



Mass-Forming Chronic Pancreatitis: Diagnostic Performance of PET/CT

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Abstract

Mass-forming chronic pancreatitis and pancreatic ductal adenocarcinoma are most commonly located in the head of pancreas, and there is a marked overlap in clinical features and imaging findings that makes it diagnostically challenging, although prognosis and management of both these entities differ. Differentiation is made even more difficult when surgical exploratory biopsy is obtained. Radical surgical resection remains the standard of care for pancreatic ductal adenocarcinoma and conservative treatment is effective for mass-forming chronic pancreatitis. Misdiagnosis of mass-forming chronic pancreatitis as pancreatic ductal adenocarcinoma results in unnecessary surgical intervention, and misdiagnosis of pancreatic ductal adenocarcinoma as mass-forming chronic pancreatitis results in delay in surgical intervention when required. Fluorodeoxyglucose-positron emission tomography/computed tomography can reliably be used for tissue characterization of mass-forming chronic pancreatitis and for monitoring disease response following treatment. Although differentiation of mass-like lesions of pancreas is reliably made on histopathology, significant false-negative rate is a major drawback that has a negative effect on diagnosis. This case report describes a rare presentation of mass-forming chronic pancreatitis with florid dystrophic calcifications in a 60-year-old male.

Keywords

- ▶ mass-forming chronic pancreatitis
- ▶ pancreatic ductal adenocarcinoma
- ▶ dystrophic calcifications
- ▶ computed tomography
- ▶ PET/CT
- ▶ histopathology

Introduction

Mass-forming chronic pancreatitis is commonly noted in elderly patients with head of the pancreas being the most common location.¹ On histopathology, progressive interstitial fibrosis with chronic inflammatory infiltrate is the characteristic finding. However, pancreatic ductal adenocarcinoma presents in the same age group with similar clinical findings that makes the differentiation between these entities diagnostically challenging. Pancreatic ductal adenocarcinoma is a hypovascular tumor with ill-defined margins that may not deform the contours of the pancreas

and is characterized by marked interstitial fibrosis. On imaging, difficulties arise when pancreatic ductal adenocarcinoma occurs on a background of pre-existing fibrosis as seen in chronic pancreatitis. On positron emission tomography/computed tomography (PET/CT), malignant lesions generally demonstrate avid fluorodeoxyglucose (FDG) uptake, whereas most benign lesions are characterized by normal or minimally increased FDG accumulation. Focal areas of abnormally increased FDG uptake are considered suspicious for malignant disease, and in many cases, metabolic alterations precede the morphologic changes

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associated with malignant tumors such pancreatic ductal adenocarcinoma.

Case Report

A 60-year-old male presented to the department of general surgery with complaints of jaundice for 4 weeks. He gave a history of chronic alcoholism since the age of 30 years and was immunocompromised with recently diagnosed type-2 diabetes mellitus. Clinical examination revealed moderate hepatomegaly. Liver function tests were deranged with elevated serum aspartate transaminase at 97 U/L (0–31), serum alanine transaminase at 241 U/L (0–37), serum alkaline phosphatase at 682 U/L (35–104), and serum total bilirubin at 5.4 mg/dL (0–1). Serum CA 19–9 was elevated at 1,382 U/mL (0–37); α -fetoprotein was normal at 1.41 ng/mL. Serum immunoglobulin G4 (IgG4) was normal at 42 mg/dL (1–290). The patient was referred for ultrasonography of the abdomen that demonstrated a hypoechoic mass lesion in the uncinate process and pancreatic head with foci of calcifications. There was associated atrophy of the pancreas and dilatation of the main pancreatic duct (► Fig. 1) Further, contrast-enhanced computed tomography (CECT) revealed a 5 × 4 × 6 cm (anteroposterior [AP] × mediolateral [ML] × craniocaudal [CC]) hypoenhancing mass in the uncinate process and head of pancreas with mild upstream dilatation of the common bile duct and intrahepatic biliary radicle dilatation. The mass lesion demonstrated exuberant cauliflower like parenchymal calcification without evidence of ductal dilatation (► Fig. 2A). Pancreatic body and tail were atrophic and were displaced posterosuperior by the mass lesion (► Fig. 2B). Main pancreatic duct showed dilatation. PET/CT imaging demonstrated a soft tissue mass with indistinct boundaries in the head and uncinate process of the pancreas with a maximum standardized uptake value (SUV) of 4.59. Due to marked elevation of serum CA-19–9 levels, the patient underwent pylorus-preserving pancreaticoduodenectomy on high suspicion of pancreatic ductal adenocarcinoma, although calcifications are not a diagnostic feature. Gross pathology of the resected specimen



Fig. 1 Longitudinal ultrasonography image demonstrating a hypoechoic mass lesion involving the uncinate process and pancreatic head with foci of calcifications. There is associated atrophy of the pancreas and dilated main pancreatic duct.

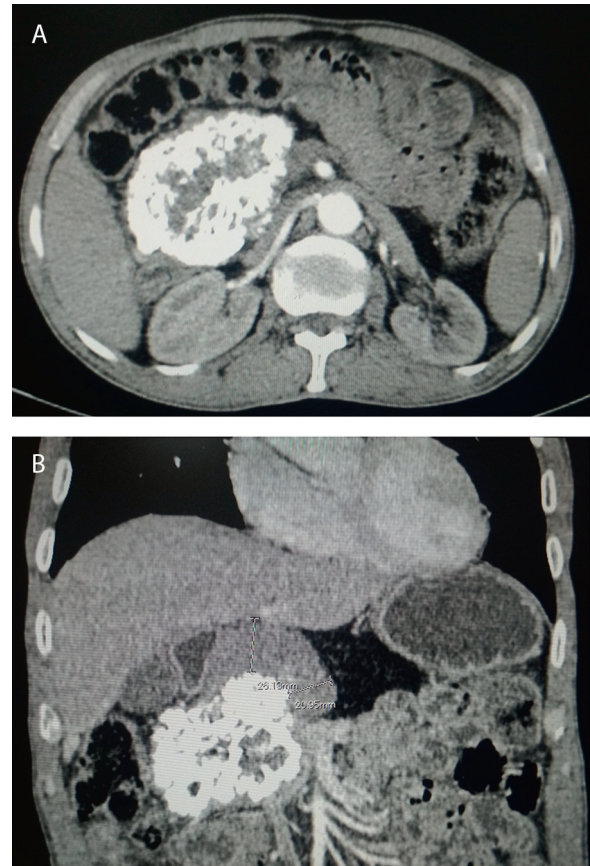


Fig. 2 (A) Axial computed tomography image in the arterial phase demonstrating a lobulated hypoenhancing mass lesion involving the uncinate process and head of pancreas with exuberant cauliflower like dystrophic calcifications. (B) Coronal reformatted computed tomography image in the portal venous phase demonstrating posterosuperior displacement of the pancreatic body and tail by the mass lesion in the uncinate process and pancreatic head. Note the atrophic pancreas with dilated main pancreatic duct consistent with features of chronic pancreatitis.

revealed an infiltrating mass lesion in the uncinate process and head of pancreas. Histopathology revealed periductal inflammation with fibrosis, dilatation of the main pancreatic duct and intralobular fibrosis, consistent with features of chronic pancreatitis (► Fig. 3). As the patient was immunocompromised, low-dose oral prednisone was initiated for 5 days to avoid recurrence of pancreatitis and the patient recovered well within 4 weeks of starting conservative treatment with nonsteroidal anti-inflammatory drugs, pancreatic enzyme supplements and intravenous fluid resuscitation for preventing dehydration. Liver function tests were reported as normal following completion of treatment.

Discussion

Mass-forming chronic pancreatitis accounts for 30% of cases of chronic pancreatitis.² Due to common clinical features and imaging findings, diagnostic differentiation of mass-forming chronic pancreatitis and pancreatic ductal adenocarcinoma can sometimes be more of a diagnostic dilemma. Approximately 33% of patients with mass-forming chronic

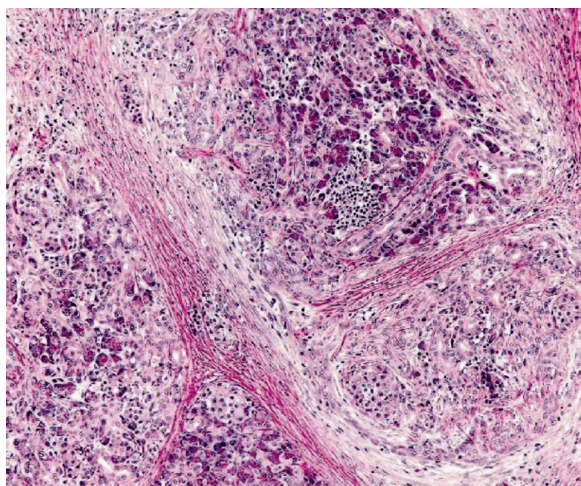


Fig. 3 Histopathology image demonstrating duct dilatation, fibrosis, and pancreatic tissue necrosis with parenchymal calcifications consistent with features of chronic pancreatitis (hematoxylin and eosin, $\times 200$).

pancreatitis have been reported to have undergone pancreatic resection because the entity was misdiagnosed as pancreatic ductal adenocarcinoma.³ However, there is no need for surgical intervention in mass-forming chronic pancreatitis and the entity usually responds well with a short course of steroids. Preoperative differentiation between mass-forming chronic pancreatitis and pancreatic ductal adenocarcinoma is of importance as clinical management varies.

CT is the imaging investigation of choice for characterization of mass lesions of the pancreas and for preoperative staging. On CT, mass-forming chronic pancreatitis appears as a lobulated hypodense and hypoenhancing mass with approximately 70% located in the pancreatic head.⁴ However, pancreatic ductal adenocarcinoma appears as hypodense infiltrating mass lesion commonly located in the head of pancreas and is noted to show delayed enhancement due to relative hypovascularity of the tumor. CT characterization of morphological features is often the preliminary step in providing a differential diagnosis of mass-forming chronic pancreatitis or pancreatic ductal adenocarcinoma. Duct penetration sign on CT helps support a diagnosis of mass-forming chronic pancreatitis over pancreatic ductal adenocarcinoma.⁵

Clinically, obstructive jaundice secondary to sclerosing cholangitis is the commonest presenting complaint in patients with mass-forming chronic pancreatitis. Jaundice associated with chronic pancreatitis is often waxing and waning type as opposed to jaundice secondary to pancreatic ductal adenocarcinoma cancer that typically increases with time. Elevated IgG4 levels were reported to be a specific diagnostic marker in chronic autoimmune pancreatitis.⁶ However, 10% of patients with pancreatic ductal adenocarcinoma and cholangiocarcinoma are positive for elevated IgG4 levels.⁷ CA19-9 tumor marker was considered to be specific for pancreatic ductal adenocarcinoma. However, CA19-9 levels are elevated in approximately 47 to 73% of cases with chronic pancreatitis.⁸ Combined measurement of serum IgG4 and CA19-9 levels might increase the diagnostic

accuracy to pancreatic ductal adenocarcinoma from mass-forming chronic pancreatitis. On CECT, mass-forming chronic pancreatitis and pancreatic ductal adenocarcinoma are visualized as hypoenhancing mass lesion in the arterial and portal venous phases that demonstrates homogeneous enhancement on delayed phase. The clinical features, laboratory investigations, and imaging findings are highly nonspecific in differentiating the above two entities and diagnosis is usually relied on findings of histopathology of the resected specimen. Differences between the two entities are shown in ► **Table 1**.

Chronic pancreatitis is characterized by evolution of irreversible structural and functional irregularities such as atrophy of pancreas, main pancreatic duct dilatation, marked fibrosis causing stricturing of the duct, and occasionally inflammatory mass-formation located in the region of pancreatic head that happens to be most common site of occurrence of pancreatic ductal adenocarcinoma. The inflammatory mass-forming chronic pancreatitis may cause stenosis of the common bile duct, main pancreatic duct, and duodenum, and even cause encasement of the vessels by the mass lesion. In such cases, the duct penetration sign on CT serves as the key differentiator between the two entities.

Approximately 60% of patients with chronic pancreatitis display parenchymal calcifications on imaging.⁹ Although ductal calcifications are most commonly encountered in chronic pancreatitis, a combination of ductal calcifications with parenchymal calcifications, glandular atrophy and cystic changes is highly specific for the diagnosis of chronic pancreatitis. However, intraductal papillary mucinous neoplasms, neuroendocrine tumors, and occasional cases of pancreatic ductal adenocarcinoma may show spotted calcifications.¹⁰ Although majority of calcifications related to chronic pancreatitis are ductal, occurrence of diffuse parenchymal calcifications is related to pancreatic ductal adenocarcinoma. A strong suspicion of pancreatic ductal adenocarcinoma should be made when there is fresh appearance of mass lesion on a background of chronic pancreatitis that reportedly causes displacement of calcifications. In the above-mentioned scenario, the differential diagnoses to be considered are mass-forming chronic pancreatitis, pancreatic ductal adenocarcinoma, autoimmune pancreatitis, neuroendocrine tumors of the pancreas, and solid pseudopapillary epithelial neoplasm.

Malignant lesions generally demonstrate avid FDG uptake, whereas most benign lesions are characterized by normal or minimally increased FDG accumulation. Mass-forming chronic pancreatitis is an exception to the above rule and it is possible to achieve the differential diagnosis between pancreatic adenocarcinoma and mass-forming pancreatitis by comparing the heights of SUVs in FDG PET/CT in the early phase.¹¹ But it is difficult to achieve the differential diagnosis between pancreatic ductal adenocarcinoma and mass-forming chronic pancreatitis by comparing the time course of SUVs in the early and delayed phase in PET/CT.¹² FDG PET/CT shows limited efficacy for differentiating pancreatic adenocarcinoma from mass-

Table 1 Differentiation of chronic mass-forming pancreatitis from pancreatic ductal adenocarcinoma

Parameter	Mass-forming chronic pancreatitis	Pancreatic ductal adenocarcinoma
Laboratory results		
Serum amylase and lipase	Usually elevated	May cause elevation in blood amylase and lipase due to impingement of the tumor on the duct system
Serum CA 19–9 levels	Not related	Elevated serum cancer antigen 19–9 levels
Serum IgG4 levels	Elevated in the autoimmune form of chronic pancreatitis	Occasionally elevated
Ultrasonography findings		
Location	Pancreatic head	Head and uncinate process
Margins	Ill-defined	Ill-defined
Double duct sign	Occasionally present	Commonly present
Pancreatic ductal system	Dilated unobstructed main duct	Abrupt truncation with upstream dilatation of main duct
Calcifications	Commonly present	Occasionally present
Vascular invasion	Occasionally present	Commonly present
Bile duct dilatation	Occasionally present	Commonly present
Cystic necrosis (collection)	Commonly present	Occasionally present
Glandular atrophy	Commonly present	Occasionally present
Lymph nodal enlargement	Commonly peripancreatic reactive nodes	Peri-pancreatic, porta hepatis, and para-aortic nodes
Metastases	Never	Commonly to liver, lung, peritoneum, adrenal, bone and distant nodes
FDG PET/CT findings		
Mean SUV (early phase—1 hour)	3.4	4.8
Maximal SUV at 1 hour	4.6	6.9
Mean SUV (delayed phase—2 hours)	4.8	5.6
Maximal SUV at 2 hours	6.8	7.6
Histopathology findings	Diffuse glandular atrophy, ductal dilatation with ductal calcifications	Infiltrating mass with ductal and vascular invasion

Abbreviations: FDG PET/CT, fluorodeoxyglucose-positron emission tomography/computed tomography; IgG4, immunoglobulin G4; SUV, standardized uptake value.

forming pancreatitis and their images should be cautiously evaluated for differentiating both diseases. Moreover, false-positive and false-negative results also may occur with FDG PET, and its inherent low spatial resolution may interfere with precise anatomic localization of findings. Relatively higher levels of ionizing radiation are also a consideration in whole-body PET. Likewise, long scanning times may affect patient compliance and increase patient motion. Finally, quantification and reproducibility of SUV may be inaccurate because of noise attenuation correction methods. Kato et al¹² performed a study on 47 patients with pancreatic masses, 33 of which were cases of pancreatic adenocarcinoma, 14 of which were cases of mass-forming chronic pancreatitis and found considerable overlapping between the SUVmax values of both entities. The findings of their study were comparable to the SUVmax value of the mass lesion in the current report.

Conclusion

In patients presenting with obstructive jaundice and a mass lesion commonly located in the pancreatic head, mass-forming chronic pancreatitis should be considered in the differential diagnosis. Duct penetration sign on computed tomography should favor the diagnosis of mass-forming chronic pancreatitis over pancreatic ductal adenocarcinoma. Imaging characteristics of mass-forming chronic pancreatitis and pancreatic ductal adenocarcinoma may be very similar and often histopathology holds the key for precise and accurate diagnosis of the entity that can drastically affect the patient management. Mass-forming chronic pancreatitis remains a diagnostic challenge and mass lesions of the head of pancreas should be reviewed with suspicion especially in patients with a background history of chronic pancreatitis. FDG PET/CT can be reliably used for tissue characterization of

mass-forming chronic pancreatitis and for monitoring disease response following treatment.

Funding

None.

Conflict of Interest

None declared.

Declaration of Patient Consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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