

REVIEW

Mimics of pancreatic ductal adenocarcinoma

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Abstract

Several uncommon primary pancreatic tumors, inflammatory conditions, metastasis to the pancreas and peripancreatic masses can mimic the appearance of pancreatic ductal adenocarcinoma (PDA). Differentiation between these lesions and PDA can be challenging, due to the overlap in imaging features; however, familiarity with their typical imaging features and clinical presentation may be helpful in their differentiation, as in some cases, invasive diagnostic tests or unnecessary surgery can be avoided. The different pathologies that can mimic PDA include inflammatory conditions such as the various forms of pancreatitis (chronic-focal mass-forming, autoimmune and groove pancreatitis), pancreatic neuroendocrine tumors, solid pseudopapillary tumors, metastasis (solid non-lymphomatous and hematologic), congenital variants (annular pancreas), as well as peripancreatic lesions (accessory spleen, adrenal masses, duodenal masses, lymph nodes and vascular lesions), and certain rare pancreatic tumors (e.g., acinar cell tumors, solid serous tumors, hamartoma and solitary fibrous tumors). The clinical presentation and imaging features of the most commonly encountered mimics of PDA are discussed in this presentation with representative illustrations.

Keywords: *Pancreas; mimics; pancreatitis; peripancreatic; primary; metastasis.*

Introduction

Pancreatic ductal adenocarcinoma (PDA) is the most commonly encountered primary tumor of the pancreas, accounting for about 80% of cases^[1]. The remaining 20% include a variety of masses (both benign and malignant) and inflammatory conditions that can involve the pancreas either primarily or secondarily^[1–6]. The different pathologies that can mimic PDA include different forms of pancreatitis, primary pancreatic neuroendocrine tumors, solid pseudopapillary tumors, metastasis, congenital variants, peripancreatic lesions as well as rare pancreatic tumors.

Pancreatitis

The various forms of pancreatitis such as chronic pancreatitis (mass-forming or focal chronic pancreatitis and groove pancreatitis) and autoimmune interstitial pancreatitis can mimic PDA.

Chronic pancreatitis

Chronic pancreatitis is characterized by repeated episodes of inflammation of the pancreas, which can eventually lead to parenchymal fibrosis and glandular atrophy^[7,8]. Most commonly, chronic pancreatitis is caused by alcohol or idiopathic causes when no other cause is identified. The most characteristic features of chronic pancreatitis seen on cross-sectional imaging are dilatation of the main pancreatic duct and side branches, diffuse parenchymal atrophy and parenchymal calcifications. These findings are pathognomonic and fairly specific for making the diagnosis of chronic pancreatitis. However, atypical presentations can be seen with asymmetric involvement of the gland or with focal chronic pancreatitis, and these can lead to localized atrophy or enlargement of part of the gland, thereby simulating PDA (Figs. 1 and 2). A smoothly stenotic or normal main pancreatic duct penetrating a pancreatic mass on magnetic resonance cholangiopancreatography (MRCP), referred to as the duct-penetrating sign, has been seen

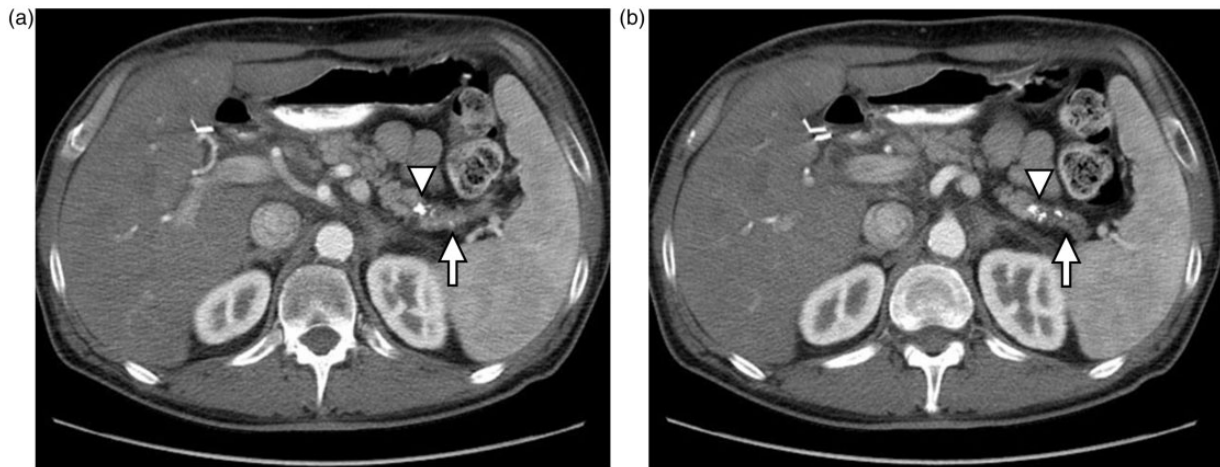


Figure 1 Focal chronic pancreatitis. (a, b) Axial CT images demonstrate focal atrophy of the pancreatic tail (arrows) compared with the rest of the gland with focal calcifications (arrowheads). The appearance can mimic pancreatic adenocarcinoma causing focal interruption of the pancreatic duct with secondary upstream atrophic changes.

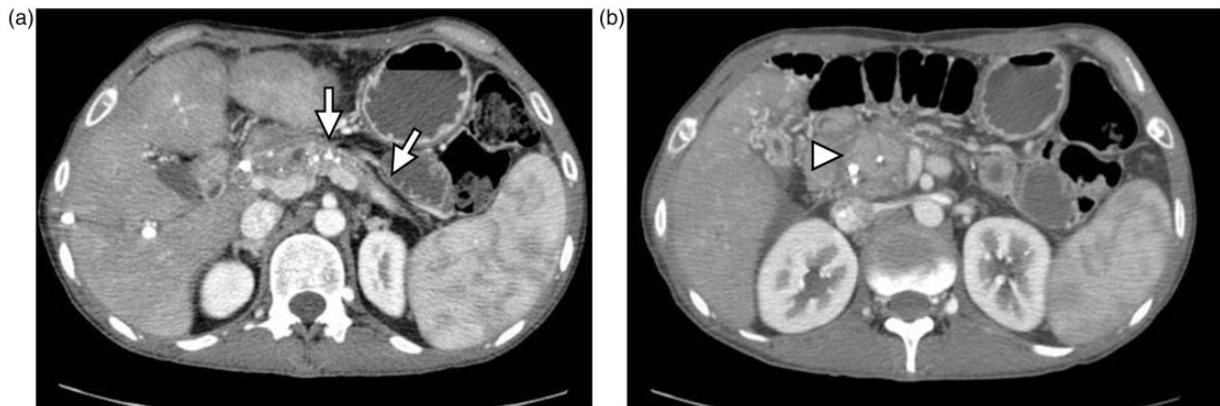


Figure 2 Mass-forming chronic pancreatitis. (a, b) Axial CT images demonstrate diffuse atrophy of the pancreatic body and tail (arrows) with parenchymal calcifications and asymmetric enlargement of the pancreatic head (arrowhead) simulating a pancreatic head mass.

more frequently in inflammatory pancreatic masses than in PDA and can be used to differentiate the two entities^[9].

Groove pancreatitis

A particular form of chronic pancreatitis affecting the pancreatobiliary space is groove pancreatitis^[10,11]. There are two forms of groove pancreatitis: the pure form, which affects the groove only and the segmental form which also involves the pancreatic head. Several causes have been described for groove pancreatitis, and these include peptic ulcer disease, gastric resection, true duodenal wall cysts, pancreatic heterotopia or disturbances of pancreatic juice outflow. Commonly, groove pancreatitis of the pure form demonstrates a sheet-like soft tissue mass filling the groove region in between the second portion of the duodenum and the pancreatic

head. This mass may demonstrate delayed contrast enhancement on computed tomography (CT) and magnetic resonance imaging (MRI), and is believed to be due to its fibrotic tissue component. In the segmental form, the process extends to involve the pancreatic head. Additional features that can be seen with groove pancreatitis are the presence of circumferential duodenal wall thickening and duodenal stenosis (Fig. 3). Both forms of groove pancreatitis can mimic PDA and differentiation must be based on histologic confirmation. The presence of peripancreatic vascular invasion or metastatic disease can help in differentiating PDA from groove pancreatitis.

Autoimmune pancreatitis

Autoimmune pancreatitis (AIP) is a more recently recognized form of pancreatitis, which can present either as a

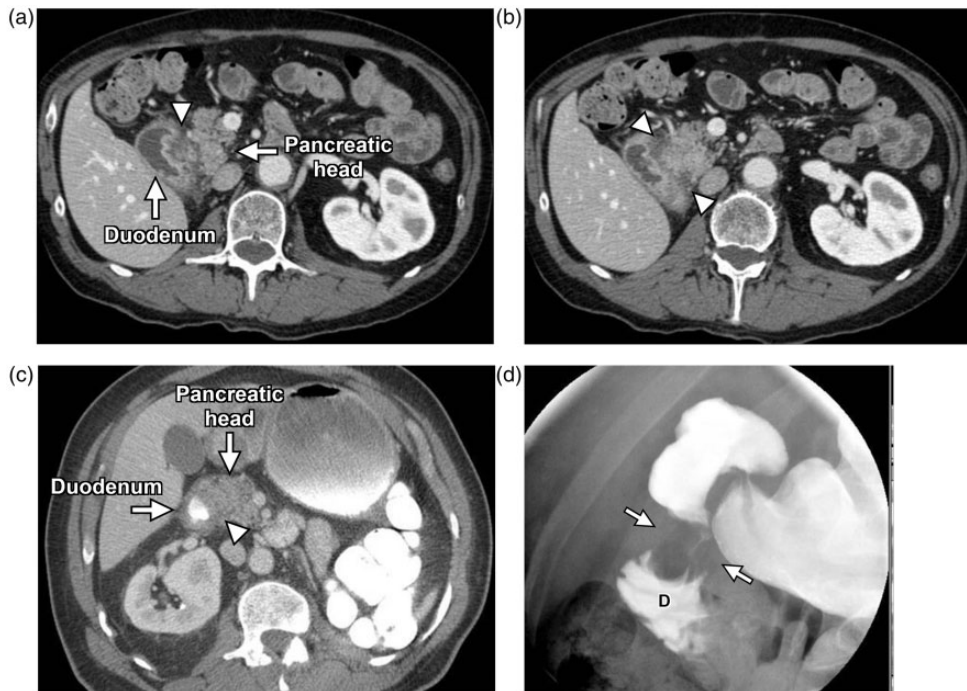


Figure 3 Groove pancreatitis. (a, b) Pure form of groove pancreatitis. Axial CT images demonstrate a sheet-like hypodense lesion in the pancreatic groove (arrowhead) interposed between the pancreatic head and duodenum. (c, d) Duodenal stenosis in groove pancreatitis. (c) Axial CT image demonstrates loss of the fat plane in the pancreatic groove (arrowhead) with circumferential thickening of the duodenum. (d) Upper gastrointestinal examination demonstrates a focal stenosis (arrows) of the duodenum (D).

focal or diffuse abnormality and may be associated with pancreatic duct/biliary strictures, thereby mimicking PDA^[12–15]. AIP is divided into two general forms with distinctly different clinical features: (1) lymphoplasmacytic sclerosing pancreatitis (type 1) and (2) idiopathic duct-centric pancreatitis (type 2). Type 1 AIP is characterized by increased serum IgG4 concentration, extrapancreatic involvement (e.g., renal, retroperitoneal fibrosis, sclerosing cholangitis, and sialadenitis), and predominant occurrence in elderly men. Type 2 AIP lacks these features and is more commonly observed in younger patients with no sex predilection. Histopathologically, type 1 AIP is characterized by extensive periductal IgG4-positive lymphoplasmacytic infiltration, storiform fibrosis, and obliterative phlebitis. Type 2 AIP typically manifests granulocyte epithelial lesions and no or very few IgG4-positive plasma cells. The typical imaging findings of AIP with diffuse involvement of the pancreas include a diffuse sausage-like enlargement of the pancreas and symmetric halo rim of low attenuation surrounding the pancreas. Endoscopic retrograde cholangiopancreatography or MRCP typically demonstrates diffuse or multifocal irregular narrowing of the main pancreatic duct with mild or no upstream dilatation. Focal involvement of the pancreas, reported in 28–41% of cases, can mimic PDA and differentiation can be made based on biopsy, response to steroids or characteristic extrapancreatic involvement (Fig. 4).



Figure 4 Autoimmune pancreatitis (AIP), Focal type. Axial CT image demonstrates a focal hypodense mass-like area in the pancreatic head (arrow) mimicking pancreatic adenocarcinoma in a patient with proven AIP.

Pancreatic neuroendocrine tumors

Pancreatic neuroendocrine tumors account for 5% of pancreatic tumors and can be benign or malignant. Most tumors secrete endocrine hormones such as insulin, glucagon, vasoactive intestinal peptide, gastrin,

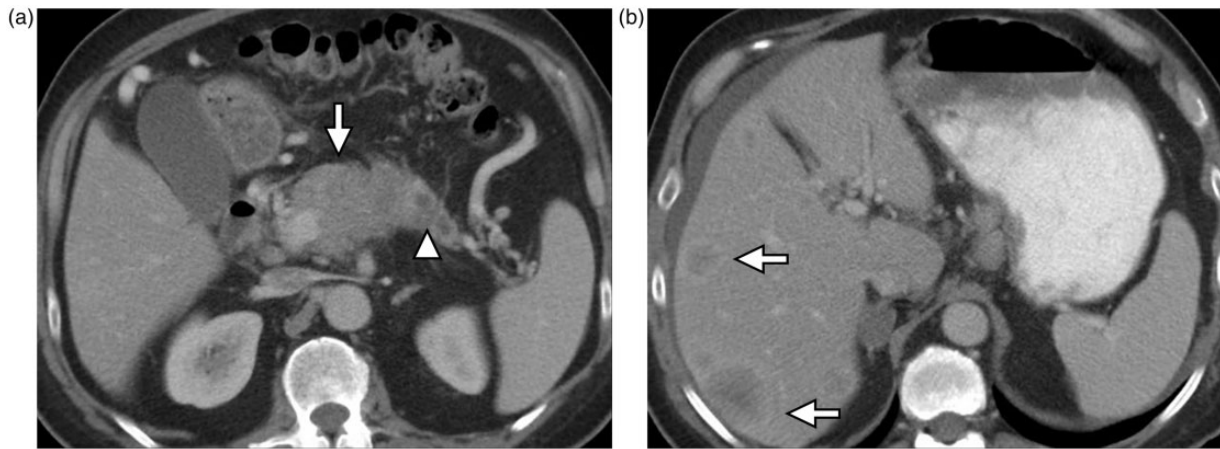


Figure 5 Pancreatic neuroendocrine tumor. (a) Axial CT image demonstrates a focal heterogeneous mass in the proximal pancreatic body (arrow) with secondary proximal atrophy and upstream pancreatic duct dilatation (arrowhead) mimicking pancreatic adenocarcinoma. (b) CT image demonstrates multiple hypervascular metastatic liver lesions (arrows) that are more typical of neuroendocrine tumor than pancreatic adenocarcinoma.

or somatostatin; however, only a small fraction of patients are symptomatic from hormone overexcretion. Neuroendocrine tumors can be sporadic or associated with well-known genetic syndromes including Von Hippel–Lindau disease, neurofibromatosis-1, tuberous sclerosis, and multiple endocrine neoplasia type 1^[3,4]. On CT and MR imaging, these tumors typically are solid and avidly enhance with intravenous contrast, and smaller lesions in particular are best appreciated on the pancreatic parenchymal phase of contrast enhancement; however, less commonly they can demonstrate heterogeneous and atypical enhancement and then can mimic PDA (Fig. 5). Correlation with serum markers of the commonly excreted hormones by these neuroendocrine tumors or biopsy is needed to differentiate them from PDA. In addition, several functional imaging agents are available for detecting and evaluating the extent of spread of neuroendocrine tumors, including somatostatin receptor scintigraphy with [¹¹¹In]diethylenetriaminepentaacetic acid-octreotide (Octreoscan) and more recently [⁶⁸Ga]tetraazocyclodecanetetraacetic acid-octreotate positron emission tomography (PET)/CT, which has been shown to be significantly more sensitive for detecting small tumors compared with Octreoscan^[16].

Solid pseudopapillary tumor

Solid pseudopapillary tumor is a rare pancreatic tumor accounting for approximately 1–2% of all exocrine tumors of the pancreas and is typically diagnosed in young women^[17,18]. Most cases are benign or low-grade malignant neoplasms. These tumors are usually large and encapsulated and are composed of a mixture of cystic, solid and hemorrhagic components (Fig. 6).

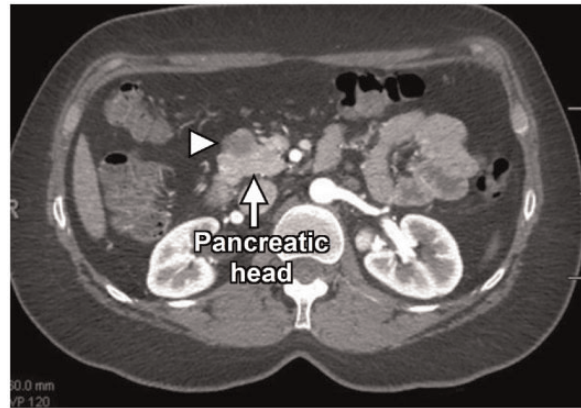


Figure 6 Solid pseudopapillary tumor. Axial CT image in a young female patient demonstrates a small hypodense lesion (arrowhead) in the pancreatic head that mimics pancreatic adenocarcinoma.

The predominantly solid and smaller lesions can mimic PDA, however, younger patient age or identification of intratumoral hemorrhage or a capsule should help in distinguishing these tumors.

Metastasis

Metastatic lesions to the pancreas from both non-lymphomatous and hematologic primary malignancies can mimic PDA.

Solid non-lymphomatous metastasis

Solid non-lymphomatous metastasis to the pancreas is rarely seen on imaging and is more frequently found at

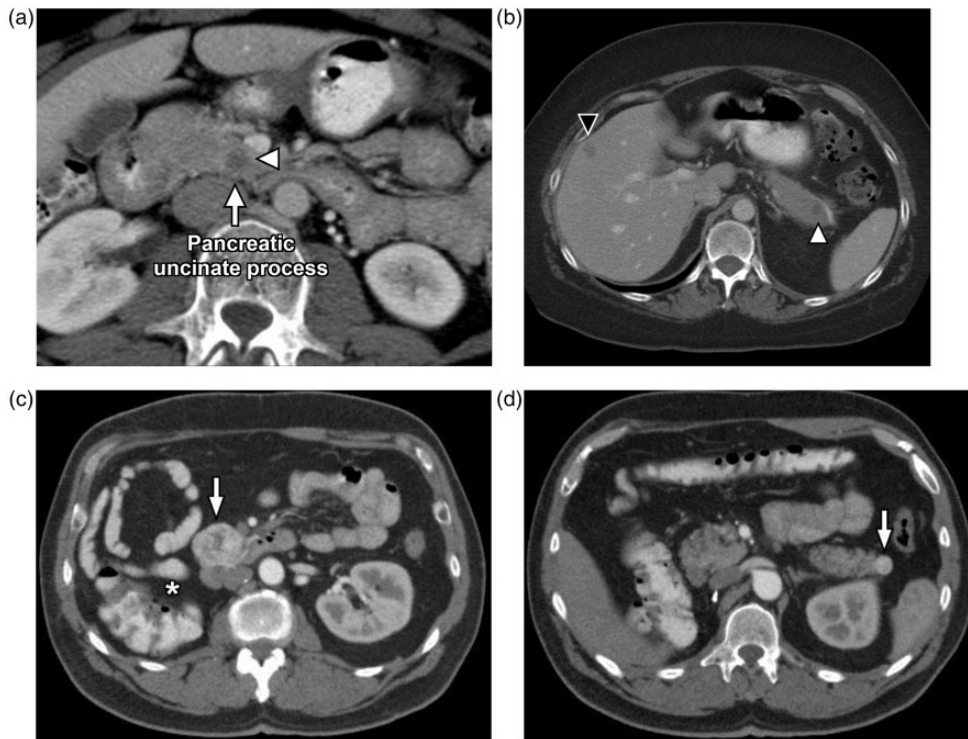


Figure 7 Metastasis to the pancreas. (a) Axial CT image demonstrates a small hypodense lesion (arrowhead) in the uncinuate process which mimics pancreatic adenocarcinoma. The patient was previously diagnosed with breast cancer and the pancreatic lesion was confirmed on cytology to represent metastasis. (b) Small hypodense lesion is seen in the pancreatic tail (white arrowhead). The patient had widespread metastasis including the liver (black arrowhead). The lesion in the pancreas was presumed to be a metastatic deposit from the patient's known advanced non-small cell lung tumor. (c, d) Axial CT images demonstrate two hyperdense lesions in the pancreatic head and tail (arrows) representing metastatic lesions from renal cell carcinoma. Absent right kidney (*) from previous nephrectomy.

autopsy; it is seen in approximately 3–12% of patients with advanced malignancy^[19]. The most frequently reported cancers that metastasize to the pancreas are melanoma, breast, renal (renal cell carcinoma), and lung and less commonly gastrointestinal tract (adenocarcinoma), thyroid, liver (hepatocellular carcinoma) and bone (osteosarcoma)^[19,20]. Most metastatic lesions, from hypovascular primary malignancies, are hypodense and simulate PDA (Fig. 7a,b). Metastases from hypervascular tumors such as renal cell carcinoma are usually hyperdense and often multiple (Fig. 7c,d). Rarely they can be solitary and if imaged in the delayed phase of contrast enhancement can mimic PDA. Pancreatic metastases do not usually present before the detection of the primary neoplasm.

Hematologic metastasis

Hematologic malignancies, particularly non-Hodgkin lymphoma can often involve extranodal locations, including the pancreas, and can be seen in 5–30% of cases^[21–23]. Involvement of the pancreas can be either by direct extension from the surrounding contiguous lymph nodes or by hematogenous spread of disease (Fig. 8). Primary pancreatic lymphoma accounts for

less than 0.5% of all pancreatic malignancies and 1% of extranodal lymphomas. Suggesting the diagnosis of lymphomatous involvement of the pancreas prospectively, in particular when there is diffuse lymph node enlargement, and confirmation with histology can avoid unnecessary surgery.

Congenital variants

Annular pancreas, a congenital variant related to pancreatic development, can pose a diagnostic challenge as the appearance may mimic a pancreatic head mass. This variant is a rare congenital anomaly in which pancreatic tissue encircles the second portion of the duodenum^[24,25]. Annular pancreas in children usually manifests with symptoms resulting from gastric outlet obstruction secondary to mass effect; however, it is mostly asymptomatic in adults and is discovered incidentally or may present in certain patients with peptic ulcers, duodenal obstruction, or pancreatitis. The unopacified duodenum in the center of the encircling pancreatic parenchyma can mimic a solid pancreatic mass (Fig. 9).

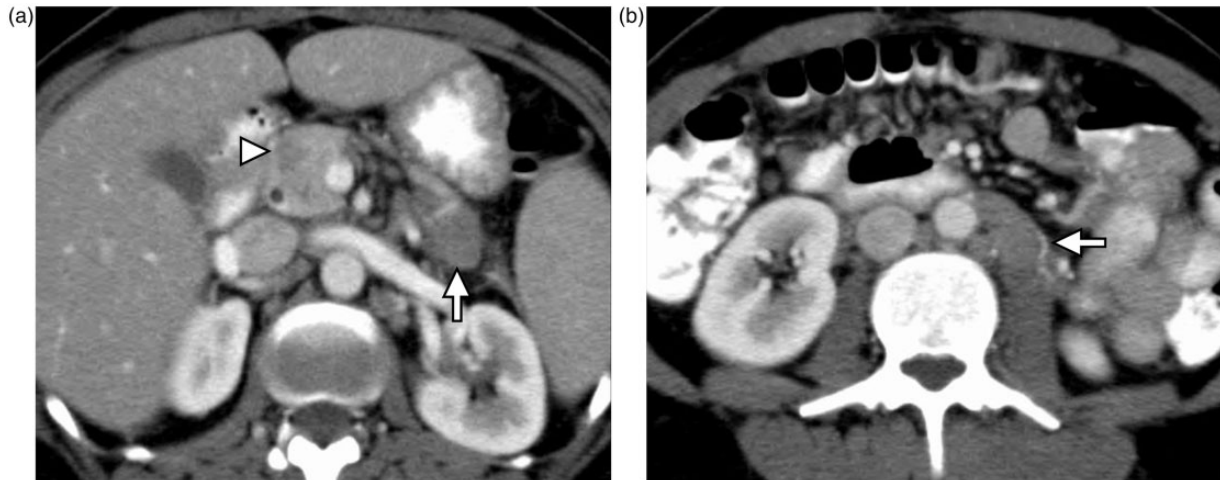


Figure 8 Non-Hodgkin lymphoma involvement of the pancreas. (a) Axial CT image demonstrates a small hypodense lesion (arrowhead) in the pancreatic head that mimics pancreatic adenocarcinoma. Note enlarged lymph nodes inferior to the body and tail of the pancreas (arrow) in (a) and left para-aortic region (arrow) in (b). The patient was diagnosed with non-Hodgkin lymphoma with hematogenous spread to the pancreas. The pancreatic lesion resolved after chemotherapy.

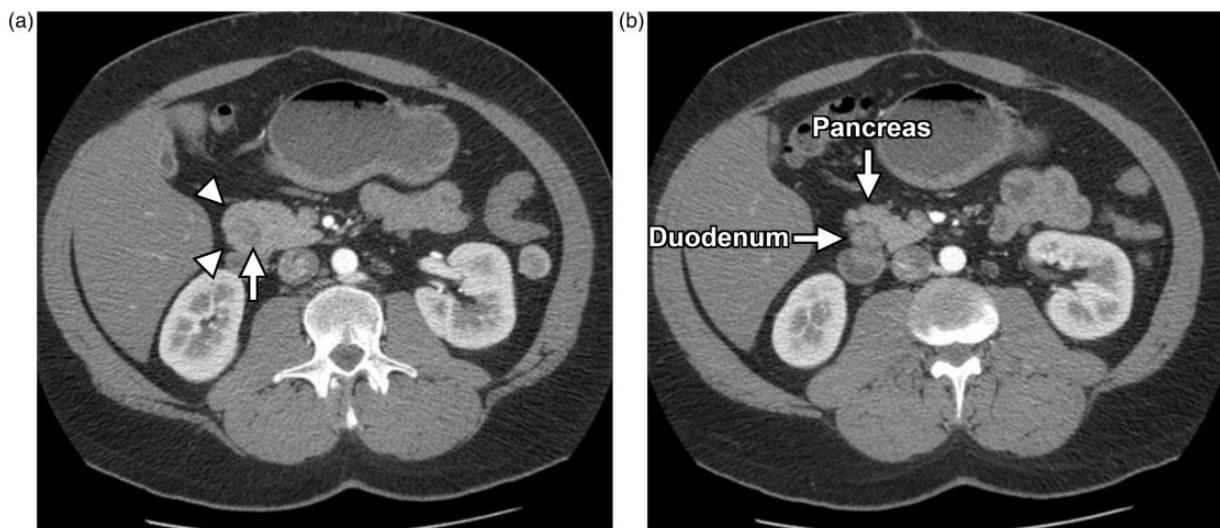


Figure 9 Annular pancreas. (a) Axial CT image demonstrates a small hypodense lesion representing the duodenal lumen (arrow) with the encircling pancreatic parenchyma (arrowheads); the appearance mimics a pancreatic head mass. (b) CT image at a lower level demonstrates the duodenum now as a separate structure from the more anteriorly located pancreas.

Peripancreatic lesions

Masses arising from the anterior pararenal space surrounding the pancreas can occasionally mimic a focal pancreatic mass. These include ectopic splenic tissue or tumors arising from the adrenal gland, duodenum, lymph nodes or vascular structures^[26]. One of the commonly encountered mimics is intraparenchymal ectopic splenic tissue commonly seen in the pancreatic tail^[27]. Accessory spleens are relatively common and are seen in 10–30% of patients at autopsy. Larger lesions are

homogeneously enhancing and mostly mimic pancreatic endocrine tumors but smaller lesions measuring less than 1 cm can have a lower or heterogeneous attenuation and can mimic PDA (Fig. 10). Other possible peripancreatic lesions that can mimic pancreatic adenocarcinoma include adrenal and duodenal masses (Fig. 11).

Rare pancreatic tumors

Several other rare pancreatic masses can mimic pancreatic adenocarcinoma, including acinar cell tumors^[28,29],

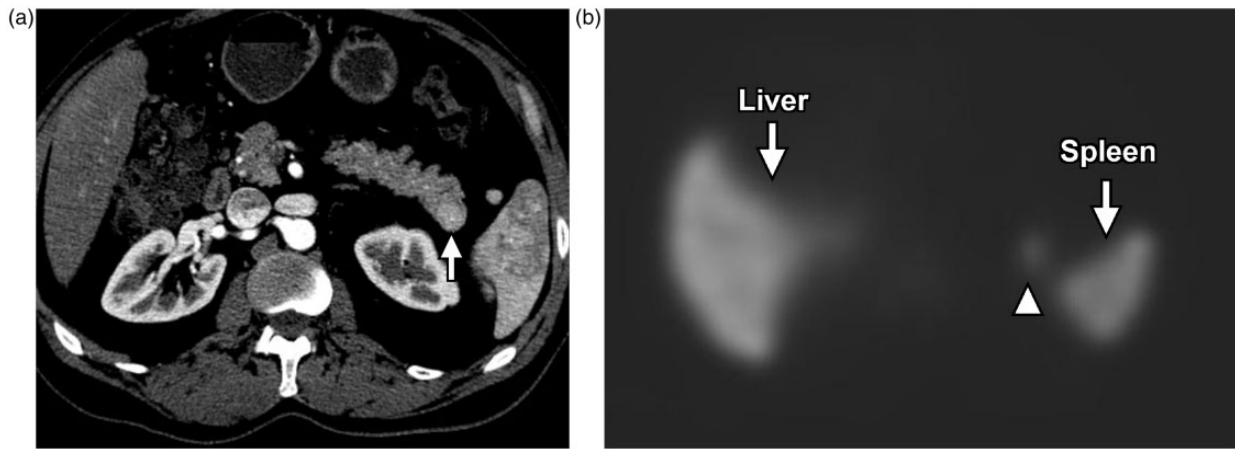


Figure 10 Accessory ectopic spleen. (a) Axial CT image demonstrates a small heterogeneously enhancing mass in the pancreatic tail (arrow). (b) Axial sulfur colloid single photon emission-computed tomography Tc-99m image confirms uptake in the mass (arrowhead), which is of similar intensity to the spleen confirming the diagnosis of splenic tissue.

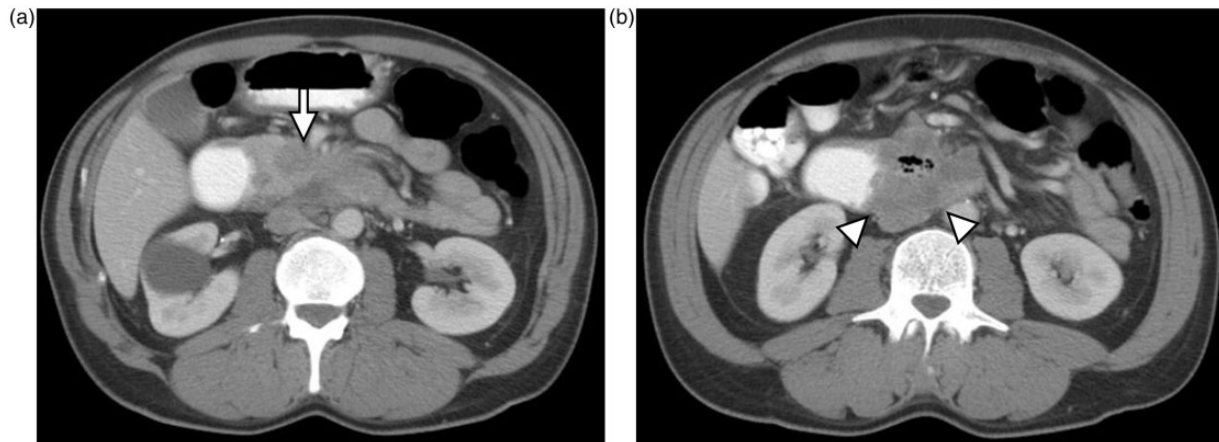


Figure 11 Peripancreatic lesions mimicking pancreatic adenocarcinoma. (a) Axial CT image demonstrates an ill-defined hypodense lesion in the pancreatic uncinus process (arrow). (b) Image at a lower level shows that the mass is arising from the transverse duodenum (arrowheads); this was later confirmed to be a duodenal adenocarcinoma.

solid serous tumors^[30,31], hamartoma^[32] and solitary fibrous tumors^[33].

Conclusion

Several neoplastic and inflammatory diseases, either originating from the pancreas or arising from the peripancreatic region, can mimic PDA. Differentiation between these diseases and PDA can be challenging, due to overlap in the imaging features. Radiologists should be familiar with the typical imaging features and clinical presentation of these less commonly encountered pathologies that can mimic pancreatic adenocarcinoma, as invasive diagnostic tests and surgery can be avoided if the correct diagnosis can be made.

Conflict of interest

The authors have no conflicts of interest to declare.

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