Solid-Pseudopapillary Neoplasm (SPN) of the Pancreas

Radiology-Pathology Correlation

Thomas Loehfelm, MD, PhD
Aarti Sekhar, MD

Department of Radiology and Imaging Sciences
Emory University School of Medicine
Neither the authors nor their immediate family members have a financial relationship with a commercial organization that may have a direct or indirect interest in the content.
[Solid-pseudopapillary neoplasm of the pancreas is a] low-grade malignant neoplasm composed of poorly cohesive monomorphic epithelial cells forming solid and pseudopapillary structures. These neoplasms frequently undergo haemorrhagic-cystic degeneration, and occur predominantly in young women.
Epidemiology

A Systematic Review of Solid-Pseudopapillary Neoplasms – Are These Rare Lesions?

- **Rare**
  - 2800 cases reported in past 51 yrs
  - 90% of these reported in past 15 yrs
- **Females**: 88%, mean age 28.5 yo
- **No ethnic predilection**
- **No preferential location in the pancreas**
  - Head: 36%
  - Body/tail: 59%
  - Extrapancreatic or unknown: 5%
- **Mean size at diagnosis**: 8.6 cm
  - Mean size decreasing as more SPNs (up to 40%) now discovered incidentally
- **Rarely metastatic**
  - Lymph nodes: 0.5-2.5% Rare
  - Distant spread: 5.6 – 9%
- **Diagnostic yield of pre-op biopsy**
  - Overall: 65% (percutaneous: 63%; endoscopic ultrasound: 70%)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>64%</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>38%</td>
</tr>
<tr>
<td>Abdominal mass</td>
<td>33%</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>20%</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>10%</td>
</tr>
<tr>
<td>Weight loss</td>
<td>8%</td>
</tr>
<tr>
<td>Jaundice</td>
<td>5%</td>
</tr>
<tr>
<td>Other</td>
<td>14%</td>
</tr>
</tbody>
</table>
Treatment and Prognosis

A Systematic Review of Solid-Pseudopapillary Neoplasms – Are These Rare Lesions?

Good prognosis after primary resection

- 96% disease free after mean follow-up of 36 mo
- 4% recurrence rate, with mean time to recurrence of 51 mo

∴ 5yr minimum follow-up recommended
- 1.5% case fatality rate

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distal pancreatectomy</td>
<td>49%</td>
</tr>
<tr>
<td>Pancreaticoduodenectomy</td>
<td>24%</td>
</tr>
<tr>
<td>Enucleation</td>
<td>9%</td>
</tr>
<tr>
<td>Central pancreatectomy</td>
<td>4%</td>
</tr>
<tr>
<td>Total pancreatectomy</td>
<td>1%</td>
</tr>
<tr>
<td>Pancreatectomy, unspecified</td>
<td>14%</td>
</tr>
</tbody>
</table>
Pathogenesis

Two theories on cell-of-origin

**Theory 1: Genital Ridge Cells**
Primordial germ cells destined for the genital ridge migrate through the mesentery in close proximity to the developing dorsal pancreatic bud. A migrational anomaly of primordial ovarian cells could lead to deposition in the tail of the pancreas, predisposing to SPNs later in life. The same theory is proposed for other pancreatic tumors with a female preponderance such as mucinous cystic neoplasms.

This theory might explain the progesterone receptor status of SPNs, and the peaks and troughs of this trophic hormone during the reproductive cycle provide a mechanistic explanation for the hemorrhagic necrotic appearance of many SPNs.

![Graphic representing a 5 week human embryo in axial cross section, demonstrating the migration of ovarian anlage germ cells to the genital ridge. Image copyright © 2012 by Saunders, Elsevier. Modified from Netter’s Atlas of Embryology, Updated Edition (Online Access).](image)

**Theory 2: Multipotential primordial cells with neuroendocrine differentiation**
SPN resembles PancNET histologically and immunohistochemically (IHC), but the IHC profile is not specifically characteristic of any known cell of origin. It could be the case that the neuroendocrine lineage is merely a potential line of tumor differentiation rarely than indicative of a neuroendocrine cell of origin.
Variety of Imaging Appearances

- Heterogeneous masses, with variable solid and hemorrhagic necrotic components
- Calcification in up to 40%

Pathology-proven SPNs from 8 separate patients, some of which will be presented in more detail on later slides
Imaging Appearance

- Progressive enhancement, less than normal pancreas
SPNs from 3 separate patients show the range of gross appearance, including solid areas with zones of hemorrhage and cystic degeneration filled with necrotic debris. Corresponding diagnostic images are not available for the specimen in the middle.
Distinctive microscopic appearance: pseudopapillary and hemorrhagic-necrotic pseudocysts; confirm diagnosis with Immunohistochemical (IHC) markers as below

More specific for SPN:
- CD10: Diffuse reactivity is characteristic of SPN
- β-catenin: Nuclear reactivity is characteristic of SPN
- Progesterone receptor
- α-1-antitrypsin: Intense staining of small clusters is characteristic
- Vimentin: Diffuse

Positive in both SPN and PancNET:
- CD56: SPN and PancNET are the only CD56+ pancreatic tumors
- Synaptophysin

More specific for PancNET:
- Chromogranin
- Cytokeratin

WHO 2010 recommends a panel of β-catenin (+), CD10 (+), Chromogranin (-) and Vimentin (+) to establish the diagnosis of SPN
**Histologic features**

<table>
<thead>
<tr>
<th>Feature</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solid</td>
<td></td>
</tr>
<tr>
<td>Pseudopapillae</td>
<td></td>
</tr>
<tr>
<td>Infiltrative</td>
<td></td>
</tr>
<tr>
<td>Hyaline, with whorled calcifications</td>
<td></td>
</tr>
<tr>
<td>Hyaline globules</td>
<td></td>
</tr>
<tr>
<td>Calcification</td>
<td></td>
</tr>
<tr>
<td>$\beta$-catenin positive</td>
<td></td>
</tr>
<tr>
<td>Progesterone receptor</td>
<td>positive</td>
</tr>
</tbody>
</table>
Case 1

24yoF, incidental mass on CT for acute RLQ pain

Dynamic contrast-enhanced MR reveals a T2-hyperintense, T1-hypointense progressively enhancing solid mass in the tail of the pancreas.

The enhancement pattern resembles the spleen on all but the arterial phase, so a differential diagnosis of intrapancreatic splenule, PancNET, and SPN was given.
Pathology was diagnostic of SPN. The gross specimen was characteristic, with a lobulated circumscribed solid mass that bulges from the pancreas but does not invade surrounding tissues, closely matching the MRI appearance.

Histology showed:
- Pseudopapillary architecture (above left) w/ hyaline granules (inset)
- Microscopic infiltration of the surrounding normal pancreas (above right), commonly seen as the tumor does not instigate a stromal rxn (this is not a marker of aggressiveness)
- β-catenin and synaptophysin positive, cytokeratin and chromogranin A negative
Case 2

26yoM, 7 mos progressive, bandlike abdominal pain

• Solid mass with progressive enhancement in the tail of the pancreas was initially thought to be a torsed splenule, and after the liver-spleen scan was negative, an atypical PancNET. SPN was not considered pre-operatively due to male gender.
• Pathology proved SPN based on histologic appearance and confirmed with β-catenin nuclear labeling. The tumor was also positive for the SPN/NET overlap makers CD56 and synaptophysin and the NET marker chromogranin (rarely positive in SPN).
Case 3

36yoM, incidental partially calcified mass on workup for kidney stones

Partially calcified mass in the head of the pancreas, with cystic areas and progressive enhancement of the solid components. The imaging appearance alone does not differentiate SPN and PancNET.
Case 3

36yoM, incidental partially calcified mass on workup for kidney stones

Recipe for incorrect pre-op diagnosis – each step biases the next

- **EUS:** Heterogeneous mass with salt-and-pepper appearance **suggestive of PancNET**
- **FNA at outside hospital:** **PancNET, low grade**
  - **IHC**
    - Synaptophysin: focal positive
    - Trypsin and chromogranin: negative
- **MR**
  - Indication: “Gastrin-producing tumor”
  - Findings: T1/T2 heterogeneous mass with progressive enhancement **represents patient’s known gastrinoma**
- **CT**
  - Indication: “Biopsy-proven low-grade PancNET”
  - Findings: Heterogeneously enhancing partially calcified mass **in keeping with known PancNET**
- **Final Pathology from Whipple specimen:** **SPN!**
  - **IHC**
    - β-catenin: nuclear and cytoplasmic positivity (specific for SPN)
    - Chromogranin A: Negative
    - Synaptophysin: Patchy positivity
    - Cytokeratin and CAM: negative

**SPN specific markers were not checked, perhaps due to male gender and atypical appearance**
Case 4

15yoF, occasional nausea, vomiting, and abdominal pain

MRCP: mass causes pancreatic duct dilation (blue arrow)

Final pathology: SPN
• B-catenin strongly positive

MRI: 13 cm cystic mass w/ progressive enhancement of solid component. Ddx included SPN and MCN.
Case 5

67yoF, 2mos LUQ pain radiating to left, around to her back

4 cm pancreatic head mass with extensive T1 bright hemorrhage; no definite enhancement

T2: Multiple cystic spaces, pancreatic duct obstruction

Subtle susceptibility on the in-phase sequence indicates egg-shell calcification
Case 5

67yoF, 2mos LUQ pain radiating to left, around to her back

• MR
  — "Complex hemorrhagic and cystic mass with questionable solid components...nonspecific, but favored to represent an MCN or atypical PancNET...SPN is felt to be less likely given patient age.”

• Pathology: SPN
  — Extends to vascular bed surface
  — “Mass is peripherally calcified (egg-shell type) and contains copious brown, gritty, friable necrotic material.”
  — IHC
    • β-catenin, CD10, and progesterone-receptor positive
Mimic 1
34yoF, abdominal pain

MR: Cystic and solid mass with cystic locules, small areas of T1 hyperintensity and scattered foci of enhancement.

Differential included SPN (particularly given patient’s age) and MCN (given multiple cystic locules).

Final diagnosis: MCN
45yoM, asymptomatic, CT for abnormality on routine labs

MRCP and T2 demonstrate a 3.5 cm cystic lesion in the pancreatic tail w/ peripheral nodules.

MR+ shows early enhancement of the peripheral nodular soft tissue.

Ddx of NET, MCN and SPN given → Final pathology: Cystic NET, grade 1
Mimic 3

21yoF, severe epigastric pain, nodule in pancreas found on u/s

- **MR**
  - T1/T2 hypointense mass with no significant delayed enhancement
    - MR report favored SPN based on age and appearance, with a DDx of autoimmune pancreatitis
    - In retrospect, it does not have the typical progressive enhancement of SPN

- **Pathology**
  - **FNA:** PancNET, intermediate grade
    - NET markers +
      - CD56 +
      - Chromogranin +
      - Synaptophysin +
  - **Surgical path**
    - PancNET, intermediate grade
58yoF, hepatomegaly on exam

MR: T2-hyperintense multicystic progressively enhancing mass in the head of the pancreas, draped over aorta, favored to represent a NET, with ddx of SPN

Pathology:

- FNA: Neoplastic
- IHC:
  - + CD56, + Chromogranin, + Synaptophysin
  - - β-catenin
- Surgical path: Paraganglioma
Mimic 5

64yoF, adenocarcinoma in head, cystic mass in tail

Liver lesions + multicystic mass in the pancreatic tail with progressive enhancement of the solid component.

Geographic hypoenhancement of the spleen suggesting vascular involvement.

Given the multiplicity of lesions, metastatic disease from patient’s adenocarcinoma in the pancreatic head was suspected and confirmed on biopsy of a liver lesion.
Solid-Pseudopapillary Neoplasm (SPN) Summary

SPNs have certain characteristic epidemiologic findings
- Young females: 88% female (but not 100%!), mean age of 29 yo, no ethnic predilection
- Mean size 8.6 cm, but decreasing as more are found incidentally
- Metastases rare, usually to liver and peritoneum (lymph nodes very rare)

Imaging
- Well-circumscribed, found anywhere in pancreas
- Ranges from solid to cystic with varying degrees of hemorrhagic necrosis
- Progressive enhancement, Ca+ in 30-40%
- Imaging features most commonly overlap with MCN, PancNET, and intra-pancreatic splenule

Resection is definitive treatment, with excellent post-op prognosis
- 4% recurrence, mean time to recur of 51 months: follow-up for at least 5 years

Pathology: SPNs have characteristic pseudopapillary architecture, however share some morphologic and immunohistochemical features of neuroendocrine tumor
- To confirm SPN, utilize SPN specific markers: β-catenin, progesterone receptor, CD10, vimentin
- Markers that overlap with NET: CD56, synaptophysin
References

Acknowledgements

• The authors are grateful to:
  – Aalok Turakhia, MD (Stanford University, Radiologist) for generously sharing diagnostic imaging cases
  – Gabriela Bedolla, MD (Emory University, Pathologist) for providing the gross and histopathology images

Thank you!

Contact Information: Thomas Loehfelm (twloehfelm@gmail.com)