

REVIEW ARTICLE

Imaging Paradigm of Cystic Lesions in Pancreas

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ABSTRACT

This review article will acquaint the readers with the list and imaging characteristics of various common and uncommon cystic lesions encountered in pancreas. The new "CYSTIC" model approach proposed by the authors will ease in narrowing down the list of differential diagnosis. Since the use of cross-sectional body imaging has increased three fold in the last two decades, the radiologists should be aware of the various types of pancreatic cystic lesions.

INTRODUCTION

There has been a significant increase in the usage of advanced diagnostic imaging modalities, with almost tripling the use of multi-detector computed tomography (MDCT), magnetic resonance imaging (MRI) and magnetic resonance cholangio-pancreatography (MRCP) in the last two decades [1]. With this increasing use of radiology resources, there has been an overall increase in healthcare costs. The detection of incidental pancreatic cysts has increased which not only is scary for the patient but also adds anxiety to the gastroenterologist, pathologist and the radiologist. The gamut of pancreatic cysts can span from benign to borderline malignant to frankly malignant cysts. Accurate preoperative imaging diagnosis of these pancreatic cystic lesions is essential so as to reduce unnecessary intervention, healthcare costs and also guide the clinician and the patient for follow-up imaging if required.

METHODOLOGY

We made a literature review of articles published in English language using PubMed-library database search between the time periods January 2010 to April 2016. The following individual and combined keywords were used:

cystic [All Fields], lesions [All Fields], tumours [All Fields], pancreas [All Fields], imaging [All Fields], radiology [All Fields]. We also reviewed the citations of the references obtained from the articles. From a total of 139 articles, only 98 related articles were selected. All the case report and case series, original, review and pictorial articles were reviewed.

RESULTS

The first task is to classify the cysts into neoplastic and non-neoplastic cysts (**Table 1**) and the second task is to study the imaging morphology of the pancreatic cysts (**Table 2; Figure 1**). MDCT has an accuracy of 56–85% for characterization of cystic pancreatic lesions [2, 3, 4]. MRI together with MRCP is superior in characterizing the cystic lesions as it has excellent soft tissue contrast resolution and spatial resolution. Previous studies indicate that MDCT and MRI are comparable in identifying malignant behaviour of cystic pancreatic lesions [5]. 3D MRCP sequences can better identify the communication of cystic lesions with the main pancreatic duct and also the internal content of these lesions [6]. Secretin-enhanced MRCP is further advancement and refinement in MRCP technique for better study of ductal anatomy and identifying communication of pancreatic cystic lesions with the pancreatic duct [7]. The role of PET in characterizing incidental cystic lesion of pancreas is unknown. However, PET can be used for evaluation of metastatic spread [8]. Moreover, higher costs and availability of PET particularly in developing countries is a concern and practically not feasible in the current scenario. Contrast-enhanced ultrasound (CEUS) is another refinement in ultrasound technique which uses microbubbles (2-6 µm) containing air or gas with high molecular weight and high solubility, within a shell of biocompatible materials. Microbubbles can also be used during endoscopic ultrasound [9]. The European

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Abbreviations IPMN intraductal papillary mucinous neoplasm; MDCT multi-detector computed tomography; MRI magnetic resonance imaging; MRCP magnetic resonance cholangio-pancreatography

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Table 1: Classification of cystic lesions of pancreas.

| Neoplastic cysts | Non-neoplastic cysts |
|--|--|
| Intraductal-papillary mucinous neoplasm (IPMN) | Pseudocyst |
| Mucinous Cystic Neoplasm (MCN) | Infectious cysts |
| Serous Cystic Neoplasm (SCN) | Hydatid cyst |
| Solid Pseudopapillary Neoplasm (SPN) | Cysticercus |
| Cystic degeneration of solid neoplasms | Tuberculosis |
| Cystic ductal adenocarcinoma | Abscess |
| Cystic neuroendocrine tumour | Squamous-lined cysts |
| Cystic acinar cell carcinoma | Lymphoepithelial cyst |
| Cystic teratoma | Epidermoid cysts in intrapancreatic spleen |
| Cystic metastases | Squamoid cyst |
| Sarcoma | Rare cystic lesions |
| Cystic mesenchymal neoplasms | Lymphangioma |
| Schwannoma | Cystic hamartomas |
| Sarcoma | Congenital or developmental cysts |
| GIST | Retention cyst |
| Paraganglioma | Simple cyst |
| | Endometriotic cyst |
| | Duplication cyst |
| | Unclassified cysts |
| | Hemangioma |
| | True epithelial cysts |
| | Von Hippel–Lindau disease |
| | Autosomal-dominant polycystic kidney disease |
| | Cystic fibrosis |

Table 2. Classification according to imaging morphology of cystic lesions of pancreas.

| Unilocular | Microcystic | Macroscopic | Cystic transformation of pancreas | Cyst with ductal communication | Multifocal | Solid-cystic |
|---|--|---|--|--|--|---|
| <ul style="list-style-type: none"> • Pseudocyst • Cystic neuroendocrine tumour • Unilocular serous cystadenoma • Unilocular mucinous cystadenoma • Retention cyst • Developmental cyst • Epithelial cyst • Epidermoid cyst in intrapancreatic accessory spleen • Endometrial cyst • Infectious cyst | <ul style="list-style-type: none"> • Serous cystadenoma • Microcystic variant of ductal adenocarcinoma (very rare) | <ul style="list-style-type: none"> • Mucinous cystadenoma • BD-IPMN • Oligocystic serous cystadenoma • Lymphangioma • Lymphoepithelial cyst • Infectious cyst • Duplication cyst • Mesothelial cyst | <ul style="list-style-type: none"> • Dysontogenetic cyst • Cystic fibrosis • Disseminated serous cystadenoma • Congenital syndromes - Von Hippel Lindau, polycystic kidney disease, Ivemark, Trisomy 13 or 15, Meckel-Gruber, etc. | <ul style="list-style-type: none"> • IPMN • Collections post-pancreatitis as a part of disconnected duct syndrome • Retention cyst/ Squamoid cyst | <ul style="list-style-type: none"> • BD-IPMN • Pseudocysts • Serous cystadenoma • Neuroendocrine tumour • Developmental cyst • Epithelial cyst | <ul style="list-style-type: none"> • SPN • Pancreatoblastoma • Cystic metastasis • Cystic degeneration in solid tumours • Malignant transformation in cystic tumours • Hemorrhagic pseudocyst |

Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) in the updated guidelines in 2011 has recommended CEUS in the study of focal pancreatic lesions found during routine ultrasound. Endoscopic ultrasound (EUS) can be used for fine needle aspiration (FNA) and cytological analysis of aspirated fluid to study CEA, CA 19-9, amylase, lipase and viscosity of the fluid (**Table 3**). However, EUS is invasive, operator dependent and a difficult modality in aspirating lesions less than 3 cm.

In this review article, we try to simplify the classification of cystic pancreatic lesions on the basis of pathological-radiological approach. We have discussed in detail the common and uncommon cystic lesions of pancreas, typical and atypical imaging features and imaging predictors of malignancy of these lesions. In addition, we have tried to develop a new “CYSTIC” model for characterization of the

cystic lesions of pancreas (**Table 4**). This model would help the radiologists in reporting and for systematic narrowing down the list of differentials. In the end we provide a flowchart regarding management and follow-up of these cystic pancreatic lesions.

DISCUSSION

Pseudocyst

The most common non-neoplastic cystic lesion of pancreas is a pseudocyst. Pseudocyst is a circumscribed collection of fluid rich in pancreatic enzymes. It is sometimes also called as false cysts as these cysts do not have an epithelial lining. Pseudocyst occurs after sequelae of pancreatitis or trauma and usually takes around 4 weeks for the formation of wall around them. It can be seen in virtually any age group. The pathophysiology is continuous steady leakage of pancreatic juice due to separation of the

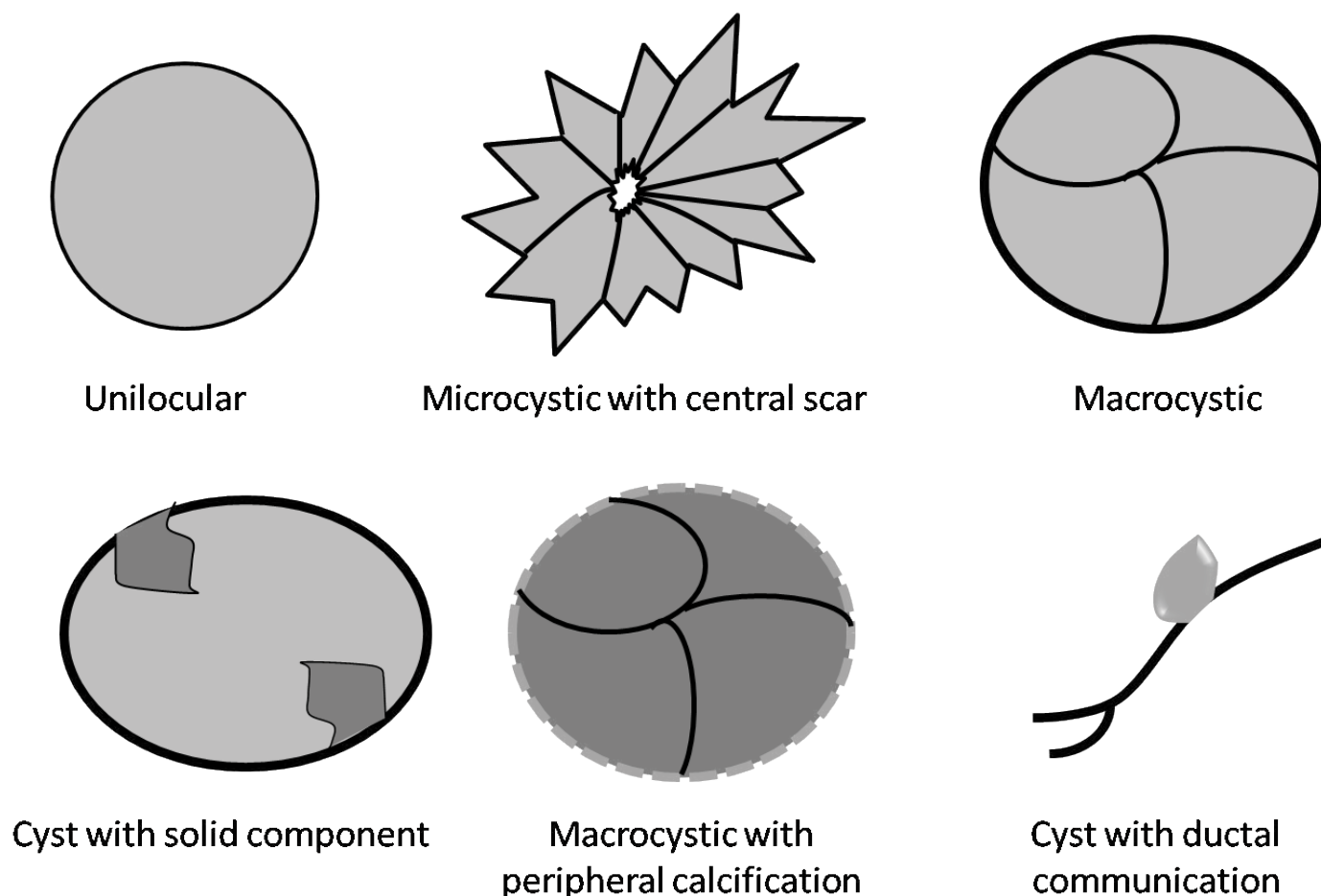


Figure 1. Line diagram illustrating various morphology of cystic pancreatic lesions.

Table 3. Fluid Analysis of cystic pancreatic lesions.

| Fluid Characteristics | Pseudocyst | SCN | MCN | IPMN | SPN | CPEN |
|-----------------------|---------------|---------------------|---------------------|---------------------|----------------------------------|---------------------------|
| Cytology | No epithelium | Cuboidal epithelium | Columnar epithelium | Columnar epithelium | Branching papilla, myxoid stroma | Salt-and-pepper chromatin |
| Viscosity | Low | Low | High | High | Bloody fluid | Low |
| Mucin | Low | Low | Very High | Very High | NA | Low |
| CEA | Low | Low | High | High | NA | Low |
| CA 19-9 | Low | Low | High | Variable | NA | Unknown |
| CA 72-4 | Low | Low | High | High | NA | Unknown |
| Amylase | Very high | Low | Variable | High | Low | Low |
| Glycogen | Absent | Very High | Absent | Absent | NA | Absent |
| DNA kRAS | Absent | Absent | Present | Present | Unknown | Unknown |

CPEN cystic pancreatic endocrine neoplasm; IPMN intraductal-papillary mucinous neoplasm; MCN mucinous cystic neoplasm; NA not applicable; SCN serous cystic neoplasm; SPN solid pseudopapillary neoplasm

main pancreatic duct (MPD) or its side branches in the absence of pancreatic parenchymal necrosis. In the absence of a history of pancreatitis or trauma, this diagnosis is very unlikely. On imaging, pseudocysts are usually unilocular, have a very well-defined regular wall, rim calcification may or may not be present (Figure 2). Antecedent features of pancreatitis (inflammation, parenchymal calcification and atrophy) if present may clinch the diagnosis. Thick enhancing walls, gas within the collection and restriction on diffusion-weighted imaging on MRI is suggestive of secondary infection. Connection with the MPD and internal debris within the cyst may or may not be present [10, 11].

No malignant potential is documented. The fluid within the pseudocyst may be turbid or hemorrhagic, has a low mucin content, Carcinoembryonic antigen (CEA) concentration is <5 ng/mL whereas amylase concentration is usually higher than 250U/L [10, 12, 13].

Mucinous Cystadenoma

This cystic neoplasm of pancreas is exclusively spotted in females in the 4th – 5th decade of life and because of which these lesions are also referred to as lesions seen in “Mother” age group. The location is commonly in the body or tail of pancreas. These lesions are usually oval shaped with thick

Table 4: “CYSTIC” model approach in cystic pancreatic lesions.

| “CYSTIC” Model approach in cystic pancreatic lesions | | | | | | |
|--|---|---|---|---|---|--|
| | ‘C’ | ‘Y’ | ‘S’ | ‘T’ | ‘I’ | ‘C’ |
| Pancreatic Cystic Lesions | Characteristic Location and Loculation | Years-age Group | Sex Size Shape | Tumour Enhancement Pattern | Incidence Imaging Prognosticators for Malignancy | Communication with Duct Calcification Central scar |
| Pseudocyst | Head, body, tail Unilocular/ multilocular | Any age group | M>F Any size Variable shape | No enhancement Enhancing wall s/o infection | Very common No malignant potential | Disconnected duct syndrome Rim calcification ± No scar |
| MCN | Body, tail Macrocystic (<6, each >2 cm) | 4 th -5 th decade | F>>M Any size Oval | Thick peripheral wall enhancement, subtle thin septal enhancement | Moderately common Solid enhancing component; irregular wall; peripheral calcification | Absent Peripheral calcification No scar |
| BD-IPMN | Head, body, tail Macrocystic | 6 th -7 th decade | M>F (3:2) Usually < 3cm Bunch of grapes | Thin peripheral enhancement ± | Common Size > 3 cm; MPD >> 6 mm; thick irregular wall; septa; mural nodules | Present Septal calcification ± No scar |
| MD-IPMN | Head, body, tail Diffuse MPD dilatation | 6 th -7 th decade | M>F (3:2) MPD ≥ 5mm Elongated | No enhancement | Rare MPD > 10 mm; mural enhancing nodules | Present Calcification ± No scar |
| SCN | Head, body, tail Microcystic (>6, each <2 cm) | 6 th -7 th decade | F > M (3:1) Variable Lobulated | Thin wall and septal enhancement | Moderately common Rarely malignant - enhancing solid component; retroperitoneal lymph nodes | Absent Central calcification Central scar present |
| SPN | Body, tail Unilocular | 2 nd -4 th decade | F>>>M Variable Oval/Round | Hemangioma like progressive enhancement | Rare Large size; local Invasion; enlarged nodes | Absent Uncommon No scar |
| Cystic NET | Head, body, tail | 5 th -6 th decade | F=M Variable Oval | Thick peripheral; solid-cystic enhancement | Moderately common Large size; invasion; metastasis | Absent Calcification ± Absent |
| Lymphoepithelial cysts | Extrapancreatic/ exophytic Variable shape | 3 rd -8 th decade | M>>F (4:1) Variable Lobulated | Negative or low CT HU value Hyperintense T1-W MR Subtle diffusion restriction | Very rare No malignant potential | Absent Septal/peripheral calcification ± Absent |
| Lymphangioma | Body, tail Macrocystic | Any age group | F>M Usually large Variable | Predominantly cystic with very thin septations | Very rare No malignant potential | Absent Septal calcification ± Absent |
| Cystic pancreatic hamartoma | Head, body, tail Unilocular/ multilocular | 3 rd -6 th decade | M>F Variable Variable | Solid-cystic, chronological change in morphology | Extremely rare No malignant potential | Absent Variable Absent |
| Dermoid cyst | Head, body, tail Unilocular/ multilocular | Any age group | M=F Variable Variable | Fat, calcium, Negative CT HU | Extremely rare No malignant potential | Absent Usually present Absent |
| Epidermoid cyst | Tail Unilocular | 4 th decade | M=F Small Smooth | Enhancement similar to splenic parenchyma; accessory spleen | Extremely rare No malignant potential | Absent Absent Absent |
| Retention cyst | Head, body, tail Unilocular | 3 rd -7 th decade | M=F Variable Smooth | Variable peripheral enhancement; ductal anomaly; stricture/ stone/tumour | Extremely rare Solid component, macro-septations, mural nodules | Present – uniform upstream dilatation Variable Absent |
| Dysontogenetic cyst | Diffuse involvement Solitary or polycystic | Congenital | M=F Variable Variable | Simple cysts without nodule/septa/ wall thickening/ enhancement | Extremely rare No malignant potential | Absent Absent Absent |
| Duplication cyst | Head, body, tail Unilocular | Any age group | M=F Small-medium size Smooth | Cyst with smooth enhancing walls; Associated with anomalies of pancreas and ducts | Rare No malignant potential | Communication ± Absent Absent |

HU Hounsfield units; MCN mucinous cystic neoplasm; MPD main pancreatic duct; NET neuroendocrine tumour; SCN serous cystic neoplasm; SPN solid pseudopapillary neoplasm

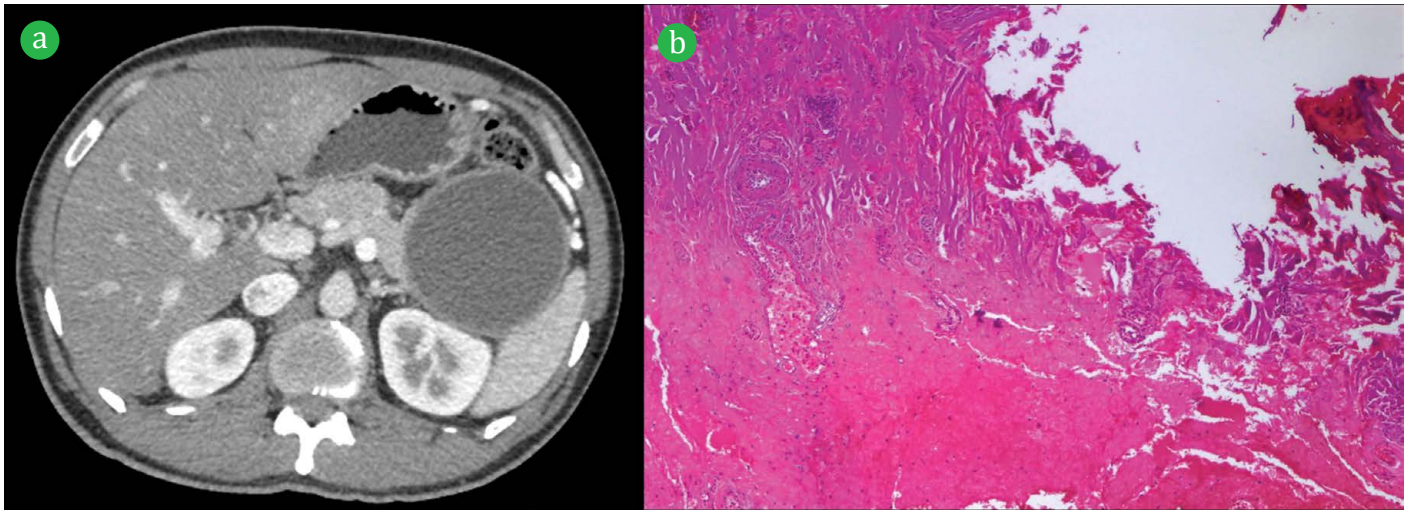


Figure 2. Pseudocyst in a 35-year-old male: **(a).** Axial CT image showing a well-defined unilocular cystic lesion with a well-defined wall without calcification, septations or solid component in a patient of prior history of pancreatitis. **(b).** Section of pseudocyst wall comprising of fibrocollagenous wall with inflammation and no lining epithelium (200X, HE).

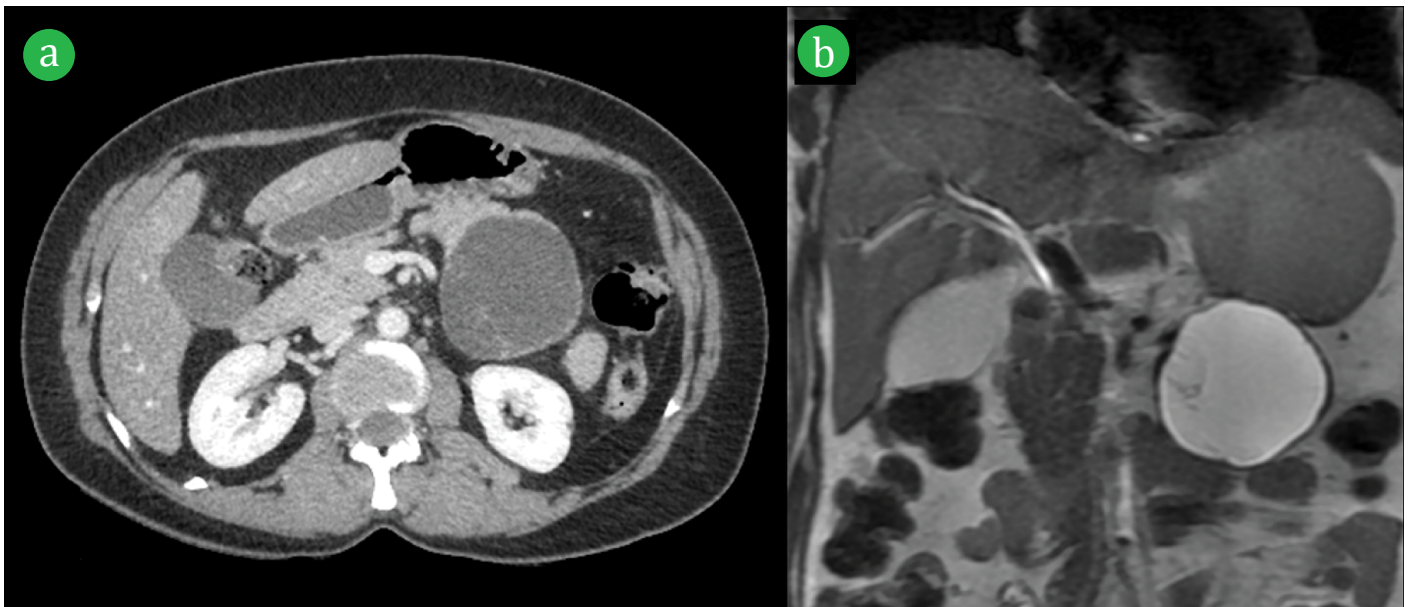


Figure 3. Mucinous cystadenoma in a 46-year-old-female: **(a).** Axial contrast-enhanced CT image showing well-defined cystic lesion in tail of pancreas with thin enhancing septations **(b).** Coronal T2-weighted MR image showing hyperintense cystic lesion with linear hypointense internal septations.

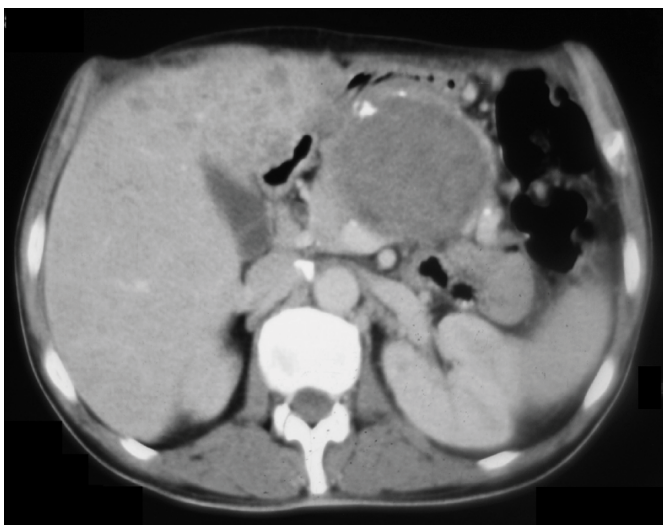


Figure 4. Malignant MCN with liver metastases in a 48-year-old male: Axial CT image showing solid-cystic lesion in the body of pancreas with peripheral calcification. Enhancing solid components is seen within the lesion. Liver metastases are also evident.

walls, macrocystic and multilocular (>2 cm, <6 in number) [14]. Peripheral calcification may or may not be seen and central scar is absent (**Figure 3**). They do not communicate with the MPD which distinguishes this entity from side-branch IPMN. The cysts may occasionally be unilocular and contain debris or hemorrhage. Imaging predictors for malignant transformation (6-36% prevalence) [15] into mucinous cystadenocarcinoma are peripheral calcification, solid component and irregular enhancing walls (**Figure 4**). The fluid within mucinous cystic neoplasm is rich in mucin, thick and highly viscous, CEA levels >192 ng/mL with variable amylase concentrations [10, 12, 13]. The most characteristic histological finding in MCN which differentiates it from IPMN is the presence of a unique ovarian-type stroma not found in other pancreatic neoplasms. Ovarian stroma cells have occasional 'luteinized' cells – epithelioid cells with abundant clear cytoplasm and like its ovarian counterpart, the stroma of pancreatic MCN variably stains for estrogen, progesterone receptors and human chorionic gonadotropin.

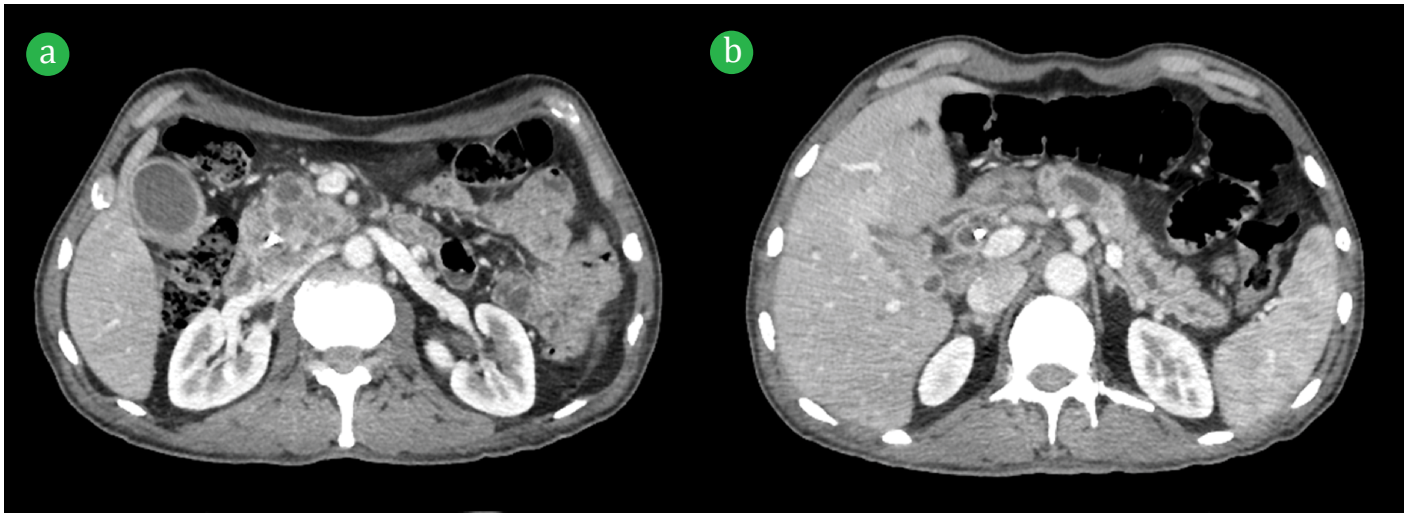


Figure 5. Malignant mixed IPMN in a 62-year-old-male: **(a)**. Contrast-enhanced CT image showing dilatation of side ducts involving the head of pancreas with enhancing solid component within these cysts **(b)**. CT image showing diffuse dilatation of the MPD.

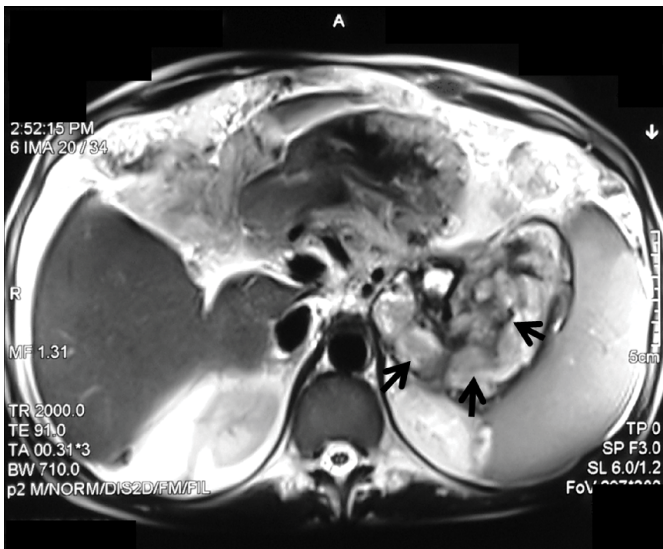


Figure 6. Colonizing variant of IPMN in 45-year-old-male: Axial T2-weighted MR image showing macrocystic lesion with dilated side ducts in tail of pancreas and hypointense frond like projections (arrows) within the cysts.

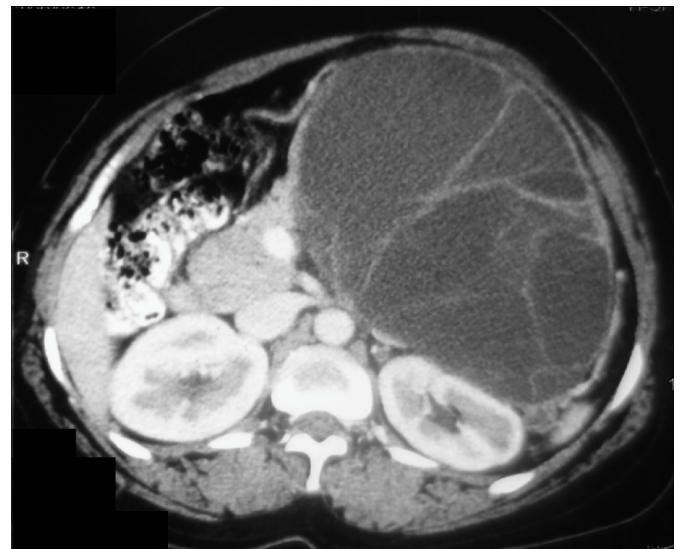


Figure 7. Macrocystic serous cystadenoma in a 61-year-old female: Axial CT image showing lobulated cystic lesion in the body of pancreas showing thin peripheral enhancement.



Figure 8. Serous cystadenocarcinoma in a 63-year-old-female: Axial contrast-enhanced CT image showing multicystic lesion with central calcification (arrow) with enhancing solid component within the cysts.

Intraductal Papillary Mucinous Neoplasm (IPMN)

IPMNs are characterized by cystic dilation of pancreatic ducts due to over production of mucin. It shows an adenoma-carcinoma sequence eventually culminating

in invasive carcinoma in few patients. IPMNs are more common in elderly males in 6th-7th decade and sometimes referred to as “Grandfather” lesions. Three types of IPMNs may be observed – main duct (MD), branch-duct (BD) and mixed variant. MD-IPMNs originate from the main pancreatic duct and are known as “Primary IPMNs”. BD-IPMNs develop from secondary branches of MPD, and also reported as “Secondary IPMNs”. Mixed variant involves the MPD as well as its side branches [16].

Typical imaging feature of MD-IPMN is dilatation of the MPD more than 5 mm in the absence of history of pancreatitis or any other cause explaining the dilatation. The dilatation may be segmental or diffuse (pan-ductal). Diameter of 5–9 mm is considered a “worrisome feature,” whereas main duct measurement ≥ 10 mm, enhancing nodules, abrupt change in the main pancreatic duct calibre with distal pancreatic atrophy, and lymphadenopathy are considered as “high-risk stigmata” (**Figure 5**). Another typical finding observed in MD-IPMNs is the dilatation of the major papilla, the minor papilla, or both, with a bulging of the MPD into the duodenal lumen [16]. Segmental

variant of MD-IPMN may be difficult to diagnose on imaging but may be suggested if communication with the MPD and upstream dilatation of the MPD is seen [17]. Primary IPMNs should also be differentiated from chronic pancreatitis. Duct dilatation without stricture, bulging papilla, nodule within the dilated duct, grape-like appearance of the cyst and nodule within the cyst are features which could differentiate MD-IPMN from chronic pancreatitis [18]. Rarely, a colonizing variant of IPMN (**Figure 6**) may be seen due to erosion and fistulisation into stomach, duodenum or the bile duct [19]. The chance of malignant transformation in MD-IPMN is about 60-92% [20, 21].

BD-IPMNs can involve any region of pancreas (predominantly uncinata) and can have a microcystic or macrocystic appearance. The macrocystic pattern is more common with a uni- or multilocular architecture. The microcystic pattern appears as bunch of grapes separated by thin septa similar to serous cystadenoma. BD-IPMNs can be multifocal or may show a diffuse morphology [22]. Only clue to the diagnosis of BD-IPMN is demonstration of communication with the MPD. Features indicative of malignant transformation are increased thickness of cyst wall, enhancement after contrast administration, mural nodules, cyst size greater than 3 cm and MPD calibre of 5-9 mm. The possibility of malignant degeneration in a BD-IPMN is approximately 6-40% [20, 21]. Secretin-enhanced MRCP is an innovative technique that can be used to differentiate BD-IPMN from other cystic neoplasms [23].

Serous Cystic Neoplasm (SCN)

Serous cystic neoplasms are more common in females (F:M=3:1) and are seen in the 6th-7th decade of life, therefore are also known as “Grandma” lesions. On imaging, these lesions are typical microcystic (>6 cysts, each <2 cm) and have thin wall with thin internal septations. It can involve any portion of the pancreas. Presence of fibrous central scar or central sunburst calcification is pathognomic, but seen in only 30% of cases [12]. Enhancement of thin septations may be seen on delayed contrast-enhanced scans. Atypical variants of these neoplasms are macrocystic (**Figure 7**) or oligocystic, unilocular, diffuse or disseminated, solid variant, and those associated with ductal dilatation

or haemorrhage. These atypical variants cannot be differentiated from mucinous cystic neoplasm, islet cell tumours or solid pseudopapillary tumor very confidently on imaging. Lobulated contour, thin wall, homogeneity of each locule on T1-weighted imaging and location in head of pancreas favours serous cystadenoma over mucinous cystadenoma [24, 25, 26]. Disseminated variant is associated with von Hippel Lindau (vHL) disease and seen at a younger age. These tumours are typically benign and malignant transformation is rarely seen. Average growth rate of this neoplasm is 1-4 mm per year, so surgeons usually recommend imaging follow-up in asymptomatic patients. Pointers towards malignant transformation are enhancing solid component and retroperitoneal lymphadenopathy (**Figure 8**). Biochemical analysis of fluid aspirate reveals clear non-mucinous fluid with high glycogen content and low CEA and amylase levels.

Solid Pseudopapillary Neoplasm (SPN)

SPNs are seen predominantly in young females in 2nd - 4th decade and so also known as “Daughter” lesions. Previously these tumours were known by various names like Hamoudi tumor or Franz tumor.²⁷ These tumours are usually seen in body or tail region, have solid-cystic component, well defined capsule and internal haemorrhage. ‘Hemangioma’ like progressive enhancement has been described and is characteristic of these lesions (**Figure 9**). SPNs rarely cause biliary or pancreatic ductal obstruction, even when located in the head of the pancreas [28, 29]. Although these tumours have very low malignant potential but local invasion, very large size and lymphadenopathy may be suggestive of malignant transformation. Occasionally peripheral calcification may be seen. The differential diagnosis considering the age of the patient are islet cell tumours, pancreaticoblastoma and calcified hemorrhagic pseudocyst. Features that distinguish SPN from neuroendocrine tumor of the pancreas are the signal intensity on T1-weighted images and enhancement pattern. SPN show some amount of increased signal on T1-weighted images while islet cell tumors show low signal on T1-weighted images. Islet cell tumors are more hypervascular than SPN [30].

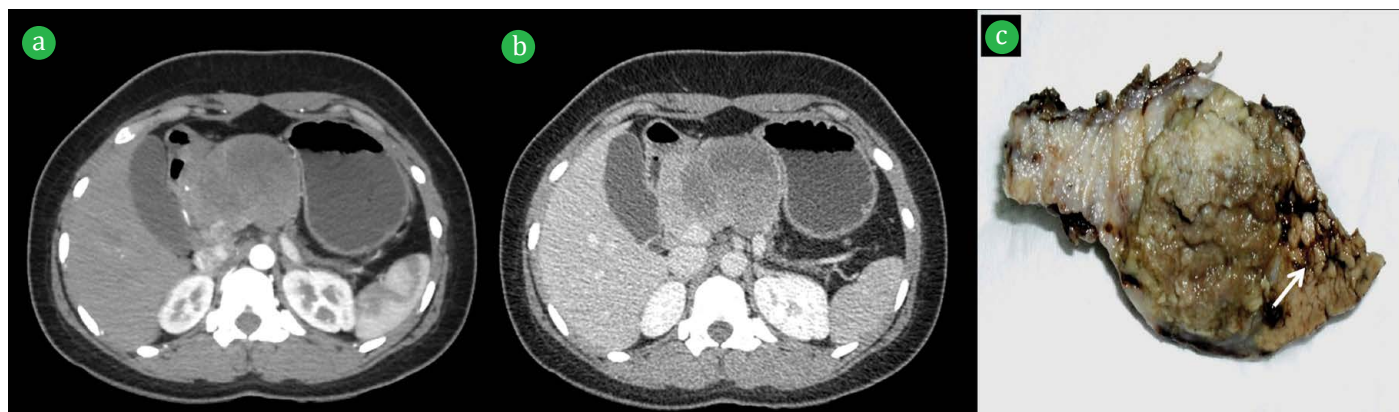


Figure 9. Solid pseudopapillary tumour in a 25-year-old female: (a). Axial contrast-enhanced CT arterial phase image showing solid-cystic mass lesion involving the head and body of pancreas (b). delayed phase CT image showing gradual progressive enhancement of solid component within the lesion (c). Gross section of tumor showing cystic degeneration (arrow).

Cystic Neuroendocrine Neoplasm

Neuroendocrine tumours (NET) of pancreas with cystic degeneration are rare non-functional islet cell tumours. These tumours are seen with equal incidence in both males and females usually in the 5th-6th decade. Peripheral enhancement of small cystic tumours and cystic degeneration in large hypervascular tumours favours the diagnosis of this tumour (**Figure 10**). Occasionally, thin septa, small solid component or calcification may also be seen. Patients with a cystic variant of NET have associations with multiple endocrine neoplasia (MEN type 1), von Hippel-Lindau and Wermer syndromes [31]. Cystic NETs are less likely to demonstrate perineural invasion, vascular invasion, regional lymph node metastasis, and synchronous distant metastasis in comparison with the solid variant of NET [32, 33].

Lymphoepithelial Cysts

Lymphoepithelial cysts of the pancreas are extremely rare and comprise only about 0.5% of the cystic neoplasms. These cysts are lined by stratified squamous epithelium. These cysts are predominantly seen in middle-aged or older male patients. Various hypotheses regarding its formation have been postulated - squamous metaplasia following ductal obstruction, which subsequently erodes into the surrounding peripancreatic lymph node; ectopic pancreatic tissue in the peripancreatic lymph nodes which has undergone liquefaction. Some theories regarding branchial origin has also been mentioned in the literature [34, 35]. The cysts contain granular keratinized material within. On imaging, the size varies from 1-6 cm. These cysts appear hyperattenuating on non-contrast CT. Negative CT attenuation may also be recognized when the lipid content is high. On T1-weighted MR images, these cysts may show subtle higher signal intensity and may not appear very bright on T2-weighted images as these are not just simple cysts. Sometimes, diffusion restriction may be seen due to keratinized material within the cyst. Thick peripheral wall, thin septae and faint calcifications

may be seen. Characteristic feature of these cysts are its epicentre being mainly extrapancreatic or exophytic nature (**Figure 11**) [36, 37].

Lymphangioma

Cystic lymphangiomas are rare cystic neoplasms which account for less than 1% of tumours. The age group varies from child to middle age. The tumour has a female preponderance. The pathogenesis is believed to be congenital malformation of lymphatic vessels or inflammation secondary to obstruction of lymphatic channels. Tumor size may vary between 3 and 20 cm [38]. On imaging, the tumor is a well-circumscribed, encapsulated, water density macrocystic lesion with thin septa similar in appearance to the cystadenoma (**Figure 12**). EUS (endoscopic ultrasound) guided fluid aspirate analysis shows chylous nature of fluid and elevated triglyceride levels [39].

Cystic Pancreatic Hamartoma

This is an extremely rare entity and accounts for <1 % of tumor-like cystic lesions of the pancreas with only 30 cases being reported so far in the literature.⁴⁰ It can be solid-cystic or purely solid. Any age group can be affected. Pancreatic hamartoma is usually a histopathological diagnosis after pancreatectomy. Only clue to the imaging diagnosis is chronological change in the morphology of the lesion, its indolent course and normal tumour marker levels [40, 41].

Pancreatic Ductal Adenocarcinoma with Cystic Degeneration

Ductal adenocarcinoma is the most common solid pancreatic neoplasms. Cystic degeneration is seen in nearly 8% of ductal adenocarcinomas. Cystic change in a pancreatic ductal adenocarcinoma is due to necrosis or intratumoral mucin cyst formation (**Figure 13**) [42]. Retention cysts and pseudocysts may be attached or lie in close vicinity to ductal adenocarcinoma [43]. In such cases it is extremely difficult to differentiate from other cystic neoplasms. However, certain imaging features

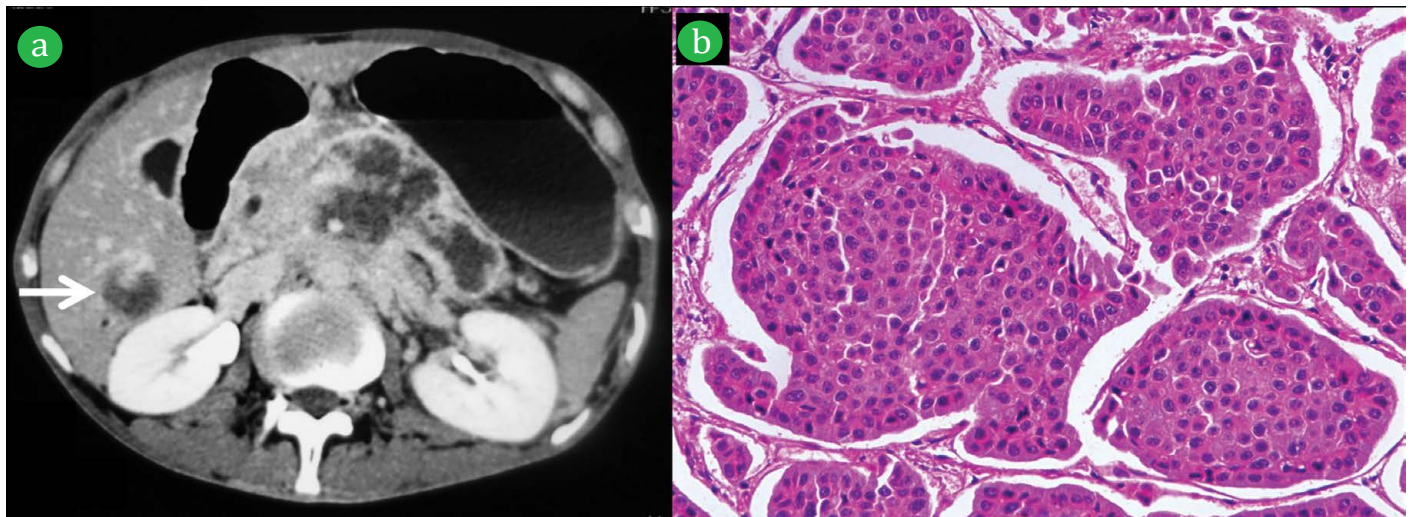


Figure 10. Cystic neuroendocrine tumour with liver metastasis in a 43-year-old-male: (a). Axial contrast-enhanced CT image depicting lobulated macrocystic lesion showing strong peripheral enhancement with liver metastasis (arrow). (b). Section from the viable areas of the NET with cystic degeneration showing tumor islands separated by fibrous stroma and cells showing finely stippled chromatin (200X, HE).

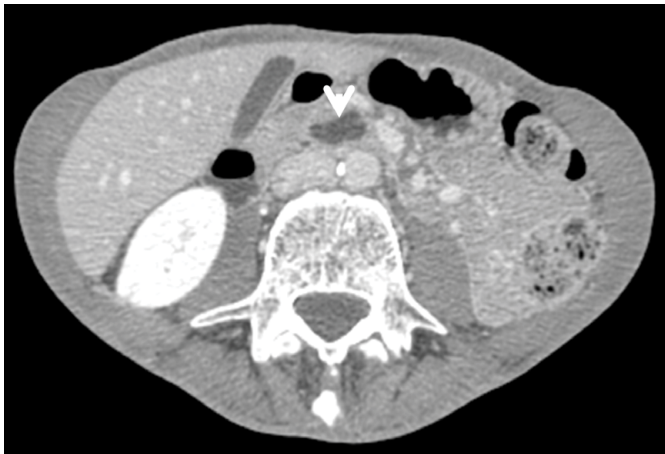


Figure 11. 59-year-old-female with lymphoepithelial cyst: Axial CT image showing lobulated partially exophytic cystic lesion (arrow) with thin septations.

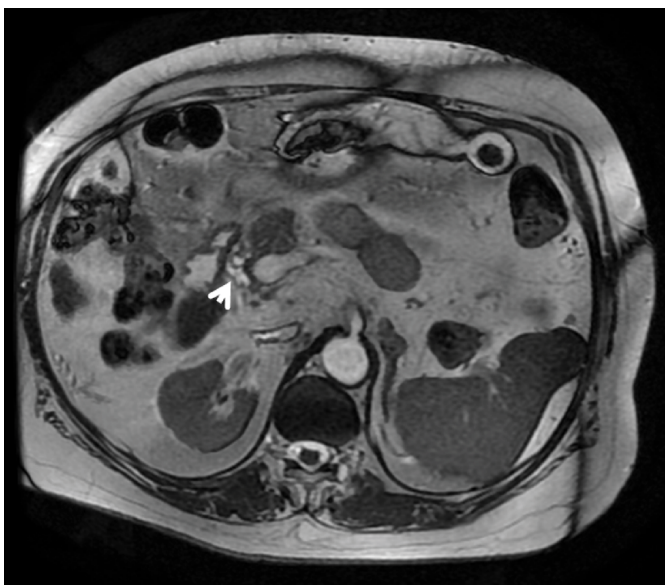


Figure 12. 67-year-old-asymptomatic female with incidental lymphangioma: Axial FIESTA image showing small lobulated cystic lesion (arrow) with thin septations abutting the head of pancreas.



Figure 13. 57-year-old-female with pancreatic ductal adenocarcinoma: Axial CT image showing cystic degeneration in ductal adenocarcinoma with liver metastases.

may be helpful - irregular contour, mural nodule, localized thickening, dilatation of the MPD, peripancreatic fat

infiltration, perineural and perivascular invasion [44]. Rarely, a microcystic variant of ductal adenocarcinoma can be encountered which may look similar to SCN [19, 45].

Acinar Cell Neoplasm/Acinar Cystic Transformation of Pancreas

Acinar cell cystadenoma (ACC) or cystadenocarcinoma is now recognized as a distinct pathologic entity that belongs to a family of acinar cell neoplasms. It is extremely difficult to diagnose preoperatively on imaging [46]. ACC was first described by Albores-Saavedra in 2002 [47]. Acinar cystic transformation (ACT) of the pancreas is also known as ACC. Multiple microcysts may be seen in the body or head region giving the appearance of ‘spongy pancreas’. Lack of ductal dilatation, well-margined hypovascular multi-cystic mass, chronic inflammatory changes in the vicinity could possibly suggest a diagnosis [48].

Dermoid Cyst

Dermoid cyst (cystic teratoma) of pancreas is a rare entity in the form of case reports. There is no gender predominance. It is characterised by presence of a cystic lesion with a Hounsfield unit of -20 to -140 HU [49]. On imaging, presence of macroscopic fat, fluid-fat levels, and calcium within the same lesion is pathognomic of a mature teratoma [50]. Suppurative infections are more common in dermoid cyst. Serum markers, such as CEA and CA19-9 are lower compared to other pancreatic cystic neoplasms [51].

Epidermoid Cyst in Intrapancreatic Spleen

The incidence of ectopic splenic tissue in the abdomen is nearly 10% in the general population [52]. Intrapancreatic accessory spleen is very rare and cyst formation even rare. Epidermoid cysts in intrapancreatic accessory spleens are usually seen in the fourth decade and are located exclusively in the tail of the pancreas. It is an extremely difficult diagnosis, however solid component if present and the cyst wall may show enhancement pattern similar to splenic parenchyma [52]. Identification of the accessory spleen around the cyst is also another clue for the diagnosis [53].

Hydatid Cyst

Hydatid cyst of pancreas is extremely rare. Its incidence varies from 0.19-2% of the various sites of hydatid disease. These lesions can be solitary or multifocal involving the entire pancreas. The differential diagnosis of pancreatic hydatid is to be considered only when daughter cysts, curvilinear laminated membrane, faint calcification are seen inside the mother cyst on imaging (Figure 14). This is particularly true for patients living in regions where the disease is endemic. In this category of patients, serologic tests may be helpful [54].

Retention Cyst

The pancreatic retention cyst is a rare benign cystic disease of the pancreas. In other words, cystic dilatation of the pancreatic duct is a retention cyst. It may or may not be associated with an obstructive cause like calculi, stricture, mucin plugs, tumours, etc. Communication with the MPD

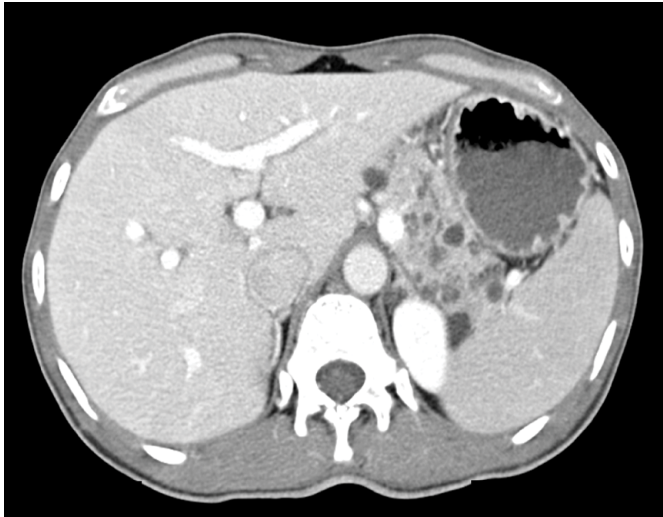


Figure 14. Pancreatic atypical hydatid cysts in a 30-year-old-male: Axial contrast-enhanced CT image showing multiple tiny cysts in body and tail of pancreas with thin septations within the lesions in a known case of disseminated hydatid disease.

and smooth upstream dilatation of the pancreatic duct without any mural nodule may be suggestive of retention cyst [55]. Retention cysts may be associated with pancreas divisum [55]. Some researchers consider these cysts to be biliary counterparts of choledochal cysts [56]. CA19-9 levels should be checked whenever retention cyst is encountered as it may be an indirect clue to co-presence of proximal ductal adenocarcinoma [55, 56].

Mesothelial Cyst

Mesothelial cysts are rare benign cysts originating in the serous cavities and are very rarely seen in visceral organs. These cysts are lined by cuboidal to flattened epithelium. On imaging, these cysts appear as unilocular cyst. Combination of radiological findings and mesothelial markers of aspirated fluid are key to preoperative diagnosis [57].

Dysontogenetic Cyst

Polycystic disease of pancreas is also known as Dysontogenetic cysts or congenital cysts of pancreas. It is a very rare entity that may occur as a solitary cyst, polycystic disease with association with renal cysts, liver, and central nervous system or retinal abnormalities. The most important differential diagnosis is IPMN [58, 59].

Enteric/Pancreatic Duplication Cyst

This is an extremely rare entity. The patients typically present with pancreatitis. On imaging, these cystic lesions are in close vicinity to the stomach or a bowel loop abutting the pancreas (**Figure 15**). It is a difficult diagnosis on imaging; however one should keep a differential whenever an aberrant pancreatic lobe, bifid pancreas or ductal anomaly is encountered [60, 61].

Pancreatic Cysticercal Cyst

Pancreatic cysticercosis is extremely rare and should be kept in the list only in endemic and developing countries. Isolated pancreatic involvement is even

rarer and involvement of pancreas is usually seen in disseminated cysticercosis [62]. MR is an excellent modality because of superior soft tissue contrast. Cysticercal cyst appears hyperintense on T2-weighted images, dark on T1-weighted images. On post-contrast sequences, enhancing eccentric mural nodule if seen is diagnostic.

Pancreatic Abscess

Pancreatic abscess is a late complication of acute necrotizing pancreatitis. It is usually seen in infected collections post-pancreatitis. On imaging, presence of gas, thick irregular enhancing walls, diffusion restriction on MR in the background of clinical setting is suggestive of pancreatic abscess [63]. On aspiration, if pus is drained and culture reveals growth of microorganisms, pancreatic abscess is confirmatory.

True Epithelial Cysts

True epithelial cysts are usually syndromic and associated with von Hippel-Lindau, autosomal-dominant polycystic kidney disease, and cystic fibrosis. On imaging, unilocular cyst with no perceptible wall and no internal septa is seen without any enhancement [64].

Cystic Metastasis

Cystic metastases to the pancreas are uncommon, but can be seen from ovarian, lung (**Figure 16**), renal cell carcinoma [65].

Other Rare Cystic Lesions

Mesenchymal tumours of the pancreas are rare and can have solid-cystic component. Schwannoma, sarcoma, GISTs, praganglioma, etc. has been described in the literature as case reports [66, 67]. Cystic transformation of the pancreas has also been described in a variety of congenital syndromes including Ivemark, Trisomy 13 or 15, Meckel-Gruber, cystic fibrosis, von Hippel Lindau, polycystic kidney disease [65, 68]. Pancreatic tuberculosis should also be kept in the

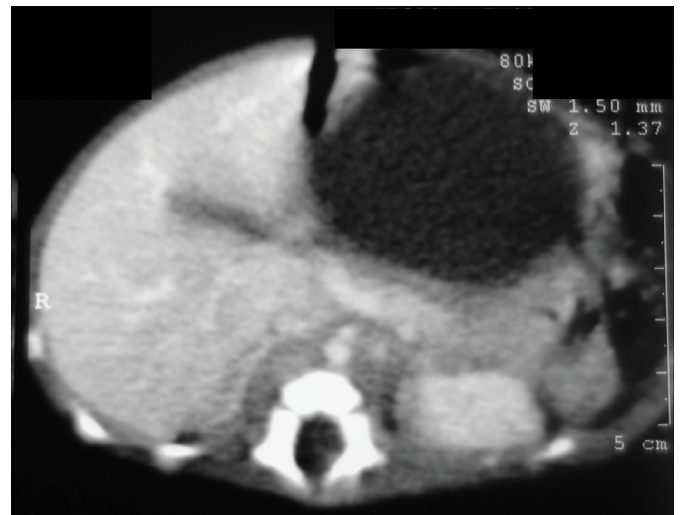


Figure 15. Duplication cyst in a 1-year-old-child: Axial CT image showing a unilocular cystic lesion in close relation to the body and tail of pancreas which on histopathology turned out to have gastric epithelial lining.

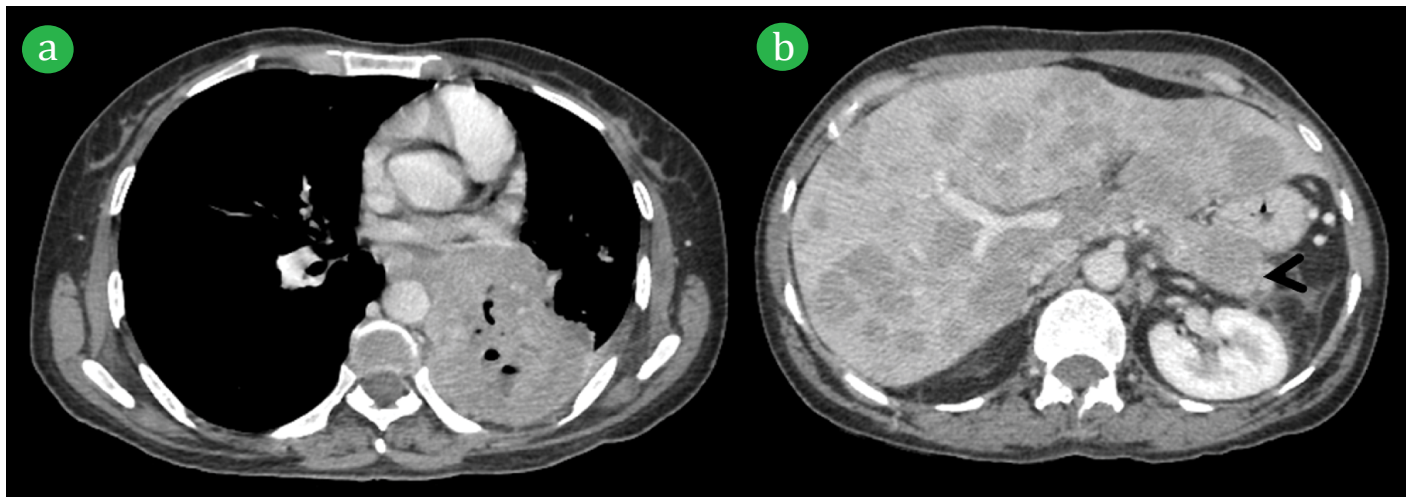


Figure 16. 50-year-old-female with pancreatic metastasis from lung cancer: (a). Axial CT image showing left lung cancer (b). with metastases in liver and pancreas (arrow).

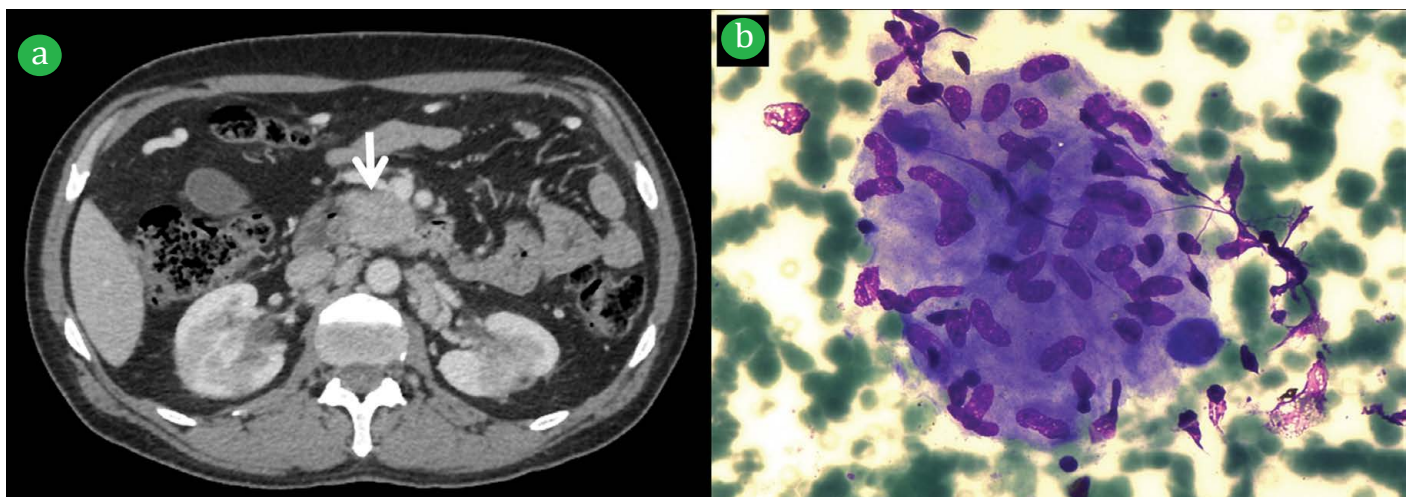


Figure 17. 48-year-old-male with pancreatic tuberculosis: (a). Axial CT image showing bulky heterogeneous head of pancreas (arrow) with retroperitoneal lymphadenopathy and hypodense lesions in both kidneys which on histopathology was suggestive of granulomatous pathology (b). Smear showing epithelioid cell granulomas (200X, Geimsa)

list of differentials in the endemic regions especially pancreatic necrotic mass with necrotic peripancreatic lymphadenopathy is seen in cases of long standing fever and weight loss (**Figure 17**) [69].

Anatomic Variants, Pseudolesions Mimicking Cystic Pancreatic Lesions

Various anatomic variations and pseudolesions in and around pancreas can mimic cystic neoplasm of pancreas [70]. These lesions can be divided according to various parts of pancreas viz., head and neck, body or tail region. In the head, neck and body region - the lesions could be unenhanced bowel, paraduodenal pseudocyst (sequelae to groove pancreatitis), juxtaampullary duodenal diverticula, fatty replacement, duodenal duplication cyst, choledochocoele, wirsungocoele, santorinocele, adrenal lesions, and vascular lesions. In the neck region the pseudolesions can be renal or adrenal lesions, bowel pathologies or accessory spleen.

Recent Advances

Acoustic radiation force impulse (ARFI) with shear wave speed (SWS) quantification can be used for

characterization of pancreatic masses. D’Onofrio *et al.* have used this technique. SWS of more than 2.74 m/s suggest ductal adenocarcinoma if the lesion is solid. For the cystic lesions, non-numerical ARFI value XXXX/0 is typical of simple fluids that may suggest serous cystic neoplasm and if the numerical value is more than zero, it is a pointer towards mucinous cystic neoplasm [71, 72]. Contrast-enhanced ultrasonography (CEUS) of the pancreas can be used for the characterization of cystic pancreatic masses. Moreover, CEUS is particularly useful in the follow up of borderline cystic pancreatic lesions [73]. Diffusion-weighted MRI has a very limited role in the evaluation of cystic lesions of pancreas as diffusivity is highly dependent upon the tissue characteristics of the tumour [74, 75].

Management Guidelines of Cystic Pancreatic Lesions

Encountering a cystic lesion in pancreas is scary for the patient, radiologist, gastroenterologist and also the pathologist. Usually, when there is a history of pancreatitis, there is not much of a problem. However, the problem arises in the absence of a history of pancreatitis, trauma and other relevant parameters that deviates from the

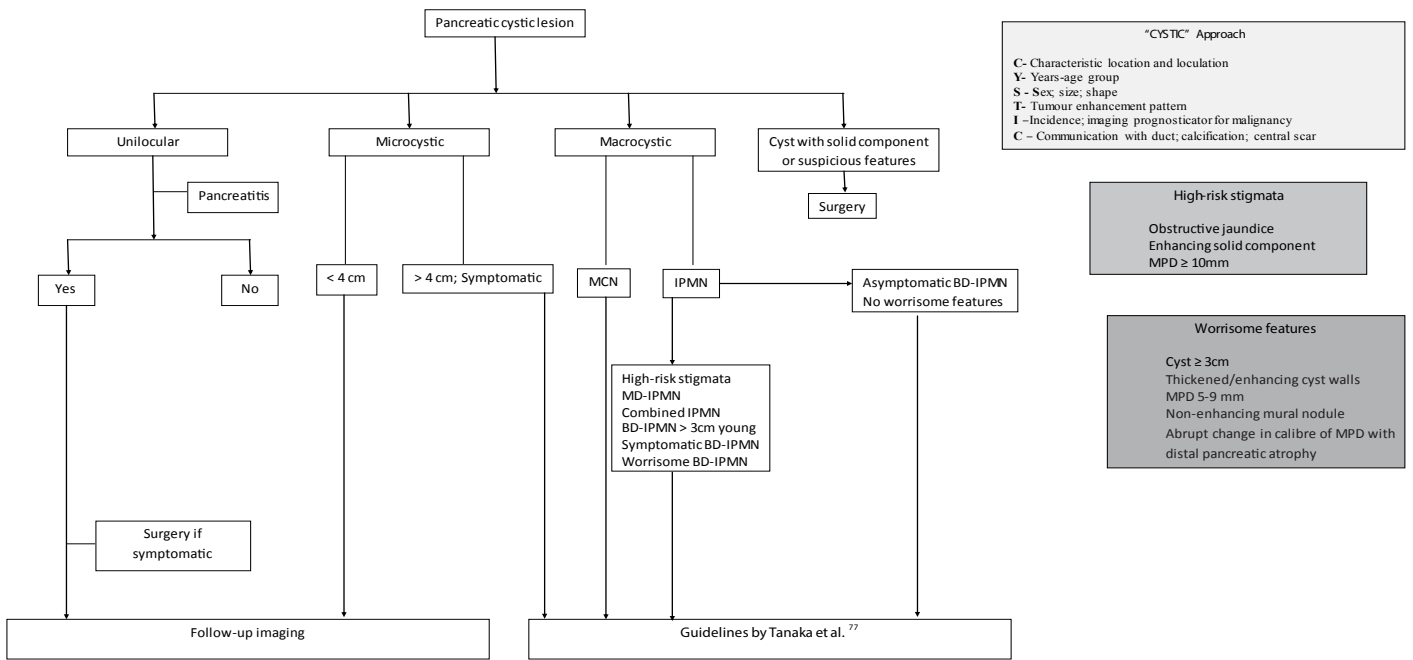


Figure 18. Flowchart depicting the management guidelines of cystic pancreatic lesions.

diagnosis of a pseudocyst. Mucinous cystic neoplasms are of concern and therefore the Sendai Consensus Guidelines were formulated in 2006 which was updated in Fukuoka in 2012 to guide the management of cystic mucinous neoplasms of the pancreas [76, 77]. Simplified flowchart regarding follow-up and management of the cystic lesion of pancreas has been detailed in **Figure 18**. For management of MCN and IPMN we follow the guidelines by Tanaka *et al.* [77].

CONCLUSION

Detecting a cystic pancreatic lesion is not uncommon in everyday radiology practice. Familiarity of the typical and atypical imaging features is crucial in helping narrow down the list of differential diagnosis. The authors hope that use of the new “CYSTIC” model as detailed above will help the radiologists in accurately diagnosing benign, borderline malignant and malignant cystic lesions preoperatively. This would avoid unnecessary delays in managing premalignant and malignant lesions, guide follow up and avoid surgery in cases of benign cystic lesions.

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Conflict of Interests

Authors declare no conflict of interests for this article.

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