EUS evaluation of Pancreatic Cyst Lesions

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Frequency of Incidental Cysts

• Pancreatic cysts increasingly identified due to wide-spread use of cross-sectional imaging

• 2.6% of outpatient CT scans
  – Increased incidence as patients age

Laffan et al, Am J Roent 2008
### Pancreatic cysts

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Demographic</th>
<th>Location</th>
<th>Cyst fluid characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Viscos.</td>
<td>Cytology</td>
</tr>
<tr>
<td>Non-mucinous</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serous cystadenoma</td>
<td>7th decade; F&gt;M</td>
<td>Body/tail &gt; head</td>
<td>Low Glycogen staining cuboidal cells</td>
</tr>
<tr>
<td>Pancreatic neuroendocrine tumors</td>
<td>3rd-6th decade; M&gt;F</td>
<td>Body/tail &gt; head</td>
<td>Low Small cells staining positive for chromogranin and synaptophysin</td>
</tr>
<tr>
<td>Solid pseudopapillary tumors</td>
<td>2nd and 3rd decade; F&gt;M</td>
<td>Body/tail &gt; head</td>
<td>Low Branching papillae with myxoid stroma</td>
</tr>
<tr>
<td>Mucinous</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intraductal papillary mucinous neoplasm</td>
<td>M=F</td>
<td>Main duct or side branch; head &gt; body/tail</td>
<td>High Occasional mucinous epithelial cells and variable atypia</td>
</tr>
<tr>
<td>Mucinous cystic neoplasm</td>
<td>5th and 6th decade; F&gt;M</td>
<td>Body/tail &gt; head</td>
<td>High Acellular with background mucin</td>
</tr>
</tbody>
</table>

**ACG/FGS Spring Symposium - Bonita Springs, FL**
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IPMN

Al Haddad M: CGH 2011

Mucinous Cystic Neoplasm
Symptomatic = Resection
Attn: Jaundice, Pancreatitis, Diabetes

Asymptomatic?

SURGERY
OBSERVATION

Risk of Invasive Malignancy

- Main Duct IPMNs: 30-50%
- Mucinous Cystic Neoplasms: 10-20%
- BD-IPMNs: 10-20%
- Referral bias in surgical series likely overstates true malignancy risk

Le Borgne J. Ann Surg 1999
Kiely JM. J Gastrointest Surg 2003
Sohn TA. Ann Surg 2004
Spinelli KS. Ann Surg 2004
Rodriguez JR. Gastroenterology 2007
Schmidt M. Ann Surg 2007
Survival after surgery

<table>
<thead>
<tr>
<th>Cyst Type</th>
<th>N</th>
<th>5-year survival (Benign vs. Malignant)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Main Duct-IPMN¹</td>
<td>140</td>
<td>100% vs. 60%</td>
</tr>
<tr>
<td>BD-IPMN²</td>
<td>145</td>
<td>100% vs. 63%</td>
</tr>
<tr>
<td>MCN³</td>
<td>163</td>
<td>100% vs. 57%</td>
</tr>
</tbody>
</table>


What’s the diagnosis?
What’s the diagnosis?

MCA

SCA

PC SPT

No reliable imaging modality!
CT versus MRCP

- CT superior to MRCP for:
  - Mural calcifications and intracystic septations

- MRCP superior to CT for:
  - Numbering cysts and detection of main pancreatic duct communication\(^1\)

- Better differentiating aggressive vs. non-aggressive than mucinous vs. nonmucinous

Sainani NI, Am J Roentgenol 2009

Imaging studies

- Increasing concern regarding repeated imaging
  - 1.5-2% of cancers related to CT scan radiation

Brenner et al, NEJM 2007
Key Issues in EUS Morphology

- MPD: >10mm
  - Cyst communication
  - Mass or nodule
  - Focal dilation

- Cyst: Thick wall
  - Mucin or nodule

Mucin vs. Mural Nodule

Mobile Fragments

>10mm: Cancer Vascular
Your diagnosis?

How accurate is EUS in diagnosing mucinous lesions?

50-78%

How can the performance of EUS be improved?

Cytology
Tumor markers
Molecular markers

Cytology

- Sensitivity variable: 55-95%
- GI epithelium secretes mucin
- Cellular atypia is patchy

Brugge WR, Gastroenterology 2004; Frossard, JL, Am J Gastro 2003
## Mucinous vs. Non Mucinous Neoplasm

<table>
<thead>
<tr>
<th>Viscosity</th>
<th>Mucinous</th>
<th>&gt;1.6</th>
<th>&lt;1.5</th>
<th>Non Mucinous</th>
</tr>
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</table>


## Tumor Markers

- CEA >192ng/ml: 79% accurate
- CEA >800 ng/ml: 98% specific
- Requirement: 0.5 to 1ml

Brugge WR, Gastroenterology 2004; Maire F, GI Endosc 2013
EUS-FNA

Thornton GD: Panreatology 2013

Genetic profiling

- Non-dysplasia → Dysplasia → Pancreatic Cancer
- Mutations: K-ras, p16 and p53
- Markers: K-ras, GNAS, allelic LOH, IL 1B, miR 21, MUC 2 & 4
- 132 IPMNs: 66% GNAS; 81% K-ras mutation
  - 96.2% at least 1 GNAS or K-ras mutation
  - Higher rate of GNAS mutations in advanced/dysplastic IPMNs

Wu: Sci Trans Med 2011
Genetic profiling

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**The Future!**

Wu: Sci Trans Med 2011

2012 Guidelines – Indications for Resection

- MD-IPMN
  - Surgery: high incidence of malignant/invasive lesions and low 5 yr survival rates
- MCN
  - Surgery: afflicts young patients, risk of progression, need for long term surveillance

Tanaka et al, Panreatology 2012
BD-IPMN: Indications for resection

• BD-IPMN
  – High risk stigmata: Obstructive jaundice + pancreatic head cyst, enhancing solid component within the cyst, main PD dilation >10 mm
  – Worrisome features: cyst >3 cm, thickened cyst walls, MPD = 5-9mm, non-enhancing mural nodule, abrupt change in caliber of PD with distal atrophy AND any of the following on EUS
    • Definite mural nodule, MPD involvement, cytology suspicious or positive for malignancy
    • Cyst rapidly enlarging OR high grade atypia in cytology

BD-IPMN 2012 Guidelines

Tanaka et al, Pancreatology 2012
BD-IPMN 2012 Guidelines

Tanaka et al, Pancreatology 2012

High-risk candidates

Endoscopic ablation
EUS-guided cyst ablation

- EUS-FNI ethanol
- ↓ viable epithelium
- smaller size

Cyst resolution

Time and follow up imaging

Epithelium

Cyst

EUS-guided ethanol lavage

- 4 studies in ~ 100 patients\(^1\)-\(^4\)
- Ablation rates of 33-79%
- Varying degrees of histologic ablation in operative patients
- Complications:
  - Pancreatitis in 5-10%
  - Abdominal pain in 10-20%
- Persistent resolution in those with initial radiographic remission\(^5\)
- ETOH + Paclitaxel\(^6\):
  Complete resolution 67.4%

1. Gan SI. GIE 2005
2. Oh HC. GIE 2008
3. Oh HC. Scan J Gastro 2009
4. DeWitt J. GIE 2009
5. DeWitt J. GIE 2010
6. Oh HC: Gastro 2011

Courtesy: DeWitt J
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Dr. Muhammad Hasan
Dr. Shaneel Hebert-Magee
Dr. Robert Hawes

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Dr. Paul Fockens, Netherlands
Dr. Takao Itoi, Japan
Dr. Darshana Jhala, USA
Dr. Michael Levy, USA
Dr. Fauze Maluf-Filho, Brazil
Dr. Anand Sahai, Canada
Dr. Peter Vilmann, Denmark

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