Pancreas Cysts & Pancreatitis

Stefanie Owczarski, PA-C, MPAS
Medical University of South Carolina
Department of Surgery
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Pancreas Cyst Objectives

- Epidemiology
- Classification
- Treatment
  - Surveillance
  - Surgery
Pancreatic Cancer Is Estimated to Be the Second Leading Cause of Cancer-Related Death by 2020

Low prevalence disease, so widespread, population-based screening is not feasible

Pancan.org
SEER.cancer.gov
Source: Estimated New Cancer Cases and Deaths for 2018
## Pancreatic Cysts

<table>
<thead>
<tr>
<th>Age band</th>
<th>Total number of subjects</th>
<th>Cyst prevalence (95% CI)</th>
<th>Cyst prevalence &gt; 2cm</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40</td>
<td>557</td>
<td>0.5% (0.07-1.21%)</td>
<td>0.03%</td>
</tr>
<tr>
<td>40-49</td>
<td>1027</td>
<td>2.6% (0.4-6.7%)</td>
<td>0.17%</td>
</tr>
<tr>
<td>50-59</td>
<td>970</td>
<td>4.0% (1-10%)</td>
<td>0.27%</td>
</tr>
<tr>
<td>60-69</td>
<td>665</td>
<td>10% (0.3-32%)</td>
<td>0.67%</td>
</tr>
<tr>
<td>70-79</td>
<td>154</td>
<td>25% (3-60%)</td>
<td>1.67%</td>
</tr>
<tr>
<td>80+</td>
<td>46</td>
<td>37% (24-51%)</td>
<td>2.47%</td>
</tr>
</tbody>
</table>

Simplified Overview of WHO Classification

Non-neoplastic
- Pseudocyst
- Congenital
- Lymphoepithelial

Mucinous
- Mucinous cystadenoma
- MD-IPMN
- BD-IPMN

Non-mucinous
- Serous cystadenoma
- Solid pseudopapillary tumor
- Cystic neuroendocrine tumors

Pancreas Cystic Lesions
Honeycomb Pattern of SCN
Use consistent terminology when describing cysts.

**Locularity**
- Unilocular with smooth contour
- Bilocular with lobulating contour and thick septum
- Oligolecular
- Multilocular

**Size of cyst components**
- Multiple microcysts
- Macrocysts with mural nodule
- Honeycomb-like appearance
- Mixed micro- and macrocysts

**Communication with main pancreatic duct**
- Branch-duct (IPMN); grape-like cluster with communication
- Main-duct (IPMN); Saccular dilation of main pancreatic duct with mass
- Mucinous cystadenocarcinoma without communication

Most Common Pancreas Cystic Lesions

- Inflammatory neoplasm
  - Pancreas Pseudocyst

- Serous Cystic Neoplasm
  - Serous Cystic Neoplasm (SCN)

- Mucinous Cystic Neoplasms
  - Mucinous cystadenoma (MCN)
    - SB-IPMN
    - MD-IPMN
    - Mixed Variant IPMN
Imaging Modalities

- TUS
- CT
- EUS
- MRI
- ERCP
MRI/MRCP

- left hepatic duct
- common hepatic duct
- common bile duct
- pancreatic duct
- right hepatic duct
- gallbladder
- cystic duct
- sphincter of Oddi
- C loop of duodenum
• Cyst morphology
• Cyst fluid analysis
  – Cytology
  – Amylase
  – CEA
  – Cyst fluid genetics
<table>
<thead>
<tr>
<th>LESION</th>
<th>DEMOGRAPHICS</th>
<th>Viscosity</th>
<th>CEA ng/mL</th>
<th>Amylase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreas pseudocyst</td>
<td>HO pancreatitis</td>
<td>Low</td>
<td>Low/ ND</td>
<td>High</td>
</tr>
<tr>
<td>Serous cystic neoplasm</td>
<td>60s, F&gt;M</td>
<td>Low</td>
<td>Low/ ND</td>
<td>Low</td>
</tr>
<tr>
<td>MCN</td>
<td>40-50s, F</td>
<td>High</td>
<td>&gt;192</td>
<td>Variable</td>
</tr>
<tr>
<td>IPMN</td>
<td>M=F</td>
<td>High</td>
<td>&gt;192</td>
<td>High</td>
</tr>
</tbody>
</table>
Table 4. Accuracy of the 3 Primary Tests for Differentiating Between Mucinous and Nonmucinous Cystic Lesions

<table>
<thead>
<tr>
<th></th>
<th>EUS morphology</th>
<th>Cytology</th>
<th>CEA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>32/57 (56.1%)</td>
<td>19/55 (34.5%)</td>
<td>42/56 (75%)</td>
</tr>
<tr>
<td>Specificity</td>
<td>25/55 (45.4%)</td>
<td>45/54 (83.3%)</td>
<td>46/55 (83.6%)</td>
</tr>
<tr>
<td>Accuracy</td>
<td>57/112 (50.9%)</td>
<td>64/109 (58.7%)</td>
<td>88/111 (79.2%)</td>
</tr>
</tbody>
</table>

*Three patients did not have cytology result.
One patient did not have a CEA result.
P<0.05 vs cytology, EUS morphology.

Performance of CEA and Amylase

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amylase &lt; 250</td>
<td>44%</td>
<td>98%</td>
<td>Serous/Mucinous vs. Pseudocyst</td>
</tr>
<tr>
<td>CEA &lt; 5</td>
<td>50%</td>
<td>95%</td>
<td>Pseudocyst vs. Serous/Mucinous</td>
</tr>
<tr>
<td>CEA &gt; 800</td>
<td>48%</td>
<td>98%</td>
<td>Mucinous vs. all others</td>
</tr>
</tbody>
</table>

EUS morphology + cytology + cyst CEA vs. CEA alone
- Sensitivity 91% vs. 75%
- Lower specificity and AUC

Cyst Fluid Genetics

- CEA alone (>148)
  - Sensitivity 67%

- + K-ras
  - Sensitivity 84%

- + Loss of heterozygosity
  - Sensitivity 91% (Specificity 93%)

Combining elevated CEA >192 and any mutation in K-ras or allelic LOH was able to identify all mucinous cysts that were missed by cytological exam.

Case 1:

- 65yo woman presents to your clinic with asymptomatic 5cm tail of pancreas (TOP) lesion
  - CT + EUS show 5cm cyst comprised of many small fluid filled cysts clustered together (AKA microcystic lesion)
  - Imaging also shows central stellate scar or “sunburst calcification”
  - EUS demonstrates a honeycombing appearance
  - EUS FNA cyst fluid CEA is not detectable
  - What is your diagnosis?
• Generally considered benign and do not require surgery
• Follow-up surveillance imaging not needed
• Demonstration of a central scar or “sunburst” calcification by CT or MRI is highly diagnostic, but only see this about 20% of cases
• Consider surgery if symptomatic or if diagnosis remains in doubt
Case 2:

- 40 yo woman with asymptomatic 7cm cystic lesion in body of pancreas (BOP)
  - CT shows macrocystic lesion with a thick fibrous wall
  - CT also shows peripheral calcifications
  - MRI indicates the lesion does not communicate with the MPD
  - EUS FNA shows thick fluid with fluid CEA level in the 400s
  - What is your diagnosis?
MCN

- Mostly in women (95%)
- Mostly in the body or tail of the pancreas (97%)
- **Does not communicate with the main pancreas duct**
- Eccentric calcifications are specific to MCNs but present in only about 15% of cases
- EUS cyst fluid CEA concentration is above 200 in approximately 80% of MCN
• 13% risk of invasive adenocarcinoma
• 15% risk of pre-cancerous cells
• Treatment is surgical resection
  – Size or presence of high risk features do not matter here, remove with surgery
• Surgery is curative, no further surveillance required long term
66yo male with new onset diabetes x 2 months was hospitalized last month with acute pancreatitis. No prior history of pancreatitis, never drinker or smoker, had cholecystectomy in his 30s.

- CT showed dilated main pancreas duct to 11mm
- EUS confirmed MPD dilation and noted mucin extruding from a widely patent “fish mouth” ampulla

What is your diagnosis?
Main Duct IPMN

• Defined as having main duct dilation >5mm without other identifiable reason for obstruction

• MD-IPMN is essentially a malignant lesion
  – 70% risk of already harboring cancer cells or of turning into cancer with time

• Treatment is surgical excision
  – Partial pancreatectomy possible total pancreatectomy
MD-IPMN

- New onset diabetes in patient >50yo, consider possible pancreas cancer
- New onset acute pancreatitis >65yo is rare, consider pancreas cancer
Side Branch vs Main Duct IPMN

Main Duct - IPMN

Branch Duct - IPMN

Mixed Type - IPMN

National Cancer Institute
Three Categories of All IPMN

• IPMN with high-risk stigmata
• IPMN with worrisome features
• Low risk IPMN

IPMN With High-Risk Stigmata

- 70% risk of already harboring cancer or pre-cancer cells

- High risk stigmata
  - Obstructive jaundice with cystic lesions in pancreatic head
  - Enhanced mural nodule $\geq 5\text{mm}$
  - MPD $\geq 10\text{mm}$

- Treatment is surgery
  - Partial pancreatectomy possible
  - Total pancreatectomy
IPMN With Worrisome Features

• 20-30% risk of already harboring pre-cancer or cancer cells

• Worrisome features:
  – Cyst size $\geq$ 3cm
  – Enhancing mural nodule $<5$mm
  – MPD dilated to 5-9mm
  – Abrupt change in the MPD
  – Rapid cyst growth rate (more than 5mm over 2 years)
  – Elevated CA 19-9
  – Lymphadenopathy

• Treatment:
  – Surgery
Low Risk IPMN

- Low risk IPMN
  - Most common type of IPMN
  - SB-IPMN without any identifiable worrisome features
  - Safe to monitor with serial imaging

- Risk of complication or death with surgery is higher than the risk of degeneration to cancer

- Goal is to monitor them for life to ensure they don’t develop higher risk stigmata
Fukuoka Guidelines

• Surgical excision of IPMN if:
  – Worrisome features
  – High risk stigmata

• Serial imaging if low risk IPMN
  – We often get CT, MRCP, and EUS at first diagnosis to ensure no higher risk features
  – Imaging at 6 months to confirm stability
  – Then annual imaging
Less Common Cysts Requiring Resection

Cystic neuroendocrine

Solid pseudopapillary tumor
Summary

- Careful history, radiographic (MRI >>> CT) characterization
  - Not all cysts require EUS, especially not right away
- Selective use of EUS-FNA with advanced tissue and biomarker acquisition
- Menu of surveillance strategies for branch duct IPMNs
  - Fukuoka – AGA – ACG
  - Many cysts included in surveillance are not BD-IPMN!
- Better diagnostics and prognostics anticipated
Case 4

35 yo man comes to the ER with worsening epigastric abdominal pain x 4 months that is stabbing like a knife and radiates to his back

- Labs
  - Serum amylase 5,000
  - WBC 28k

- CT
  - Large cystic structure body of pancreas
  - Edematous pancreas parenchyma

- What is your diagnosis?
Pancreatic Pseudocyst

- Benign cyst
- Collection of leaked pancreatic enzymes
- Caused by acute and/or chronic pancreatitis
- Can result in disconnected pancreas duct
Pancreatitis

- **Acute pancreatitis**
  - Acute pancreas inflammation
  - Usually subsides

- **Recurrent acute pancreatitis**
  - Repeated episodes of acute pancreatitis
  - Can go on to become chronic pancreatitis

- **Chronic pancreatitis**
  - Permanent damage to the gland from prolonged inflammation and scarring
  - Often develops between ages 30-40yo
  - M>F
Chronic Pancreatitis

• 8-10 new patients per 100,000 population per year in the US
• Incidence has quadrupled in the last 30 years
• No cure for the disease
• Risk factors
  – Gallstones
  – Alcohol
Risk Factors for Chronic Pancreatitis at MUSC
Chronic Pancreatitis

- 70% develop Type 3c insulin dependent diabetes
- 30-85% develop exocrine pancreas insufficiency
- Shortened life expectancy
  - 10 year survival 70%
  - 20 year survival 45%
  - About 20% of deaths are related to pancreas cancer
  - Death also from complications of DM, ETOH, and opioids
CP Diagnosis

- Need objective evidence to make the diagnosis
- Labs
  - Amylase
  - Lipase
  - LFTs
  - CA 19-9 if older patient or suspicious findings on cross sectional imaging
- CT
- MRI / MRCP
- EUS / ERCP
CT Features of CP

- CT abdomen or pancreas protocol with IV contrast
  - Dilated main pancreas duct (<5mm)
  - Irregular main pancreas duct
  - Pancreas atrophy
  - Pancreatic calcifications
  - Pancreatic pseudocyst
CT Features of CP
MRCP Features of CP

- Allows for better imaging of the pancreas and biliary ductal systems
- Dilated MPD (<5mm)
- Irregular MPD
- Stricture of MPD
- Ductal filling defects
  - Suctal stones
  - Strictures from scar tissue
- Dilated side branches
- Parenchymal atrophy or enlargement
MRCP

a. MRCP with normal MPD

b. MRCP with MPD dilation and visible side branches in body and tail
## EUS Rosemont Criteria Diagnosis of CP

<table>
<thead>
<tr>
<th>Major Criteria</th>
<th>Minor Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major A</td>
<td>Major A</td>
</tr>
<tr>
<td>Cysts</td>
<td>Hyperechoic foci with shadowing</td>
</tr>
<tr>
<td>MPD calibre ≥3.5 mm</td>
<td>MPD calculi</td>
</tr>
<tr>
<td>Side branch ectasia ≥1 mm</td>
<td>Lobularity with honeycombing</td>
</tr>
<tr>
<td>Echogenic duct walls and strands</td>
<td>Non-shadowing hyperechoic foci</td>
</tr>
<tr>
<td>Lobularity with non-contiguous lobules</td>
<td></td>
</tr>
<tr>
<td>I. Consistent with CP</td>
<td>II. Suggestive of CP</td>
</tr>
<tr>
<td>A. 1 major A (+) ≥3 minor features</td>
<td>A. 1 major A feature (+) &lt;3 minor features</td>
</tr>
<tr>
<td>A. 3 to 4 minor features, no major features</td>
<td>≤2 minor features and no major features</td>
</tr>
<tr>
<td>B. 1 major A feature (+) major B feature</td>
<td>B. 1 major B feature (+) ≥3 minor features</td>
</tr>
<tr>
<td>B. major B feature alone or with &lt;3 minor features</td>
<td></td>
</tr>
<tr>
<td>C. 2 major A features</td>
<td>C. ≥5 minor features (any)</td>
</tr>
</tbody>
</table>
Treatment Options

• Medical
  – Opioids

• Endoscopic
  – ERCP
  – EUS with celiac plexus block

• Surgical
  – Primary indication for surgery is intractable pain
  – 40-67% of patients with CP require surgery at some point
  – Goals of Surgery
    • Improve pain control
    • Improve QOL
Inflammatory pancreas pseudocysts are a finding in pancreatitis. Patients with chronic pancreatitis often don’t have elevations in their serum lab values. May need CT, MRI / MRCP, and EUS to make the diagnosis of CP. Many patients with CP will experience improved pain control and quality of life with surgical intervention.
Thank You