Pancreatic Cystic Neoplasms: Imaging Characteristics, Differential Diagnosis and Management

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Learning Objectives

• To demonstrate imaging findings of the key pancreatic cystic neoplasms and their differential diagnoses

• To describe patient demographics and clinical history essential for diagnosis

• To describe the role of EUS as a problem solving tool in management and treatment planning
Pancreatic Cystic Lesions

Pathological Classification of Cystic Lesions

- **Injury/inflammatory related cysts**
  - Pseudocysts and walled off necrosis

- **Neoplastic cysts**
  - **Ductal lineage**
    - Serous cystadenoma
    - Mucin-producing lesions
      - Mucinous cystic neoplasm (MCN)
        - Mucinous cyst adenoma
        - Mucinous cyst adenocarcinoma
      - Intraductal papillary mucinous neoplasms (IPMN)
    - Ductal adenocarcinoma with cystic features
  - **Not otherwise specified**
    - Intraductal tubular carcinoma

- **Endocrine lineage**
  - Cystic neuroendocrine tumors

- **Acinar lineage**
  - Acinar cell cystadenocarcinoma

- **Undetermined lineage**
  - Solid pseudopapillary neoplasm (SPN)

- **Other miscellaneous**
  - Lymphoepithelial cysts
  - Squamoid cyst of pancreatic ducts
  - Epidermoid cysts within the intrapancreatic accessory spleen
  - Abscess

Characterization

- MR modality of choice – superior contrast resolution
  - Type of fluid
  - Cyst morphology and size
  - Hemorrhage
  - Septation/scar
  - Soft-tissue components/nodularity
  - Communication with the pancreatic duct
  - Surrounding pancreatic parenchyma

- Patient demographics and clinical history are essential for diagnosis

Serous Cystadenoma

**Background**

- Serous producing neoplasm
- 20-30% of cystic neoplasms
- Despite benign nature, tend to grow slowly and achieve larger size but do not predict malignancy

**Demographics**

- “Grandmother lesion”
- Older (median age 65)
- F>M; 75% female
- Usually incidental and asymptomatic; if larger (>4cm) may cause symptoms of abdominal pain or rarely jaundice from mass-effect and duct obstruction

EUS:
- Honey comb appearance
- Cyst fluid amylase and CEA low to undetectable
- Rich in VEGF-A (vascular epithelial growth factor> 8500, 100% sensitive and 97% specific

Serous cystadenocarcinomas should be considered and managed as benign lesions

G.H. Sakorafas. et al Surgical Oncology 20 (2011) e84-e92
Serous Cystadenoma

- Microcystic lesion composed of numerous small cysts ranging from 0.1-2 cm typically less than 1 cm separated by fibrous septae radiating from central scar (honeycomb or cluster of grapes) with external lobulations
- MR helps show simple fluid signal intensity on T2-weighted images; lesion can appear solid on CECT and CEMR from septal enhancement
- Septae demonstrate progressive enhancement
- Stellate, coarse Ca+ can be present in the central scar (30%), with a corresponding signal void (pathognomonic of SCN)
- No capsule

Serous cystadenoma: Photomicrograph x 400 [H-E] stain demonstrate typical clear cells (arrows) without cytologic atypia lining the cyst wall and forming small nests. Clearing of the cytoplasm is due to glycogen accumulation.
Serous Cystadenoma

Serous cystadenoma: 70-year-old female with history abdominal pain. Axial T2 weighted MR image reveals lobulated microcystic, T2 hyperintense and T1 hypointense mass in the tail of the pancreas (arrows). Progressively enhancing septae following contrast administration (pink arrows). On DWI, mass shows high ADC due to no restriction (green arrow).

DWI: DWI and ADC values of serous cyst adenoma depends on amount of fibrous septa or fluid in the lesion (not of much help)
Serous Cystadenoma: Variants

- **Macrocystic/Oligocystic**
  - 10% Unilocular cystic lesion with lobulated or bosselated contour with few cysts > 1 cm
  - No wall enhancement
  - Location: Pancreatic head, lacks central scar
  - DDX: MCN and Pseudocyst
  - EUS with aspiration for definite diagnosis

- **Von Hippel Lindau (Serous cystadenoma)**
  - Multiple serous cystadenomas and macrocystic variants occur in VHL
  - Typical involvement is diffuse or in patchy fashion
  - Look for manifestations of VHL (RCC, pheochromocytoma, hemangioblastomas as well neuroendocrine pancreatic tumors and cysts, etc.)

Brugge WR. J Gastrointest Oncol. 2015 Aug;6(4):375-88
Differential Diagnosis of Oligocystic Serous Cystadenoma

**Oligocystic serous cystadenoma**

- Ax T2
- Ax Post T1

70-year-old female complaining of vague abdominal pain.

**MCN**

- Ax T2
- Ax Post T1

40-year-old female complaining of vague abdominal pain. Cyst fluid with high CEA and low amylase levels.

**Pseudocyst**

- Ax T2
- Ax Post T1

55-year-old male with history of pancreatitis. Cyst fluid with high amylase levels.
Serous Cystadenoma: Variants

Solid Variant

- Only hypervascular cystic pancreatic tumor with the exception cystic neuroendocrine
- Intra-tumoral hemorrhage can occur
- Rare entity

Solid enhancing pattern - mimicking neuroendocrine tumor

Sahni and Mortele AJR 2009 Apr, 192(4):923-35
Brugge WR. J Gastrointest Oncol. 2015 Aug;6(4):375-88
Mucinous Cystic Neoplasm (MCN)

Demographics and Background

- **Exclusively** in women classically 40-50 years of age “Mother Lesion”
- Body and tail predominantly affected
- 30% patients are asymptomatic. Symptomatic patients complain of abdominal pain, palpable mass, weight loss, fatigue, anorexia or jaundice. Some patient may present with *pancreatitis*
- 10% of cystic neoplasms
- Mucin-producing neoplasm lined with thick tall columnar epithelium, surrounded by *ovarian*-type stroma
- Nearly all MCNs surrounded by a thick layer of spindle cells containing *progesterone and estrogen receptors*
- All have malignant potential
  - Spectrum of low, moderate, or high-grade dysplasia, +/- features of invasive carcinoma
  - 1/3rd reported to harbor invasive carcinoma, which can be very focal

**Ectopic ovarian stroma incorporated during embryogenesis into the pancreas and may release estrogens and progesterone causing epithelium to proliferate and form cystic tumors**

MCN Imaging Features

- MCN present as single spherical or oval mass
- Unilocular or multilocular
- Well-circumscribed, smooth margined, delayed enhancing fibrous capsule
- Peripheral Ca+ in wall/septa (10-25%), generally not seen with MR
- No communication with the PD differentiates from IPMN
- Septa, cyst wall thickening and mural nodules may or may not present
- Mucin filled Cysts
  - Usually simple fluid signal intensity (homogeneous low T1 and high T2 signal)
  - High intrinsic T1 signal intensity has been observed but is less frequent

EUS:
- Hyperechoic internal debris, wall adherent nodules or solid papillary projections
- Cyst fluid CEA levels elevated and low amylase levels
- No communication with the pancreatic duct

Resected in all cases due to malignant potential
MCN with Invasive Adenocarcinoma

Risk factors for malignancy are
- Advanced age
- Large tumor size (typically > 4cm)
- Cyst wall irregularity and thickening
- Associated mass or mural nodules
- CEA high
Mucinous Non-neoplastic Cyst Retention Cyst or Mucocele

- Mucinous differentiation of epithelial lining, lacks surrounding ovarian stroma
- No sex predilection
- No known neoplastic potential
- No PD communication, cellular atypia, or papillary projections
- Small, unilocular or thinly septated cysts, with internal simple fluid signal intensity, and no enhancing components
- Likely represent many of the small, unilocular cysts incidentally found on imaging

Retention cysts may result from ductal obstruction; it is important to ensure they are not caused by a tumor proximal to cyst
Intraductal Papillary Mucinous Neoplasms

Demographics and Background

- IPMNs are mucinous cystic lesions characterized by neoplastic, mucin producing papillary cells projecting from the pancreatic ductal surface of the main pancreatic duct or side branches.
- Location: Usually in the head of pancreas, 20-30% multifocal, 5-10% diffuse pancreatic involvement.
- Mean age is 65, “Grandfather Lesion” > 60% of patients are male.
- IPMNs are most commonly asymptomatic and discovered incidentally on routine imaging.
- Some patients may present with symptoms of pancreatitis.

Classification

- Main Duct – MD-IPMN (diffusely dilated main PD with filling defects corresponding to mucinous filling or papillary tumors)
- Branch duct-BD-IPMN affected branch ducts are dilated and communicate with the main PD
- Combined type IPMN
IPMN-MD

Characterized by PD dilatation, which may involve the entire duct or discrete segments
Risk of Malignancy 50-70%

Role of Imaging:

- To detect IPMN and exclude other cystic lesions
- Differentiate MD-IPMN and BD-IPMN
- To determine risk of malignancy and resectability
- Radiologist should look for anatomical location, size, number, locularity, septations, calcifications, PD dilatation, appearance of cysts and communication with the cysts and PD
High ADC value due to mucinous gel material within the PD allowing more freedom of water molecules. Mostly high grade dysplasia/CIS detected at pathological specimens.

Cysts with high risk stigmata – resection without further testing
Cysts with worrisome features – evaluated by EUS
Cysts >3cm and no worrisome features – evaluated by EUS (elderly patient)
Cysts <3cm without worrisome features – surveillance according to size stratification

IPMN-BD

- Unilocular or cluster of cysts (dilated ducts), lobulated margins
- Communicates with the PD, which is itself non-dilated
- Side branch type (very common) increases with age
- 15-20% risk of malignancy
- Slow progression:
  - Hyperplasia-LGD-HGD-Invasive carcinoma
- Usually multifocal 25-40%
- Probably represent a pancreatic “field defect”

EUS: High CEA reflects presence of mucinous epithelium. A cut off CEA level of 192ng/ml, sensitivity 73%, specificity 84% and accuracy 79% differentiate mucinous from non mucinous cysts. Glucose and kynurenine metabolites are high in non mucinous cysts and lower in mucinous cysts.

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IPMN

Worrisome features:
• Cyst > 3 cm
• Thickened/enhancing cyst walls
• Non enhancing mural nodules
• Main pancreatic duct size 5-9 mm
• Abrupt change in main pancreatic duct caliber with distal pancreatic atrophy
• Regional lymphadenopathy

High risk stigmata
• Obstructed common bile duct
  (Jaundice with lesion of the pancreatic head)
• Enhancing solid components within the cyst
• Main Pancreatic duct > 10 mm

Malignant transformation: Invasive adenocarcinoma developed in side branch IPMN

Progressive dilatation of the main duct (dashed arrows) and development of solid nodule (yellow arrow) in the side branch IPMN (blue arrow)
Solid Pseudopapillary Neoplasm (SPN)

Demographics and Background

- <5% of cystic lesions
- Young (mean age is 25), 96% are female, large mass with hemorrhage
- Low-grade malignant potential, <20% with local invasion or metastasis
  - 95% 5-year survival
- All suspected solid pseudo-papillary tumors are managed surgically
  - Cannot be reliably differentiated from other solid/cystic lesions by imaging alone e.g.
    - Neuroendocrine
    - Mucinous cystic neoplasm
- Can be located anywhere in the pancreas

Cavities of SPNs are not true cysts but represent a necrotic or degenerative process
Solid Pseudopapillary Tumors

MR Imaging

- Usually well circumscribed
- Varying degrees of hemorrhage, necrosis, cystic degeneration and solid components
- Predominantly solid lesions – mild T2 hyperintensity
- Predominantly cystic lesions – fluid signal intensity on T2 images
- +/- Internal hemorrhage – intrinsic high T1 signal intensity
- Thick, fibrous capsule – low T2 signal, delayed enhancement, +/- calcification (30%)
- Progressive enhancing soft-tissue components
- Large (average size ~ 9cm)

EUS: Cystic fluid Is low in CEA reflecting non mucinous epithelium and may show necrotic debris

SPNs exclusively occur in the pancreas
Solid pseudopapillary neoplasm: 26-year-old female with history of abdominal pain. Axial T2 weighted MR image reveals predominantly solid mass in the head of pancreas (white arrow) with T2 hyperintense areas due to necrosis/cystic degeneration and corresponding precontrast T1weighted image shows intermediate signal (black arrow). Following contrast administration mass show progressive enhancement (pink arrows) with areas of non enhancement due to cystic degeneration (yellow arrow). On DWI, solid portion of the mass shows low ADC due to restriction (green arrow) whereas cystic components show high ADC (blue arrow).

**DWI: Neoplastic composition like solid debris, cystic or hemorrhagic fluid determines the degree of diffusion and ADC values**

**Solid component – Low ADC**

**Cystic component – High ADC**
Ductal Adenocarcinoma with Cystic Features

Most common pancreatic neoplasm (85-90% of all pancreatic tumors)
High mortality, overall 5-year survival of 15-25% (resectable), less than 5% (unresectable)

MR Imaging:

- Hypoenhancing with progressive delayed enhancement
  - Pathology correlate: poorly vascularized, infiltrative, fibrotic tumor with surrounding desmoplastic reaction
- Location: 2/3 pancreatic head, 5-15% body, 10-15% tail
- Associated with ductal obstruction, either CBD, PD or both (MRCP & T2WI)
- Keys to differentiate from other solid lesions with cystic features:
  - Infiltrative pattern
  - ductal obstruction
  - vascular invasion

Pancreatic adenocarcinoma: 79-year-old female with history left upper quadrant pain. MRI of the abdomen demonstrates heterogeneous infiltrating mass involving body and tail of pancreas with central hyperintense T2 and hypointense T1 signal due to necrosis (blue arrows), T2 hypointense and intermediate T1 signal thick rind of soft tissue (yellow arrows) that shows enhancement following contrast administration and restricted diffusion due to dark ADC (green arrows) and no enhancement of central aspect due to necrosis (dashed arrow). The mass encases the celiac axis, hepatic artery and splenic artery by 360 degrees (white arrows).
Cystic Neuroendocrine Tumors

MR Imaging

• Small Lesions: Homogenously T1 hypointense and T2 hyperintense
  • Avid arterial enhancement (rich capillary network and vascular supply)
• Larger lesions have increased heterogeneous appearance (hemorrhage and cystic change)
• Cystic NET:
  • 90% hypervascular rim
  • nonfunctional (80%)

EUS:
- Cyst fluid CEA and amylase levels low
- Cells positive for chromogranin and synaptophysin
Lymphoepithelial Cysts

- Rare (<1% of all pancreatic cysts)
- Benign
- Usually middle aged men (mean age 55 years, M>F 4:1)
- Cysts are lined by squamous epithelium, filled with keratinaceous debris and surrounded by a band of dense lymphoid tissue
- MR Imaging:
  - findings are not well described in the literature, variable MR appearance
  - either unilocular or multilocular
Walled off Necrosis/Pseudocyst

Occur in the setting of pancreatitis
No epithelial lining

MRI :

- Irregular cyst(s) in/next to the pancreas
- Evolve over time
  - Irregular margin early, well circumscribed later, with a thick enhancing wall (granulation tissue and fibrosis)
- Internal blood products (high T1 signal)
- Dependent necrotic or proteinaceous debris (non-enhancing, low T2 signal)
  - Soft-tissue elements should never enhance
- Other changes of acute/chronic pancreatitis (e.g. fibrosis, atrophy, dilated PD, SV thrombosis, parenchymal calcification)
- May dissect along fascial planes to remote sites (e.g. liver, pleura, or even mediastinum)
- May fistulate with vascular structures

Management: Can spontaneously resolve, should evolve over short intervals, whereas other types of cysts often persist without significant change. If complicated or symptomatic may require surgical, percutaneous or endoscopic drainage.
Acinar Cell Cystadenocarcinoma

Demographics and Background

- Mean Age 58; M>F (2:1)
- 1-2% of exocrine neoplasms
  - Pancreatic enzyme production (trypsin and lipase)
- Malignant, frequently metastatic at time of presentation
- Poor prognosis: 5 year survival of 6%

MR Imaging

- Large (usually >10cm)
- Hypoenhancing
- Varying degrees of necrosis with cystic change
- Well-marginated with surrounding capsule
- Can have intratumoral calcification and hemorrhage

54-year-old male with history abdominal pain. MR axial T2 and precontrast T1 weighted images demonstrate a large lobulated heterogeneous hypointense and intermediate signal mass, respectively (white arrows), with central T2 hyperintense and T1 hypointense necrosis (black arrows) involving the pancreatic head. Post contrast T1 weighted image shows heterogeneous enhancement of solid mass (green arrow) and no enhancement of central aspect (yellow arrow). Biopsy showed (acinar cell carcinoma.)
Pancreatic cystosis (Cystic fibrosis)

25-year-old male with history of cystic fibrosis. MR axial T2 weighted image demonstrates hyperintense innumerable cysts (white arrows) throughout the pancreas which show no enhancement on post contrast axial T1 weighted image (black arrows).

Epithelial cyst within intrapancreatic splenule

67-year-old male with history of intrapancreatic splenule. MR axial T2 weighted image demonstrates hyperintense cystic lesion (white arrow) in the tail of pancreas (site of intrapancreatic splenule), which show no enhancement on post contrast axial T1 weighted image (black arrow).

Pancreatic abscess

54-year-old female with history of left upper quadrant pain and fever. MR axial T2 weighted image demonstrates heterogeneous lesion (white arrow) in the tail of pancreas, which show no central enhancement but show irregular enhancing rim on post contrast axial T1 weighted image (black arrow). Frank pus was aspirated on FNA.
Conclusions

• MR Imaging is the diagnostic solving tool for detection and characterization of a wide range of pancreatic cystic lesions because of its unsurpassed soft tissue contrast and its ability to evaluate pancreatic duct.

• MR Imaging also provides information with respect to cyst fluid contents and internal septa which are beyond the reach of ultrasound and CT.

• Knowledge of MRI findings of cystic pancreatic lesions is critical for the diagnosis and choosing the best therapeutic approach.

Thank you very much for your attention!

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