Management of Pancreatic Islet Cell Tumors

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Morbidity and Mortality Conference
• 42 yr female with chronic abdominal pain.
• PMHx: Uterine fibroids
• Medications: percocet prn for pain.

• Physical exam: non-contributory
• Labs:
  – Calcium – 9.0, amylase – 30, lipase – 70
Case Presentation

• Evaluated by patient’s gynecologist.
• CT Scan
  – Dilated pancreatic duct with abrupt cutoff.
  – No discrete mass or evidence of metastatic disease.
MRI
Octreotide Scan

- Octreotide Scan - normal study

- EUS –
  - Mass in the body of pancreas
  - Dialated duct distal to it
  - Biopsy: neuro-endocrine tumor of pancreas

PROCEDURE

- Distal pancreatectomy and hysterectomy.
Procedure

- Entered lesser sac by lifting greater omentum off transverse colon
- Posterior wall of stomach lifted off the pancreas.
- Kocherized duodenum.
- Mass was visible in the body of pancreas lateral to the SMV
Pathology

- Low-grade pancreatic endocrine neoplasm
- 2.5 x 2.2 x 1.6 cm
- Multiple satellite nodules in the tail of pancreas
- 0/10 HPF mitotic figures
- Lymph nodes and margins negative.
- Evidence of acute and chronic pancreatitis.
- Immuno-histochemistry – positive for chromogranin and serotonin.
Post-operative Course

• Complicated by post operative ileus
• Tolerated diet on pod #8 and discharged on POD #11.
Management of Pancreatic Islet Cell Tumors
Pancreatic Islet Cell Tumors

- Rare neoplasms (1/100,000)
- 1000 x common in autopsy statistics than in clinical practice.
- Most are benign / non-functional
- Malignant ones – usually metastatic at diagnosis
- All secrete Chromogranin A – detect in serum.

- Sporadic or can occur w/ inherited syndromes - MEN 1

  - Taupenot et al. 2003.
<table>
<thead>
<tr>
<th>Tumor</th>
<th>% Malignant (% Resectable)</th>
<th>% Multicentric</th>
<th>5-Year Survival</th>
<th>% Associated with MEN-1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulinoma</td>
<td>10 (&gt;90%)</td>
<td>5–10</td>
<td>97</td>
<td>5</td>
</tr>
<tr>
<td>Gastrinoma</td>
<td>60–90 (79%)</td>
<td>60–70</td>
<td>60–70</td>
<td>25</td>
</tr>
<tr>
<td>Glucagonoma</td>
<td>50–80 (35%)</td>
<td>&lt;5</td>
<td>50–60</td>
<td>1–20</td>
</tr>
<tr>
<td>VIPoma</td>
<td>40–70 (70%)</td>
<td>&lt;5</td>
<td>50</td>
<td>5</td>
</tr>
<tr>
<td>Somatostatinoma</td>
<td>75 (60%)</td>
<td>&lt;5</td>
<td>40</td>
<td>45–50</td>
</tr>
<tr>
<td>Nonfunctioning and PPoma</td>
<td>&gt;60</td>
<td>&lt;5</td>
<td>30–50</td>
<td>20–40</td>
</tr>
</tbody>
</table>

Pancreatic Islet Cell Tumors

- Anatomic distribution:
  - Gastrinomas, PPomas, and somatostatinomas - 75% right of SMA
  - Insulinomas, glucagonomas – 75% body and tail of pancreas
General Management

• Diagnosis of particular functioning tumor.
• Localization of the neoplasm.
• Surgical resection if feasible.
• Palliation of symptoms.
Efficacy of Localization of Tumors of the Pancreas

<table>
<thead>
<tr>
<th>MODALITY</th>
<th>TRUE POSITIVES (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Noninvasive</strong></td>
<td></td>
</tr>
<tr>
<td>Ultrasonography</td>
<td>23</td>
</tr>
<tr>
<td>Octreotide radioimaging (SRS)[*]</td>
<td>86</td>
</tr>
<tr>
<td>CT</td>
<td>43</td>
</tr>
<tr>
<td>MRI</td>
<td>26</td>
</tr>
<tr>
<td><strong>Invasive</strong></td>
<td></td>
</tr>
<tr>
<td>Endoscopic ultrasonography</td>
<td>82</td>
</tr>
<tr>
<td>Selective angiography</td>
<td>56</td>
</tr>
<tr>
<td>Portal venous sampling</td>
<td>76</td>
</tr>
<tr>
<td>Provocative angiography†</td>
<td>65</td>
</tr>
</tbody>
</table>

*Provocative angiography – Calcium and glucagon stimulation test for insulinoma.

Insulinoma

Most common type

- 5th & 6th decade, females
- Secrete insulin(proinsulin): Whipple's triad
- Ratio serum Insulin : glucose > 0.3.
- Provocative tests:
  - Glucagon stimulation test – 72% sensitive
  - Calcium infusion test
Insulinoma

- Localization – CT or EUS
- Octreotide scanning not useful.
- Transhepatic selective venous sampling
- Exploration with intra-operative ultrasound.
Glucagonoma

- Fifth decade of life
- Rare – 4D syndrome, necrolytic migratory erythema

Glucagon level > 500 pg/ml.
Glucagonoma

Localization:
- Large (>5cm) and metastatic (75%)
- Located in body / tail of pancreas
- CT/MRI. Octreotide scanning (75%)
- Aggressive nutritional support and DVT prophylaxis prior to intervention.
Vasoactive Intestinal Peptide – Secreting Tumor

• 30 – 50 years, rare (1/10,000,000); WDHA syndrome.

• Solitary, > 3 cm, located in tail of pancreas
• 60-80 % metastatic at diagnosis.
• CT / MRI.
• Octreotide scanning is highly sensitive.

• Pre-operative octreotide, hydration with correction of metabolic abnormalities and hypokalemia.
Somatostatinoma

- Rarest of islet cell tumors.
- Fifth decade of life, diagnosed incidentally.
- Diabetes (60%), cholelithiasis (70%), steatorrhea.
- Somatostatin level > 10 ng/ml.
- Mostly solitary, large, located in head of pancreas, metastatic (75%).
- CT/MRI; Octreotide scanning.
Pancreatic Polypeptide – Secreting Tumors

Third most common

Symptoms:
  – weight loss, jaundice, abdominal pain.

Diagnosis: PP - > 300 pg /ml

Localization
  • Large lesions – CT / MRI.
Non-Functioning Islet Cell Tumors

- Secrete low levels of hormones / chromogranin A
- Common symptom: abdominal pain (86%)
- Diagnosed with CT / MRI.

- Should be considered as aggressive as functioning tumors and with similar prognosis
  - Similar 5 yr survival

MEN I

- Parathyroid, pituitary, pancreas and occasionally adrenal gland.
- 25% of gastrinomas, 10% of insulinomas associated with MEN I
- MEN I -> 50% have gastrinomas, 20% have insulinomas.

- All patients with pancreatic endocrine tumors – check serum calcium levels
  - Elevated calcium levels: study parathyroid and pituitary
Surgical Treatment

• Only curative therapy.
• After appropriate serum marker testing and localization study.
• Operative exploration and feasibility of resection
• Formal resection except for cases of insulinoma (enucleation.)
Metastatic Disease

Surgical resection confers survival advantage and relief from symptoms.

Metastatic Disease

- Hepatic Resection – for liver only mets
- RFA / Cryoablation
- Hepatic artery embolization

- Radionuclide therapy – octreotide, MIBG
- Chemotherapy
  - Limited benefit
  - Enroll in clinical trials

www.downstatesurgery.org
Surgical Treatment Algorithm

1. Diagnosis
   - Serum chromogranin A level, tumor specific hormone level (e.g., insulin)
   - High-resolution CT scan
   - Somatostatin Receptor Scintigraphy (SRS) (except for insulinoma)

2. Localized disease
   - Surgical resection of primary tumor
     - Intraoperative ultrasound
     - Enucleation if possible
     - Distal pancreatectomy vs. pancreaticoduodenectomy for larger tumors

3. Metastatic disease
   - Liver only
     - SRS positive
       - Peptide receptor radionuclide therapy
     - SRS negative
       - Clinical trials (chemotherapy)
   - Diffuse

4. Further treatment
   - Isolated
     - Hepatic resection and/or ablation
   - Diffuse
     - Hepatic artery embolization

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Conclusions

- Pancreatic Islet cell tumors - uncommon class of neoplasms
- Can be easily diagnosed with careful history and few laboratory tests.
- Localization and complete surgical resection provides best symptom control and improves overall survival.
References