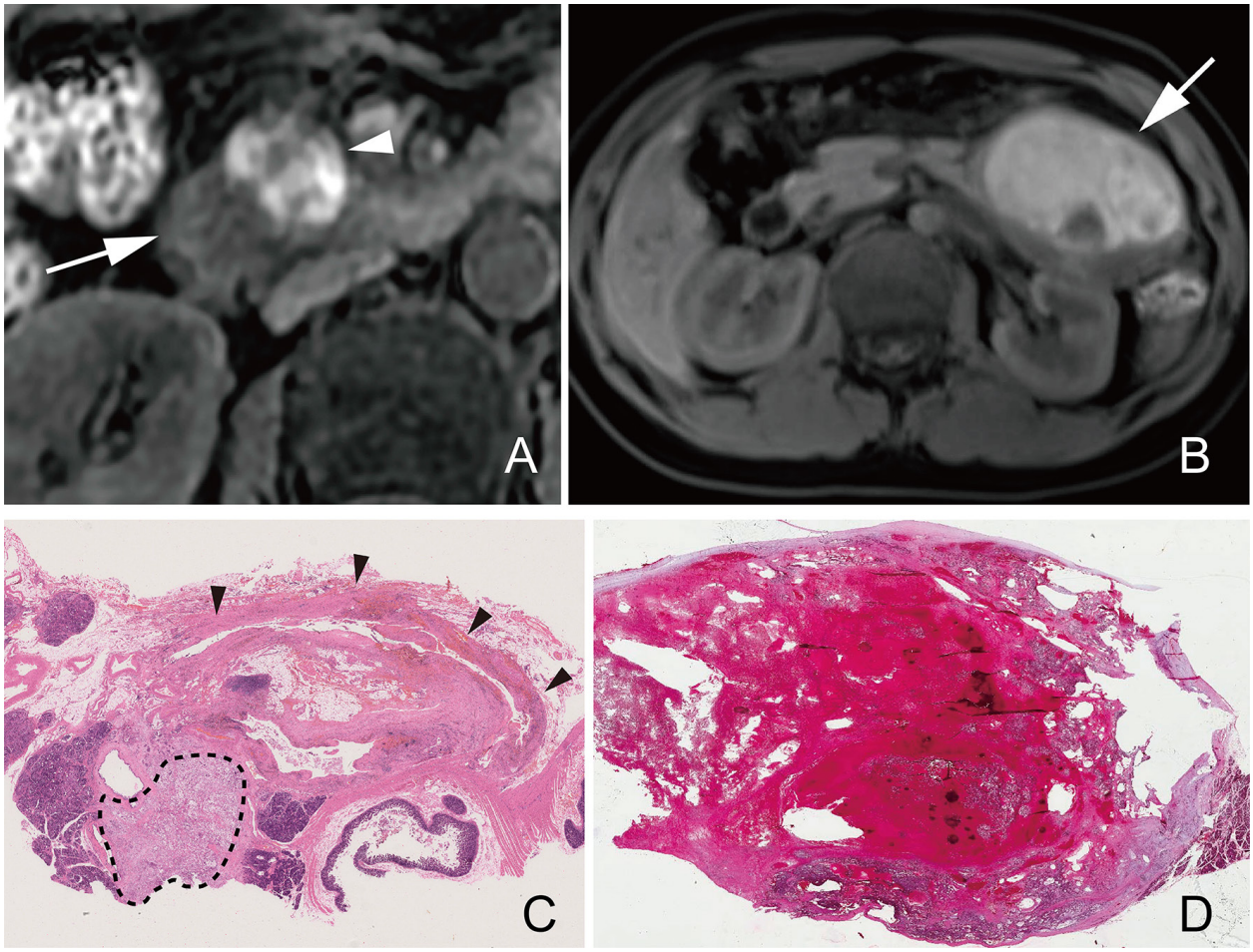

Figure 2: (A, B) Hemorrhage caused by solid-pseudopapillary neoplasm of the pancreas in an 18-year-old woman. (A) Microscopically, a large well-demarcated lesion with large hemorrhage. (B) Axial T1-weighted fat-saturated magnetic resonance image shows a large well-demarcated inhomogeneous hyperintense lesion in the pancreatic tail (arrow). (C, D) Hemorrhage caused by pancreatic ductal adenocarcinoma in a 66-year-old man. (C) Microscopically, a hemorrhagic area (arrow heads) at the edge of the tumor (black dotted line) (HE×1). (D) Axial T1-weighted fat-saturated magnetic resonance image shows a hypointense (arrow) and inhomogeneous hyperintense (arrowhead) lesion in the pancreatic head.

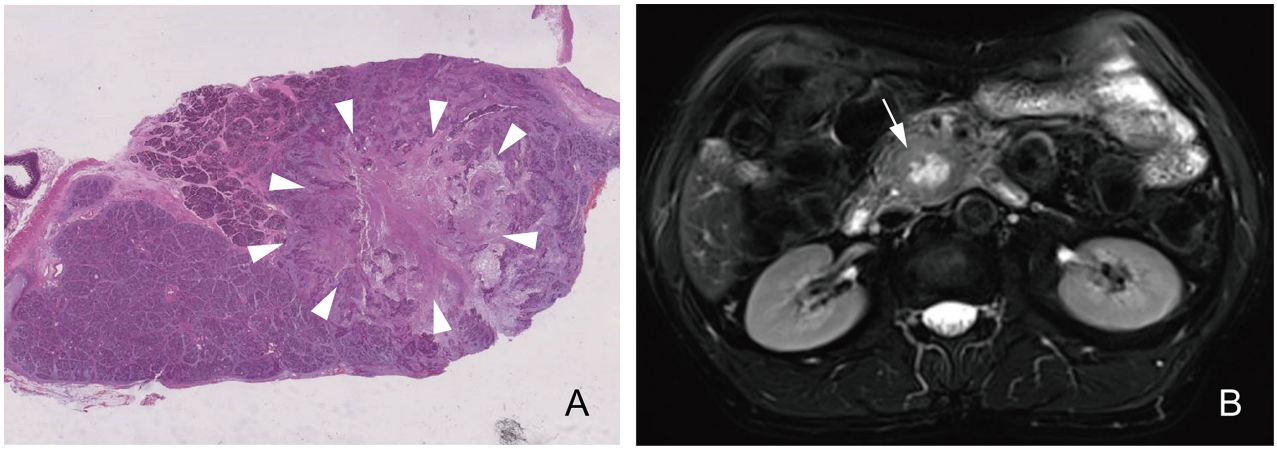

Figure 3: Cystic degeneration caused by pancreatic adenosquamous carcinoma. (A) The tumor with central necrosis (arrowheads) (HE×1). (B) Axial T2-weighted magnetic resonance image shows a round, ill-defined, mild, hypointense mass with central hyperintense necrosis (arrow).

shows a flaky, mainly interlobular distribution.[34,44] As the disease continues to advance, fibrosis extends with and between atrophic lobules and becomes confluent, forming extensive sheets of fibrosis and scar tissue with few cellularities and abundant collagen content.[44–46]

PDAC consists of highly infiltrated neoplastic epithelial tumor cells, which are embedded in a remarkable desmoplastic stroma.[47] The desmoplastic stroma is composed of fibroblasts, collagen fibers, and a scattering of inflammatory cells. The tumor stroma can vary from cellular rich with more densely packed tumor glands to less cellular and abundant collagen.[34]

Fibrosis shows low attenuation on CT, hypointense signals on MRI T1WI, and slightly hyperintense or iso-hyperintense signals on T2WI.

PANCREATIC DUCT ALTERATIONS

Pancreatic lesions can be categorized into lesions without ductal communication (pancreatic extraductal lesions) and lesions with ductal communication (partially intraductal pancreatic lesions). Pancreatic lesions can show the different patterns of pancreatic duct dilatation: upstream, downstream, and diffuse. The relationship between most pancreatic masses and pancreatic ducts can be confirmed via magnetic resonance cholangiopancreatography (MRCP) or multiplanar reformation (MPR) along the main pancreatic duct.

Parenchymal fibrosis and calculi result in pancreatic changes in CP. The spectrum of changes in the pancreatic duct is wide and may include stricture, dilatation, stenosis of intraductal calculi, and occasional side-branch duct dilatation (Figure 4A, B).[45]

Autoimmune pancreatitis (AIP) is characterized by periductal lymphoplasmacytic inflammation, phlebitis, and fibrosis.[48] The medium-sized ducts are often involved by the periductal inflammation. Segmental or diffuse stenosis of the main pancreatic duct is the characteristic finding in endoscopic retrograde cholangiopancreatography.[49,50] CT and MRI often detect mild pancreatic ductal dilation and the upstream narrowed segment.[51,52] Low-grade malignant tumors (such as pNET, SPN, or SCN) often compress the lesion areas on pancreatic ducts, resulting in stenosis or abrupt cutoff of pancreatic ducts, followed by upstream pancreatic duct dilation. However, the degree of upstream pancreatic duct dilation is usually milder than that in PDAC due to the relatively soft nature and slow growth of the mass (Figure 4C, D).

PDAC can easily compress or invade the ducts and cause variable degrees of stenosis, ultimately resulting in complete stenosis and upstream pancreatic duct dilation. A minute carcinoma may only manifest with abdominal pain and significant dilatation of the main pancreatic duct (MPD). Therefore, careful observation of minor changes in the pancreatic duct may help detect small pancreatic tumors. The typical "double-duct sign" occurs when a carcinoma located in the pancreatic head compresses or invades the pancreatic duct and the common bile duct, combining "soft-rattan" dilation of the common bile duct (Figure 4E, F).

Lesions with ductal communication mainly include IPMN, pancreatic intraductal tubulopapillary neoplasm (ITPN), and PPC; pNET rarely develops in pancreatic ducts. The communication between the main pancreatic duct and the cystic lesion is a vital feature at diagnosis.

Based on IPMN imaging[53] and gross pathological findings, the location of ductal involvement can be categorized as in the main duct, branch duct, or a mixture of both; each category accounts for approximately one third of resected IPMNs.[54,55] The imaging characteristics of IPMN lie on the location of the tumors. The main-duct type appears as diffuse or segmental duct dilation (Figure 4G, H).[56,57] The branch-duct type appears as clustered pleomorphic cysts or a unilocular cystic lesion and is often located in the uncinate process.[57] ITPN is an extremely rare pancreatic intraductal tumor that produces relatively less mucus. PPCs represent collections of pancreatic juice secondary to duct rupture due to increased pancreatic duct pressure, stenosis, calculi, and occlusion caused by protein plugs.[34]

MICROVESSEL

The arterial supply to the pancreas is derived from branches of superior mesenteric artery and the celiac trunk.[58] Lobular branches emanating from these arterial branches along interlobular connective tissues enter pancreatic lobules and give rise to intralobular arteries that provide blood to exocrine glands. Owing to the highly vascular nature of the pancreas, the normal pancreatic parenchyma demonstrates a homogeneous blush shortly after the arrival of a contrast agent in the abdominal aorta. However, the contrast agent can also wash out in the delayed phase owing to the abundant pancreatic venous drainage network.

In mild AP, the edematous pancreas shows that the collections of fibrin and neutrophils may be present in the widened interlobular septa.[34] Blood-vessel dilation and congestion are found by microscope. Therefore, edematous pancreatic parenchyma often shows a normal or mildly uneven "slow-in and slow-out" pattern of enhancement

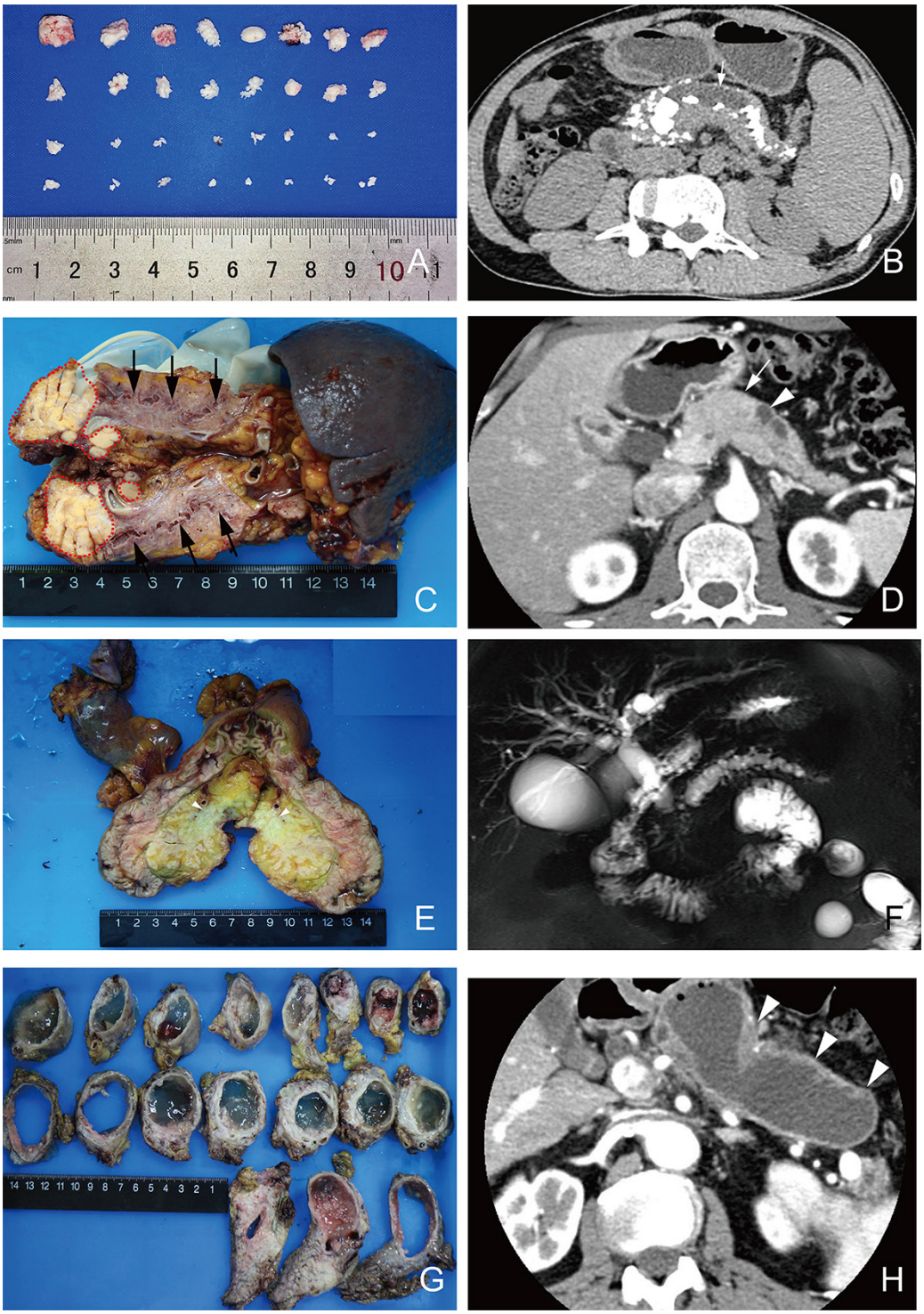

Figure 4: (A, B) Pancreatic duct alteration caused by severe chronic pancreatitis in a 58-year-old man. (A) Pancreatic stones from the specimen. (B) Axial unenhanced computed tomography image shows a dilated pancreatic duct, multiple calcifications throughout the pancreas, and parenchymal atrophy. (C, D) Pancreatic duct alteration caused by G2 nonfunctional pancreatic neuroendocrine tumor in a 72-year-old man. (C) Surgical specimen (distal pancreatectomy): a yellowish lesion (red dotted line) of pancreatic body with upstream duct dilation (black arrows). (D) Axial portal vein phase computed tomography image shows a hypervascular mass (arrow) in the pancreatic body with significantly dilated upstream main pancreatic ducts (arrow head). (E, F) Double-duct sign caused by a pancreatic ductal adenocarcinoma in a 68-year-old man. (E) Surgical specimen (pancreaticoduodenectomy): a hard, whitish lesion (arrow head) with irregular faint margins presenting infiltrative growth pattern, with involvement of the Wirsung duct and common bile duct, both upstream-dilated (double-duct sign). (F) 2D magnetic resonance cholangiopancreatography image shows significant dilation of the biliary tree and Wirsung duct (double-duct sign). (G, H) Pancreatic duct alteration caused by main-duct intraductal papillary mucinous neoplasm in a 64-year-old woman. (G) Surgical specimen (total pancreatectomy): main pancreatic duct significantly and diffusely dilated and filled with mucoid material. (H) Axial arterial phase computed tomography image shows the diffuse dilation of the main pancreatic duct (arrow).

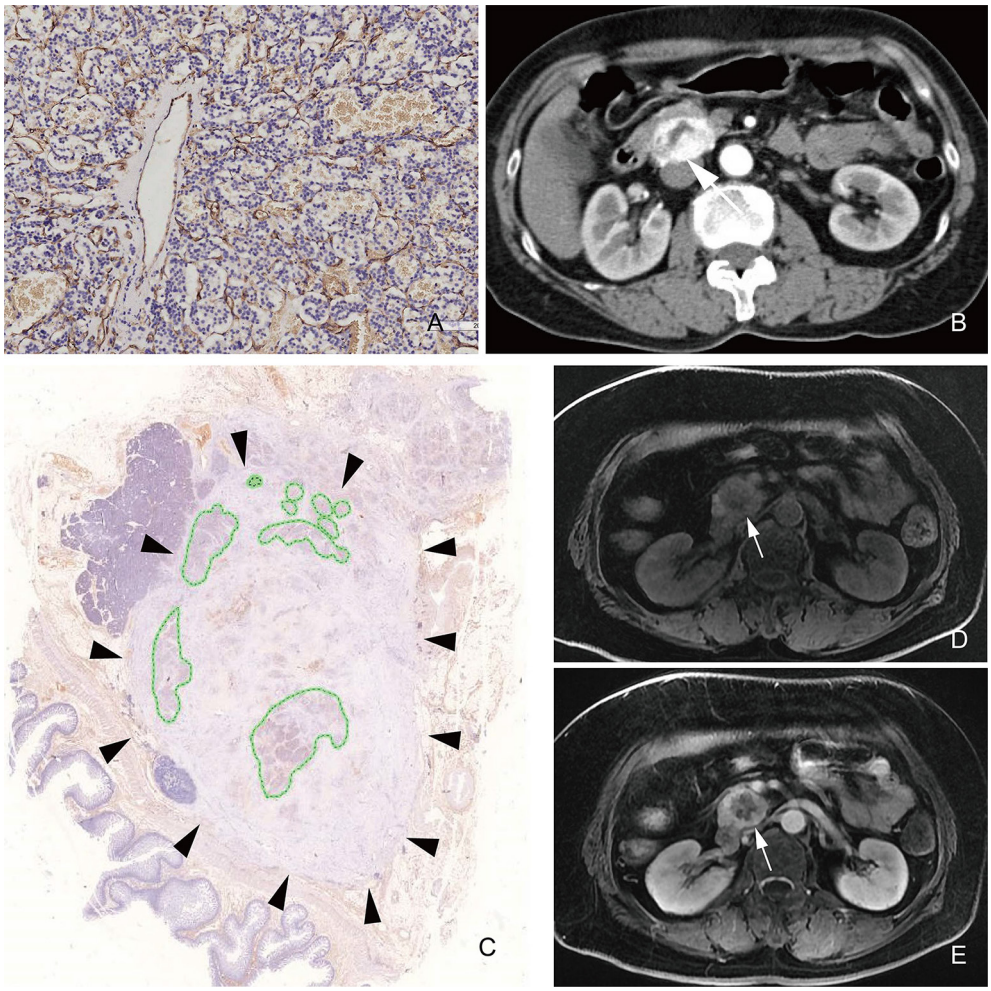

Figure 5: (A, B) Hypervascular G2 nonfunctional pancreatic neuroendocrine tumor in a 58-year-old woman. (A) High intralesional vascular network is shown with CD34 immunohistochemical staining (IHC×100). (B) Axial arterial phase computed tomography image shows inhomogeneous hypervascularity (arrows). (C–E) Enhancement feature of the pancreatic ductal adenocarcinoma in a 58-year-old man. (C) The mass (black arrowhead) with a few residual normal pancreatic tissues at its periphery (green lines) is shown with CD34 immunohistochemical staining (IHC×1). (D) Axial unenhanced computed tomography image shows a solid, round, and distinct border and a low-attenuation mass in the pancreatic head. (E) Axial computed tomography image in delayed phase shows the mass with mild progressive enhancement, especially at its periphery.

postcontrast. In severe AP, any of the tissues and the constituent cells of the pancreas can be involved. Necrosis of the pancreatic parenchyma is the important feature. The necrotic area shows nonenhancement due to the lack of blood supply. Therefore, contrast-enhanced examinations are effective for the detection of necrotic areas.

Microscopic examination shows that acinar atrophy, fibrosis, and pancreatic duct changes represent the essential triad of CP.[44–46] The enhancement characteristics for CP are determined by the proportion and distribution of residual normal pancreatic tissues and fibrosis. The sensitivity of MRI seems to be superior to that of CT, especially for the diagnosis of early-stage CP.[44] Early-stage CP is characterized by the presence of abundant normal pancreatic tissues and mild fibrosis. It is difficult to detect in unenhanced imaging and only shows minimal delayed postcontrast enhancement. As the disease progresses, CP is characterized by significant fibrosis and atrophic lobules. The pancreatic parenchyma shows significant hypointensity on T1WI and slightly hyperintense or isointense signals on T2WI with significant delayed postcontrast enhancement.

The stroma in pNET typically consists of a delicate fibrovascular network. Most pNETs are more significantly enhanced than normal pancreatic tissues (Figure 5A, B) in the arterial phase or in the portal venous phase. With a small number of poorly differentiated tumor cells, abundant stroma, and reduced fibrovascular network, pNET can be easily misdiagnosed as PC, as it may also show hypoenhancement or delayed minimal enhancement on imaging.

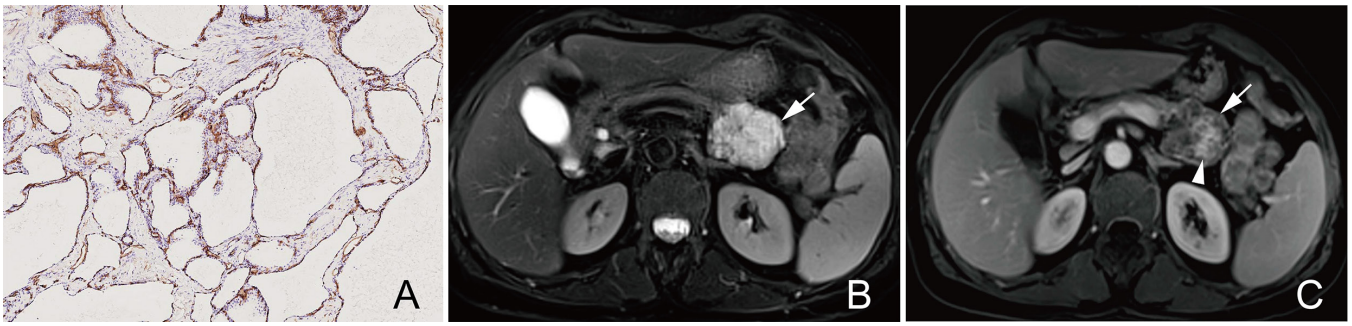

Figure 6: Enhancement feature of the serous cystic neoplasm of the pancreas in a 45-year-old woman. (A) Microscopic examination of the tumor shows the network of small capillary-sized vessels beneath the epithelium with CD34 immunohistochemical staining (IHC×40). (B) Axial T2-weighted image shows lobulated, distinct borders and a hyperintense mass (arrow). (C) T1-weighted magnetic resonance image in the arterial phase shows the mass is hypervascular (arrowhead).

Despite the presence of abundant thin-walled blood vessels in the stroma of the SPN that usually exhibit hyaline degeneration and collagenation, the contrast agent can only enter the tumor tissues slowly via thick-walled blood vessels. The mass shows hypoenhancement in the arterial phase and delayed progressive enhancement; the degree of enhancement is lower than that of its surrounding normal pancreatic parenchyma.

Previous research has shown that prognostic significance is better assessed by quantification of the total vascular area (TVA) and the branching pattern of microvessels than the microussel density (MVD) for colorectal carcinoma patients.[59] PDAC is microscopically composed of tumor cells, stoma, and residual atrophic acinus. The degree of enhancement of PDAC is determined by the MVD and TVA in the tumor.[60] PDACs have varying proportions of tumor cells and stroma, as well as varying degrees of inflammation. Moreover, there may or may not be residual normal pancreatic tissues in the tumors with varying extents and distributions. These differential microscopic observations determine the enhancement pattern of the tumor (Figure 5C–E).

The pathological basis of enhanced SCN and MCN is the network of small capillary-sized vessels immediately beneath the epithelium. After contrast administration, the vascularization of internal septa is clear, and when extremely microcystic, the SCN may even mimic a solid hypervascular lesion.[61] Currently, MRI T2WI and MRCP help diagnose the hyperintense cyst fluid (Figure 6). Additionally, the enhanced solid components of pancreatic cystic masses, such as mural nodules in the IPMN and MCN, reveal the mass's relationship with the tumor microvessel.

CONCLUSION

Although pancreatic diseases are a widely known and easily recognizable condition in its typical presentation, there are some less well-known forms that may be challenging and/or demand special attention on imaging. However, diagnosis of pancreatic diseases can be challenging due to numerous pitfalls associated with image acquisition and interpretation, including technical factors, imaging features, and cognitive errors. Accurate diagnosis requires familiarity with these pitfalls and deep understanding of pathology, as these can be minimized using systematic strategies.

To overcome the current limitations of imaging, researchers have developed radiomics. Radiomics is an emerging field that converts imaging data into a high-dimensional mineable feature space using many automatically extracted data-characterization algorithms.[62,63] The concept behind radiomics is that medical images contain much more information than is visible to the eyes of radiologists, which is called "hidden" information.[64] Radiomics combined artificial intelligence (AI) algorithms, particularly deep learning, has demonstrated remarkable progress in pancreatic image-recognition tasks including tumor classification,[65–67] grade,[68–70] survival,[71,72] treatment respond prediction,[73–76] lymphatic metastasis,[77–79] tumor microenvironment,[80–82] and so on. In the future, the diagnosis of pancreatic diseases will enter an era of precision and individuation.

Conflict of Interest

The authors have no conflicts of interest to disclose.

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