An Update on Pancreas Neoplasms

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Department of Pathology and Laboratory Medicine
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Lines of Differentiation in Pancreatic Neoplasms

<table>
<thead>
<tr>
<th>Differentiation</th>
<th>Special Stain</th>
<th>IHC</th>
<th>EM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ductal</td>
<td>Mucin stain</td>
<td>Glycoprotein markers (CEA, CA125, CA19.9)</td>
<td>Mucigen granules</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MUC1, MUC3, MUC4, MUC5AC, CK7</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>60% loss of SMAD4</td>
<td></td>
</tr>
<tr>
<td>Acinar</td>
<td>PAS-D, butyrate esterase</td>
<td>Enzyme markers (trypsin, chymotrypsin, lipase, others)</td>
<td>Zymogen granules, irregular fibrillary granules</td>
</tr>
<tr>
<td>Neuroendocrine</td>
<td>Grimelius stain</td>
<td>Neuroendocrine markers (chromogranin, synaptophysin, CD56)</td>
<td>Dense core granules</td>
</tr>
</tbody>
</table>
Pancreas Ductal Adenocarcinoma (PDAC)

<table>
<thead>
<tr>
<th>Synonyms</th>
<th>Tubular adenocarcinoma, infiltrating duct carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epidemiology</td>
<td>60-80 y.o., 4th leading cancer death in US (increasing to 2nd by 2030)</td>
</tr>
<tr>
<td>Etiology</td>
<td>Tobacco smoking (3X), chronic pancreatitis (10X), obesity, alcohol, diabetes mellitus</td>
</tr>
<tr>
<td>Signs &amp; Symptoms</td>
<td>Jaundice, pruritus, back pain, weight loss</td>
</tr>
<tr>
<td></td>
<td>New onset diabetes mellitus in 70% of patients</td>
</tr>
<tr>
<td></td>
<td>Late symptoms: liver metastasis, duodenal invasion (gastric outlet obstruction), peritoneal cavity involvement (ascites)</td>
</tr>
<tr>
<td>Tests</td>
<td>Serum tumor markers (CA19-9, CEA)</td>
</tr>
<tr>
<td></td>
<td>CT (best method) – mass, “double duct sign”, vascular invasion assessment</td>
</tr>
<tr>
<td></td>
<td>EUS – heterogenous mass, lymph node assessment, FNA biopsy</td>
</tr>
<tr>
<td>Localization</td>
<td>Head of pancreas (60-70%), body (5-15%), tail (10-15%)</td>
</tr>
</tbody>
</table>

Pancreatic adenocarcinoma
Recent Developments on PDAC

- EUS – FNA has become an established method in the initial diagnosis of pancreatic tumors
  - Cytopathology evaluation
  - Tissue procurement
- 2 tier grading system on precursor lesions
  - PanIN, IPMN, MCN
- AJCC Cancer Staging Manual, 8th edition
- Neoadjuvant chemoradiation has been widely administered
  - Resectable and nonresectable PDAC

PDAC Treatment

- Complete surgical resection remains the only potentially curative option
- Median overall survival of 28 months after resection and adjuvant chemotherapy
- Borderline resectable or locally advanced disease may have margin negative resection after neoadjuvant chemotherapy
  - Similar overall survival with resectable disease
- Neoadjuvant chemoradiation
  - Reduces micrometastases
  - Increases likelihood of complete resection and survival
Patients with BR/LA-PDAC who had a pCR after neoadjuvant chemoradiation had a significantly prolonged survival compared with those who had nCR or a limited response.

PDAC Precursors

- Pancreatic intraepithelial neoplasia (PanIN)
- Intraductal papillary mucinous neoplasm (IPMN)
- Mucinous cystic neoplasm (MCN)
• 2 tier system for all precursor lesions – low grade & high grade
  - PanIN
  - IPMN
  - MCN
• PanIN of any grade at margin in pancreas with invasive carcinoma does not have prognostic implications
• Intraductal lesions 0.5 to 1 cm can be either large PanINs or small IPMNs
• "Intraductal spread of invasive carcinoma" (aka, "colonization") is invasive carcinoma invading back into and extending along the ductal system, may morphologically mimic high-grade PanIN

**Molecular Alterations in Pancreatic Ductal Lesions**

<table>
<thead>
<tr>
<th></th>
<th>Mucinous</th>
<th>Papillary</th>
<th>Atypical</th>
<th>CIS</th>
<th>Invasive Carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>PanIN 1A</td>
<td>35%</td>
<td>45%</td>
<td>65%</td>
<td>85%</td>
<td>90%</td>
</tr>
<tr>
<td>PanIN 1B</td>
<td>35%</td>
<td>45%</td>
<td>65%</td>
<td>85%</td>
<td>90%</td>
</tr>
<tr>
<td>PanIN 2</td>
<td>35%</td>
<td>45%</td>
<td>65%</td>
<td>85%</td>
<td>90%</td>
</tr>
<tr>
<td>PanIN 3</td>
<td>35%</td>
<td>45%</td>
<td>65%</td>
<td>85%</td>
<td>90%</td>
</tr>
</tbody>
</table>

K-ras 35% 45% 65% 85% 90%
p53 0% 0% <5% 20% 70%
HER-2/neu 82% 86% 92% 100% 69%
p16 24% 19% 53% 71% 93%
SMAD4/DPC4 0% 0% 0% 31% 55%

Wilentz et al., Cancer Res 60:2002
Basturk et al., Am J Surg Pathol 2015

**Hereditary Pancreatic Carcinoma**

- Heritable factors involved in 10%

- **Familial pancreatic carcinoma**
  - At least two first degree relatives with PDAC and not associated with other known hereditary syndromes

- **PDAC-associated hereditary syndromes:**
  - Peutz-Jeghers syndrome (STK11/LKB1)
  - Hereditary pancreatitis (PRSS1 [cystic trypsinogen], SPINK1)
  - Familial atypical multiple mole melanoma syndrome (COverlap [p16:Leiden deletion])
  - Lynch syndrome (hMSH2, hMLH1)
  - Familial adenomatous polyposis
  - Hereditary breast-ovarian cancer syndrome (BRCA2)
  - Ataxia telangiectasia
Pancreatic Carcinoma Screening

- High risk individuals
  - Familial pancreatic carcinoma
  - Hereditary pancreatitis
  - Peutz Jeghers syndrome
  - Chronic pancreatitis
- Identification of precursor lesions and early resectable PDAC
- Cancer of the Pancreas Screening-5 (CAP5) Study (CAPS5)
  https://clinicaltrials.gov/ct2/show/study/NCT02000089
  - Pancreatic fluid mutations & circulating pancreatic epithelial cells

Acinar Ductal Metaplasia & Atypical Flat Lesions

- Alternative pathway – KRAS mutation
- Metaplasia – dysplasia – cancer sequence
- Seen in individuals with familial pancreatic cancer

ADM

AFL


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<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>Primary tumor cannot be excised</td>
<td></td>
</tr>
<tr>
<td>T2A</td>
<td>Carcinoma in situ (This includes high-grade PanIN, BOP, igin, MCC)</td>
<td></td>
</tr>
<tr>
<td>T2B</td>
<td>Tumor 2 cm or greater dimension</td>
<td></td>
</tr>
<tr>
<td>T2C</td>
<td>Tumor 0.5 cm to 2 cm or greater dimension</td>
<td></td>
</tr>
<tr>
<td>T3</td>
<td>Tumor &gt; 4 cm or greater dimension</td>
<td></td>
</tr>
<tr>
<td>T4</td>
<td>Tumor involves the celiac axis, superior mesenteric artery, and/or the portal vein, regardless of size</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>N0</td>
<td>Regional lymph nodes cannot be assessed</td>
<td></td>
</tr>
<tr>
<td>N1</td>
<td>Regional lymph node metastasis</td>
<td></td>
</tr>
<tr>
<td>N2</td>
<td>Metastasis in 1 or more regional lymph nodes</td>
<td></td>
</tr>
</tbody>
</table>

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Intraductal Papillary Mucinous Neoplasms

- Definition:
  "Grossly and radiographically visible (>1cm) epithelial tumor arising from the main pancreatic duct or duct branches, causing dilatation and mucin production"
- Often lack invasive carcinoma
  - 30% of surgically resected IPMNs harbor invasive carcinoma
- 5 year survival is better than PDAC
  - IPMN alone 30-50%
  - IPMN + invasive ca = 70-90%

### Genetic Features

<table>
<thead>
<tr>
<th>Genetic Features</th>
<th>K-ras</th>
<th>p53</th>
<th>DPC4</th>
<th>p16</th>
<th>STK11/LKB11</th>
<th>GNAS</th>
<th>RNF43</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ductal adenocarcinoma</td>
<td>&gt;95%</td>
<td>50-70%</td>
<td>40-60%</td>
<td>95%</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>IPMN</td>
<td>13-100%</td>
<td>0-50%</td>
<td>5%</td>
<td>0-20%</td>
<td>32%</td>
<td>50-70%</td>
<td>25-35%</td>
</tr>
</tbody>
</table>

### Synonyms

- Mucinous duct ectasia, duct ectatic mucinous cystadenoma/carcinoma, mucin producing tumor, villous adenoma, papillary adenoma/carcinoma

### Epidemiology

- 3% of pancreatic exocrine and 20% of cystic neoplasms
- Incidence is increasing (incidental, asymptomatic)
- Gender: Male = Female

### Etiology

- Cigarette smoking, Peutz-Jeghers syndrome, FAP, family history of pancreatic carcinoma, McCune-Albright syndrome

### Signs and Symptoms

- Nonspecific abdominal pain, chronic pancreatitis, weight loss, new onset diabetes mellitus, jaundice

### Clinical Findings

- C caut and CEA elevated in cases with invasive carcinoma
- Endoscopy – mucin extrusion from ampulla of Vater
- Radiology – ectasia and cystic dilatation of pancreatic duct

### Localization

- Predominantly in head of pancreas; localized, multicentric or diffusely involving the entire pancreatic ductal system, extending to ampulla or common bile duct

### IPMN Classification

<table>
<thead>
<tr>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Intraductal papillary mucinous adenoma, IPMN with low grade dysplasia</td>
<td>IPMN with low grade dysplasia</td>
<td>IPMN low grade</td>
</tr>
<tr>
<td>IPMN, borderline; IPMN with moderate dysplasia</td>
<td>IPMN with intermediate-grade dysplasia</td>
<td></td>
</tr>
<tr>
<td>Intraductal papillary mucinous carcinoma (in situ); intraductal papillary mucinous carcinoma, minimodular</td>
<td>IPMN with high-grade dysplasia</td>
<td>IPMN high grade</td>
</tr>
<tr>
<td>Intraductal papillary mucinous carcinoma, invasive</td>
<td>IPMN with an associated invasive carcinoma</td>
<td>IPMN, low grade, with an associated invasive carcinoma (includes carcinoma with an associated IPMN)</td>
</tr>
</tbody>
</table>
Classification of types of intraductal papillary-mucinous neoplasms of the pancreas: a consensus study.


Department of Medical Pathology, Tokai University School of Medicine, Ise, Isehara, Japan. takada@med.tokai.ac.jp

<table>
<thead>
<tr>
<th>Type</th>
<th>MUC1</th>
<th>MUC2</th>
<th>MUC5AC</th>
<th>MUC6</th>
<th>CDX2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastric foveolar</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Intestinal type</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Pancreatobiliary</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Oncocytic</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Tubulopapillary</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

H&E staining.
IPMN – Carcinogenesis Pathway

- Intestinal type IPMN (ductal pathway)
  - GNAS
- Pancreatobiliary type IPMN/FUN1 (aggressive pathway)
  - KRAS

IPMN – Main vs. Branch Ducts

- 70% involve main duct, 30% confined to branch ducts
- Branch duct type (Terris, et al)
  - Younger patients & low risk of progression
  - Main duct type: 20% CIS, 37% invasive carcinoma
  - Branch duct type: 15% CIS, 0% invasive carcinoma
- 5 year risk of progression (Levy, et al)
  - MD 63% vs BD 15%
Prognosis & Treatment

- Presence and size of invasive component
  - Mural nodules
  - Solid masses
  - Large tumor size
  - Dilated main pancreatic duct
  - Cyst wall thickening
  - Increase serum CA19-9
- Complete surgical resection is curative for IPMN
- Partial pancreatectomy
  - Extent
  - Status of margin – frozen section difficulties
  - Risk of local recurrence – skip nature
  - Surveillance

2 tier system for all precursor lesions
- PanIN
- IPMN
- MCN

Clinical significance of dysplasia at resection margin of IPMN lacking invasive carcinoma remains to be determined
  - Increased risk of recurrence after prolonged follow up
  - Further resection recommended on high grade dysplasia at margin

"Incipient IPMN" are lesions 0.5-1.0cm with intestinal or oncocytic papillae or GNAS mutations (intestinal or gastric type)

"Simple mucinous cyst" are cysts > 1 cm with gastric-type flat mucinous lining at most minimal atypia without ovarian-type stroma

Synonym: IPMN, oncocytic type

Form large cystic lesion with friable papillary growths in large pancreatic ducts

Distinctive feature:
  - Oncocytic cytoplasm (mitochondria)
  - Eccentric nucleoli
  - Intraepithelial lumina, often containing mucin, producing ciboriform architecture

Difference from conventional IPMNs:
  - MUC6 +, HepPar1 +, lack of KRAS mutation
• Synonym: Intraductal tubular neoplasm
• Definition: Grossly visible intraductal lesion composed of tubule-forming epithelial neoplasm with high grade dysplasia and ductal differentiation without overt production of mucin
• 3% of IPMN's
• Solid, nodular masses in dilated pancreatic ducts, no mucin
• 40% ITPN's harbor invasive carcinoma, usually localized
**Mucinous Cystic Neoplasm (MCN)**

- **Definition:**
  Cyst forming epithelial neoplasm that commonly does not communicate with the pancreatic ductal system, lined by mucin-producing epithelium and with associated ovarian-type subepithelial stroma

- Almost exclusively in women, 40-50 y.o.
  - Patients with MCNs with associated invasive carcinoma are 5-10 years older
- >95% in body and tail of pancreas
- Incidental finding, less likely to present with pancreatitis, jaundice or new onset diabetes mellitus

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**Mucinous Cystic Neoplasm**

- Noninvasive tumor: CK 7,8,18, 19, CA19-9, EMA, CEA, MUC5AC, MUC2 (goblet cells), KRAS mutation
- Invasive tumor: MUC1, loss of SMAD4, alterations of p16 and p53
- Similar molecular alterations to PanIN
### Mucinous Cystic Neoplasm Grading

<table>
<thead>
<tr>
<th>Old terms</th>
<th>WHO 2010</th>
<th>New 2-tier system</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Baltimore Consensus 2015</td>
</tr>
<tr>
<td>Mucinous cystadenoma</td>
<td>MCN with low-grade dysplasia</td>
<td>MCN low grade</td>
</tr>
<tr>
<td>Mucinous cystic tumor, borderline</td>
<td>MCN with intermediate-grade dysplasia</td>
<td></td>
</tr>
<tr>
<td>Mucinous cystadenocarcinoma</td>
<td>MCN with high-grade dysplasia</td>
<td>MCN high grade</td>
</tr>
<tr>
<td>Mucinous cystadenocarcinoma, invasive</td>
<td>MCN with an associated invasive carcinoma</td>
<td></td>
</tr>
</tbody>
</table>

- MCN, MCN grade, with an associated invasive carcinoma associated with MCN.

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![Image of Mucinous Cystic Neoplasm Grading](image-url)
Pancreatic Neoplastic Mucinous Cysts
Cytopathology

- Thick colloid-like extracellular mucin, or elevated CEA (>192 ng/ml), or KRAS/GNAS mutation, and/or presence of neoplastic mucinous epithelial cells
  - IPMN: KRAS, RNF43, GNAS
  - MCN: KRAS, RNF43
  - NMC high grade or with invasive carcinoma: KRAS and/or GNAS, TP53, PIK3CA and/or PTEN
- Two-tier grading – low and high grades

Serous Neoplasms of the Pancreas

Serous adenoma - benign
  - solid
  - microcystic
  - macrocystic/oligocystic

Serous adenocarcinoma - malignant
Serous Neoplasms of the Pancreas

Serous adenoma
- 1-2% pancreatic neoplasms
- mean age 60 y.o., slight female predominance
- 50-75% in body or tail
- associated with Von Hippel Lindau syndrome
- CK 7,8,18 and 19; EMA, inhibin, MUC6 and NSE +
- no KRAS or P53 mutation

Serous adenocarcinoma
- exceedingly rare
- direct invasion into adjacent organ or metastasize
Pancreatic Neurondocrine Neoplasms

• Non-syndromic (non-functioning), but IHC +
  - alpha-cell/glucagon producing NET
  - beta-cell/insulin producing NET
  - G-cell/gastrin-producing NET

• Syndromic (functioning) – “oma”
  - Insulinoma
  - Glucagonoma
  - Somatostatinoma
  - Gastrinoma
  - VIPoma

Pancreatic Endocrine Neoplasms
Associated Conditions

• Multiple Endocrine Neoplasia I
• von Hippel-Lindau Syndrome
• Tuberous Sclerosis
• Pheochromocytoma
• Cushing’s Syndrome
Pancreatic Neuroendocrine Neoplasms
Criteria for Malignancy

- Traditional Criteria
- Metastases
- Gross invasion
- Vascular invasion
- Correlation with clinical syndromes
- Predictors of aggressive behavior
  - Mitotic rate
  - Ki-67 index
  - Invasion
  - Necrosis
- Poorly Differentiated Neuroendocrine Carcinoma

Pancreatic Neuroendocrine Neoplasm Grading

<table>
<thead>
<tr>
<th>WHO 2010</th>
<th>WHO 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well differentiated neuroendocrine tumor</td>
<td>Well differentiated neuroendocrine tumor (PanNET)</td>
</tr>
<tr>
<td>Neuroendocrine tumor (PanNET) G1 (≤2 mitoses/10hpf and/or ≤2% Ki67 index)</td>
<td>Neuroendocrine tumor (PanNET) G1 (≤2 mitoses/10hpf and/or ≤3% Ki67 index)</td>
</tr>
<tr>
<td>Neuroendocrine tumor (PanNET) G2 (≥2-20 mitoses/10hpf and/or 2-20% Ki67 index)</td>
<td>Neuroendocrine tumor (PanNET) G2 (≥2-20 mitoses/10hpf and/or 2-20% Ki67 index)</td>
</tr>
<tr>
<td>Poorly differentiated neuroendocrine carcinoma (PanNEC)</td>
<td>Poorly differentiated neuroendocrine carcinoma (PanNEC)</td>
</tr>
<tr>
<td>Neuroendocrine carcinoma (PanNEC) G3 (≥20 mitoses/10hpf or &gt;20% Ki67 index)</td>
<td>Neuroendocrine carcinoma (PanNEC) G3 (≥20 mitoses/10hpf or &gt;20% Ki67 index)</td>
</tr>
<tr>
<td>Mixed adeno-neuroendocrine carcinoma (MANEC)</td>
<td>Mixed neuroendocrine-non-neuroendocrine neoplasm (MINEN)</td>
</tr>
</tbody>
</table>

Pancreatic Neuroendocrine Tumor (PanNET)

- Well differentiated NEN - low, intermediate or high grade
- Minimal to moderate atypia
- Typical organoid patterns, lacking necrosis
- General neuroendocrine markers +
- Associated with hormonal syndrome/functioning tumor
Pancreatic Neuroendocrine Carcinoma (PanNEC)

- Poorly differentiated high grade NEN
- Highly atypical small cells or intermediate to large cells
- General neuroendocrine markers +
- Exocrine markers -
- Rarely associated with hormonal syndromes
- TNM classification follows PDAC
### WD G3 PanNETs vs PD G3 PanNECs

<table>
<thead>
<tr>
<th>WD G3 PanNETs</th>
<th>PD G3 PanNECs</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEN1, DAX, ATRX mutations</td>
<td>P53, RB1, KRAS mutations</td>
</tr>
<tr>
<td>IHC loss of DAXX or ATRX</td>
<td>IHC loss of RB</td>
</tr>
<tr>
<td>Recognizable as NETs</td>
<td>Small cell or large cell type</td>
</tr>
<tr>
<td>Often evolve from a recognizable lower grade component (1 or 2)</td>
<td>No lower grade component</td>
</tr>
<tr>
<td>No upper limit given, but usually ki67 &lt;40 to 55%, mitotic count &lt;20/10hpf</td>
<td>Must have ki67 index &gt;20%, no lower limit given but usually &gt;55%</td>
</tr>
</tbody>
</table>

- Plasmacytoid morphology
- Smooth nuclear contour
- Abundant cytoplasm
- Apoptosis
- Nuclear tangles
**Mixed Neuroendocrine-Non-Neuroendocrine Neoplasm (MINEN)**

- Mixed neoplasm with components of a nonendocrine carcinoma (mostly ductal adenocarcinoma or acinar cell carcinoma) combined with a neuroendocrine neoplasm
- Usually both components are high grade malignant carcinomas (G3), but occasionally one of the two or both components may belong to the G1/G2 category
- Each component comprises >30% of the tumor

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**Solid-Pseudopapillary Tumor**

- 2-3% of pancreatic tumors
- Tumor of young females
  - F:M = 9.5:1; Mean age = 30.3 yrs
- Symptoms usually related to presence of mass
  - Detected during pregnancy, after trauma, incidentally
- Low grade malignant neoplasm
- Metastases in 15%
- Long survival after metastases
- Uncertain histogenesis
- Monomorphic epithelial cells with solid and pseudopapillary structures

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**Solid-Pseudopapillary Tumor: Molecular Features**

- APC / β-catenin pathway upregulation (95%)
  - β-catenin mutations
  - Overexpression of cyclin D1
  - Upregulation of genes required in Notch, Hedgehog, and androgen receptor signaling pathways
  - E-cadherin expression changes from a membranous to intracytoplasmic localization
- No abnormalities in "ductal carcinoma genes"
  - K-ras
  - p53
  - DPC4
**Solid Pseudopapillary Tumor: Staining Profile**

<table>
<thead>
<tr>
<th>Stain</th>
<th>% Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trypsin</td>
<td>0</td>
</tr>
<tr>
<td>Chymotrypsin</td>
<td>0</td>
</tr>
<tr>
<td>Lipase</td>
<td>0</td>
</tr>
<tr>
<td>Lipase</td>
<td>0</td>
</tr>
<tr>
<td>Synaptophysin</td>
<td>30</td>
</tr>
<tr>
<td>Neuron Specific Enolase</td>
<td></td>
</tr>
<tr>
<td>Lipase</td>
<td>0</td>
</tr>
<tr>
<td>Chromogranin</td>
<td>0</td>
</tr>
<tr>
<td>neuron specific enolase</td>
<td>80</td>
</tr>
<tr>
<td>CD56</td>
<td>95</td>
</tr>
<tr>
<td>Mucicarmine</td>
<td>0</td>
</tr>
<tr>
<td>CEA</td>
<td>5</td>
</tr>
<tr>
<td>Keratin</td>
<td>30</td>
</tr>
<tr>
<td>Vimentin</td>
<td>100</td>
</tr>
<tr>
<td>α1-antitrypsin</td>
<td>84</td>
</tr>
<tr>
<td>CD10</td>
<td>100</td>
</tr>
<tr>
<td>Beta catenin</td>
<td>97</td>
</tr>
<tr>
<td>Progesterone receptor</td>
<td>90</td>
</tr>
</tbody>
</table>
Acinar Cell Carcinoma
Clinical Features

- 1-2\% of pancreatic tumors
- Male predominance, mean age = 61
- Non-specific presenting symptoms
- Jaundice rare
- Lipase hypersecretion syndrome
Acinar Cell Carcinoma

<table>
<thead>
<tr>
<th>Gene</th>
<th>Ref.</th>
<th>Number of patients</th>
<th>Number of patients with mutation (frequency)</th>
</tr>
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Al Hader A et al, World J Gastroenterol 2017
BRAF fusion in 24% acinar tumors, including pure and mixed types

BRAF partners:
- SND1 (50%)
- HERPUD1 (18%)

Potential for targeted therapy to inhibit MAPK pathway activity

Treatment

- Aggressive surgical resection
  - 5-year survival on resected patients 72%
  - Resection for metastases
- No defined treatment guidelines for cure
- May be chemoresponsive to agents that have activity against pancreatic adenocarcinomas and colorectal carcinomas
- Targeted therapy
  - MMR deficient – PD-1 receptor blocker
  - SND1 -BRAF fusion – MEK inhibitor
  - JAK-1 mutation – JAK-1 & 2 inhibitor