Insulinoma Associated Protein 1 (INSM1) is a Useful Diagnostic Tool in the Differential for Pancreatic Neuroendocrine Tumors

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BACKGROUND
- Distinguishing pancreatic neuroendocrine tumors (PanNETs) from acinar cell carcinomas (ACCs) and solid pseudopapillary neoplasms (SPNs) can have significant theranostic impact.
- Overlapping cytomorphologies and non specific neuroendocrine (NE) marker expression cause diagnostic difficulty on limited material.
- We investigated the utility of insulinoma-associated protein 1 (INSM1), a novel NE marker, in differentiating PanNETs from ACCs and SPNs in cellblocks (CB) and surgical resections (SR).

MATERIALS AND METHODS
- 28 PanNETs (n=12 CBs and n=16 SRs), 11 ACCs (n=5 CBs and n=6 SRs), 15 SPNs (n=5 CBs and n=10 SRs), and 21 pancreatic ductal adenocarcinoma (PDAC, n=11 CBs and n=10 SRs) from 2000-2018 were selected.
- INSM1 (SantaCruz Biotech., C-8, 1:100) IHC was performed, graded via an H-score system (score: 0-300) and averaged for each tumor type.

RESULTS

Conclusions
- INSM1 is a highly sensitive and specific marker for distinguishing PanNETs from ACCs and SPNs.
- INSM1 expression is reduced with increasing PanNET grade.

TABLE 1. INSM1 IHC is a useful diagnostic tool for PanNET tumors

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>Number INSM1 Positive</th>
<th>% Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>PanNET</td>
<td>28/28</td>
<td>100%</td>
</tr>
<tr>
<td>ACC</td>
<td>0/11</td>
<td>0%</td>
</tr>
<tr>
<td>SPN</td>
<td>5/15</td>
<td>33%</td>
</tr>
<tr>
<td>PDAC</td>
<td>1/21</td>
<td>4.7%</td>
</tr>
</tbody>
</table>

TABLE 2. H-score distribution for ACC, SPN and PanNETs

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>Average INSM1 H-score Cytology</th>
<th>Average INSM1 H-score surgical resections</th>
</tr>
</thead>
<tbody>
<tr>
<td>PanNET</td>
<td>254/300</td>
<td>252/300</td>
</tr>
<tr>
<td>ACC</td>
<td>0/300</td>
<td>0/300</td>
</tr>
<tr>
<td>SPN</td>
<td>0/300</td>
<td>21.5/300</td>
</tr>
<tr>
<td>PDAC</td>
<td>0/300</td>
<td>2.5/300</td>
</tr>
</tbody>
</table>

TABLE 3. Sensitivity and Specificity of INSM1 for PanNETs versus other tumors in the differential on limited material

- Sensitivity: 100%
- Specificity: 88.7%
- Positive Predictive Value: 82.4%
- Negative Predictive Value: 100%