Pancreatic Neuroendocrine tumours

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Throckmorton Surgical Society Symposium
May 3rd, 2019

Objectives

- Review (Residents)
- Surgical aspects
- Confusing
Confusing

- TNM
- NCCN
- NANETS
- ENETS
- WHO

- Carcinoid
- Islet cell
- NEN
- NET
- NEC
- GPNET
- Midgut NET

Theodor Langhans
1839-1915
“Histology”

Otto Lubarsch
1860-1933
“Autopsy”

Siegfried Oberndorfer
1876-1944
“Benign carcinomas”
“Karzinoide”

Modlin IM,
Hum Pathol 2004
Pancreatic tumors

- Rising:
  - Rising incidence
  - PPI
  - Increased detection
  - More imaging

Klimstra DS. Mod Pathol. 2007; 20: 94-112

PNET
Functional status

- Functional tumors - relatively constant

- Increase in non-functional tumors - nearly doubled
  (More imaging)

- Significant increase in pancreatic carcinoid tumors - 13 fold
  (more immunohistochemical staining)

- Functional tumors – better prognosis

Kunz PL. J Clin Oncol. 2015; 33: 1855-1863
Kasumova GG et al. JACS. 2017; 224:1057-1064
PNET Presentation

- Sporadic (Majority)
- MEN-1-Pancreas
  - Gastrinoma-30-40%
  - Insulinoma-10%

Presentation

- Incidental mass
- PNET hormone symptoms
- MEN 1 syndrome symptoms
Incidental mass

- CT scan
- MRI

- Arterial phase-enhancing lesions/washout during venous phase
- Both for primary pancreas lesion and liver metastasis
- Subcentimeter lesions - ??

MEN 1 symptoms

- Radiology
- EUS
- Octreo-scan
- DOTATAE
- Venous sampling
- Intra-operative
- Tumor markers

- Non-functioning tumors:
  - Chromogranin A
  - False + ve’s
- Functioning tumors:
  - Chromogranin A
  - Specific hormone
## PNET

### Principles of treatment

- **Cancer control**
- **Symptom control**

<table>
<thead>
<tr>
<th>Classification/Grade</th>
<th>Ki-67 proliferative index</th>
<th>Mitotic index</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Well-differentiated</strong> PanNET (Tumors)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PanNET G1</td>
<td>&lt;3</td>
<td>&lt;2</td>
</tr>
<tr>
<td>PanNET G2</td>
<td>3 - 20</td>
<td>2 - 20</td>
</tr>
<tr>
<td>PanNET G3</td>
<td>&gt;20</td>
<td>&gt;20</td>
</tr>
<tr>
<td><strong>Poorly differentiated</strong> PNEC (Carcinomas)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PanNEC (G3)</td>
<td>&gt;20</td>
<td>&gt;20</td>
</tr>
</tbody>
</table>

- **Small cell type**
  - Similar to small cell carcinoma of lung
  - Large cell type better prognosis than small cell

**WHO Classification of Tumors of Endocrine Organs**, Ohike N, Adasy NV, LaRosa et al. 2017

- Nearly all functioning tumors: Well-differentiated
- Carcinoid tumors and islet cell tumors of past: are in the well-differentiated category now
- No moderately differentiated category- included in well-differentiated category
- Not known if there is progression from PNET to PNEC
**PNET**

**Who to treat**

- **Functional-YES***
  - Resection
  - Medical management (symptoms)
  - *(MEN 1)*

- **Non-functional**
  - Still resect BUT
  - Controversial based on
    - Size
    - MEN 1

**PNET**

**Extent of disease**

1. Localized
2. Non-metastatic
1. Locally advanced
2. Metastatic
PNET
Treatment caveats

1. Size: < or > 2 cm (now may be 1 cm as cut off)
2. Differentiation – Well or Poorly differentiated (FNA difficult)
3. Lymph node involvement (difficult to assess pre-op)
4. NET OR NEC
5. Adjacent organs or vessel involvement
6. Extent of resection (ex: splenectomy or not)

Pancreatic neuroendocrine tumours
Localized/non-metastatic

Non-functioning

- 64 yr F,
- Incidental lesion
### Pancreatic neuroendocrine tumours

#### Localized/non-metastatic

<table>
<thead>
<tr>
<th>Non-functioning</th>
<th>Size</th>
<th>MEN 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rule out MEN 1</td>
<td></td>
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</tr>
</tbody>
</table>

- **90-100%**: parathyroid lesions
- **30-70%**: pancreas: benign or malignant
- **30-40%**: pituitary- functioning

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### Pancreatic neuroendocrine tumours

#### Localized/non-metastatic

<table>
<thead>
<tr>
<th>Non-functioning</th>
<th>Size</th>
<th>MEN 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>2cm cut off (? 1cm) Without MEN 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- ?Resect all/&gt; 2cm/&gt; 1 cm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Distal pancreatectomy +LN</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Pancreaticoduodenectomy +LN</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- ??Enucleation- controversial: (small &lt; 2-3cm/G1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Balance risks and benefits for &lt; 2 cm + major resection (Now cut off 1 cm/Resect 1-2cm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MEN 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 2cm or &gt; 2cms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-functioning: 35-55%</td>
<td></td>
<td></td>
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</tbody>
</table>

- Controversial
- Resect: > 2 cm (tumor control NOT symptom control, ex: gastrinoma)
- ?? If < 2 cm
Pancreatic neuroendocrine tumours
Localized/non-metastatic

Functioning

Insulinoma
Most common
90% benign

Without MEN 1
- Solitary-90%/ 10% multiple
- **Laparoscopy** (intra-op search other lesions)
- Enucleation- < 2cm/duct
- Distal pancreatectomy
- +/- spleen preserving
- Pancreaticoduodenectomy

With MEN 1
- Multiple
- Resect
- **Laparotomy**
- Subtotal pancreatectomy
  +/- enucleation of head
- Pancreaticoduodenectomy

MEN 1
Pancreatic neuroendocrine tumours

Localized/non-metastatic

**Gastrinoma**

More malignant

Without MEN 1

- Observe (occult tumour)
- **Laparotomy**: exploration
- Duodenotomy +/- EGD, EUS/nodes
- Based on location
- Enucleation (criteria- 2cm)
- Distal pancreatectomy
- Pancreaticoduodenectomy

With MEN 1

- CONTROVERSIAL
- Multiple
- Good biochemical outcomes without surgery (PPI)
- Mainly for tumor control
- Observe
- ?? > 2cm - remove all

**Glucagonoma**

Usually malignant

Metastasis (50-80%)

< 2cm or > 2cm

Without MEN 1

- Usually in tail/malignant
- Enucleation
- Distal pancreatectomy
  + node dissection, +/- splenectomy
- Pancreaticoduodenectomy

With MEN 1

- Multiple
- Resect
- **Laparotomy**
- Distal pancreatectomy
- Pancreaticoduodenectomy
Loco-regional unresectable or metastatic disease: **Pancreas**

46 year female with GI bleed

- Pancreatectomy
- Splenectomy
- Gastrectomy
- Hepatectomy

Neuroendocrine tumour involving pancreas/stomach/spleen/liver

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**Loco-regional unresectable or metastatic disease: Pancreas**

**Asymptomatic**

- Observe
- Resection: R0
- Systemic Rx

**Symptomatic**

- Resection
  - R 0
  - Primary alone
  - Systemic Rx

- 90% (? 70%) cyto reductive surgery can also be considered
- Resecting primary (small bowel- now pancreas) in presence of unresectable metastatic disease

NANETS guidelines
Neuroendocrine tumours

- Rising & Confusing
- Better prognosis (Steve Jobs vs Patrick Swayze)
- Functional versus Non-functional
- Two principles: cancer control and symptom control

- Surgery is the mainstay
- Resect completely/ even R1 or R2 acceptable
- MEN I considerations

Thank you