An Algorithmic Approach to Diagnosing Neoplasms of the Pancreas

Thursday, May 28, 2009

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1. Is it Solid or Cystic?
Nature of Epithelium and Stroma

- Individual glands; desmoplastic stroma; mucin production
- Solid, cellular epithelium; minimal or hyalinized stroma

Chronic Pancreatitis vs. Ductal Adenocarcinoma

- Individual glands; desmoplastic stroma; mucin production

Features Supporting Adenocarcinoma

- Haphazard growth pattern
- Glands next to muscular vessels
- Perineural or vascular invasion
- Incomplete lumina
- Nuclear variation > 4:1
- Huge, irregular nucleoli
- Necrotic glandular debris
- Numerous or abnormal mitoses

Lobular growth = Chronic Pancreatitis
Haphazard growth = Adenocarcinoma

Chronic Pancreatitis - muscular vessels at periphery of lobules

Glands next to muscular artery = adenocarcinoma

Perineural Invasion
Four-fold variation in nuclear size in a single gland

Luminal necrosis and incomplete lumina

Glands touching fat

Loss of DPC4
Features Supporting Adenocarcinoma

1. Haphazard growth pattern
2. Glands next to muscular vessels
3. Perineural or vascular invasion
4. Nuclear variation > 4:1
5. Necrotic glandular debris
6. Incomplete lumina
7. Gland touching fat
8. Loss of dpc4 expression, expression of CEA, mesothelin

2. Solid, cellular epithelium; minimal or hyalinized stroma

1. Acinar cell carcinoma
2. Pancreatinoblastoma
3. Pancreatic endocrine neoplasm
4. Solid-pseudopapillary neoplasm

Acinar Cell Carcinoma
Acinar Cell Carcinomas
Clinical

- Age – mostly adults (mean 62 years)
- Gender – male > female
- Symptoms – usually non-specific with weight-loss, abdominal pain, and nausea and vomiting
- Lipase – about 15% develop the syndrome of arthralgias, eosinophilia and subcutaneous fat necrosis
Pancreatoblastoma

Trypsin

Klimstra et al, Am J Surg Pathol
Pancreatoblastoma

- Occurs primarily in children (1-15 years)
- Undifferentiated component – back to back small cells with a syncytial pattern
- Differentiated component – squamous, acinar, endocrine
- Survival better than for ductal adenocarcinoma

Pancreatoblastoma vs Acinar Cell Carcinoma

Squamoid Nests
Cystic Neoplasms

- Gender
- Tail vs. Head
- Relationship to larger pancreatic ducts
- Character of cyst fluid
- Lining (serous vs. mucinous vs. none)
- Stroma (ovarian-type)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Gender (F:M)</th>
<th>Head/Tail</th>
<th>Relation to Duct</th>
<th>Cyst Contents</th>
<th>Epithelium</th>
<th>Stroma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucinous Cyst Neoplasm</td>
<td>20:1</td>
<td>Tail</td>
<td>None</td>
<td>Mucinous</td>
<td>Mucinous</td>
<td>Ovarian</td>
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<tr>
<td>Intraductal papillary Mucinous Neoplasm</td>
<td>1:1.5</td>
<td>Head</td>
<td>Always</td>
<td>Mucinous</td>
<td>Mucinous</td>
<td>None</td>
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<tr>
<td>Solid-pseudopapillary Neoplasm</td>
<td>10:1</td>
<td>Tail=Head</td>
<td>Tail=Head</td>
<td>Necrotic/Hemorrhagic</td>
<td>Non-cohesive</td>
<td>None</td>
</tr>
<tr>
<td>Serous Cyst Neoplasm</td>
<td>7:3</td>
<td>Tail=Head</td>
<td>Tail=Head</td>
<td>Serous</td>
<td>Serous</td>
<td>None</td>
</tr>
</tbody>
</table>
Cystic Neoplasms

Serous Cystadenoma

Mucinous Cystic Neoplasm

Intraductal Papillary Mucinous Neoplasm
Solid-pseudopapillary

Serous Cystadenomas

- More common in women than in men
- Average age at diagnosis: 61-68 years
- Presenting signs and symptoms include:
  - abdominal pain
  - weight loss
  - palpable abdominal mass
Oligocystic Serous Cystadenoma

Solid Serous Neoplasm
Serous Cystadenoma

- Several case reports of “multifocal” disease
- One or two cases of malignant serous neoplasms
- The vast majority of serous cystadenomas are benign, even if incompletely resected.
Mucinous Cystic Neoplasms:

1. Ovarian stroma
2. Cysts do NOT Communicate with Pancreatic Ducts

Mucinous Cystic Neoplasms

- Much more common in women than in men
- Mean age at diagnosis: ~50 (younger than for patients with serous cystadenomas)
- Tail > Head
One-third of MCNs have an associated invasive ductal adenocarcinoma
Section 108

Pseudoinvasion-glands trapped in the stroma

Progesterone Receptors

Disease Specific Survival

Mucinous Cystic Neoplasm

Serous Cystic Neoplasm

<table>
<thead>
<tr>
<th></th>
<th>Mucinous Cystic Neoplasm</th>
<th>Serous Cystic Neoplasm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>40-50 years</td>
<td>61-68 years</td>
</tr>
<tr>
<td>Gender (F/M)</td>
<td>20:1</td>
<td>7:3</td>
</tr>
<tr>
<td>Head vs. body/tail</td>
<td>Body/tail</td>
<td>Head=Body/tail</td>
</tr>
<tr>
<td>Central Scar</td>
<td>Usually not</td>
<td>Usually</td>
</tr>
<tr>
<td>Cyst Contents</td>
<td>Mucoid</td>
<td>Serous</td>
</tr>
<tr>
<td>Mucin oozing from ampulla</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Stroma</td>
<td>Ovarian-type</td>
<td>Collagen</td>
</tr>
<tr>
<td>Epithelium</td>
<td>Columnar &amp; Mucinous</td>
<td>Cuboidal with Glycogen</td>
</tr>
</tbody>
</table>

Cystic Neoplasms

Serous Cystadenoma

Mucinous Cystic Neoplasm

Intraductal Papillary Mucinous Neoplasm

Solid-pseudopapillary

Intraductal Papillary Mucinous Neoplasms:

1. Collagenous stroma
2. Cysts do Communicate with Pancreatic Ducts

Intraductal Papillary Neoplasms

- Long history of symptoms
- Incidence in men equals that in women
- Head > Tail
- Mucin oozing from the ampulla of Vater
IPMN

IPMNs are grossly visible
Intraductal Papillary Mucinous Neoplasms

Surgically resected non-invasive IPMNs have a 90% 5-year survival rate. Most of the recurrences in patients with non-invasive IPMNs appear to be from multi-focal disease, because patients who undergo total pancreatectomy for a non-invasive IPMN have a close to 100% 5-year disease free survival.
Mucinous Cystic Neoplasm

**Age**: 40-50 years

**Gender**: Female>>male

**Head vs. body/tail**: Body/tail

**Connectivity to large ducts**: Usually not

**Cyst Contents**: Mucoid

**Mucin oozing from ampulla**: No

**Stroma**: Ovarian-type

**Multifocal disease**: Very rare

Intraductal Papillary Mucinous Neoplasm

**Age**: 60's

**Gender**: Male>female

**Head vs. body/tail**: Head

**Connectivity to large ducts**: Always

**Cyst Contents**: Mucoid

**Mucin oozing from ampulla**: Yes

**Stroma**: Collagen

**Multifocal disease**: 20-30%
Solid-Pseudopapillary Neoplasm

- Clinically, the vast majority occur in young women (20’s)
- Patients present with vague abdominal fullness or pain
- Grossly well demarcated masses. On cross section, they are cystic and solid with areas of hemorrhage and necrosis
Solid-Pseudopapillary Neoplasm

- >90% have β-catenin gene mutations
- K-ras wild-type
- 15% p53 mutations
- 0% DPC4, p16
Solid-Pseudopapillary Neoplasms: Outcome

Some may be locally aggressive, but most are surgically cured. Venous invasion may suggest a greater risk for metastases. All should be considered malignant with the potential to metastasize.

Solid and Pseudopapillary Neoplasm

<table>
<thead>
<tr>
<th></th>
<th>Solid–Pseudopapillary</th>
<th>Endocrine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histology</td>
<td>papillae, hyaline globules, foam cells</td>
<td>nests and sheets</td>
</tr>
<tr>
<td>Chromogranin</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>CD10</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>β-catenin</td>
<td>nuclear</td>
<td>-</td>
</tr>
</tbody>
</table>
Cystic Neoplasms

- Gender
- Tail vs. Head
- Relationship to larger pancreatic ducts
- Character of cyst fluid
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- Stroma (ovarian-type)
Case 1

1. Mucinous Cystic Neoplasm
2. Intraductal Papillary Mucinous Neoplasm
3. Serous Cystic Neoplasm
4. Solid-pseudopapillary Neoplasm
5. Acinar Cell Carcinoma
Case 2

1. Invasive adenocarcinoma
2. Intraductal Papillary Mucinous Neoplasm
3. Chronic Pancreatitis
4. Solid-pseudopapillary Neoplasm
5. Acinar Cell Carcinoma
Case 3
1. Mucinous Cystic Neoplasm
2. Intraductal Papillary Mucinous Neoplasm
3. Serous Cystic Neoplasm
4. Solid-pseudopapillary Neoplasm
5. Acinar Cell Carcinoma

Case 4
1. Mucinous Cystic Neoplasm
2. Intraductal Papillary Mucinous Neoplasm
3. Serous Cystic Neoplasm
4. Solid-pseudopapillary Neoplasm
5. Acinar Cell Carcinoma