Pathology of the Parathyroid Gland

Hyperplasia & Tumors

2015-12-15
• Function:
  – Parathyroid hormone
  – Calcium homeostasis

• Number:
  – At least 4
  – 13% with >4 up to 16

• Size:
  – 6x4x2mm
  – tot. total weight ♂ 120mg, ♀ 142mg
  – pathologic: single gland >60mg
Parathyroid Glands
- Sense low serum calcium and increase PTH secretion

Skin
- UVB exposure
  - 7-dehydrocholesterol
  - Pre-D₃
  - Vitamin D₃

Liver
- 25-hydroxylase
- 25-hydroxycholecalciferol

Kidney
- 1α-hydroxylase
- Decreases excretion of calcium
- Increases excretion of phosphorus

Bone
- Releases calcium and phosphorus
- Calcitriol (1,25-(OH)₂-D)
- 1,25-dihydroxycholecalciferol

Small Intestine
- Increases absorption of dietary calcium and phosphorus

Increased Serum Calcium and Phosphorus
Normal Parathyroid Gland

• Histology:
  – Chief cells
  – Clear cells
  – Transitional oxyphilic cells
  – Oxyphilic cells
  
  – Fat cells:
    • Child: none
    • Puberty until 30 y: Increase of fat cells (up to 10-30%)
    • Pathological in adults: >50% or no fat (fat content varies from gland to gland)
Immunohistochemistry

- Parathormone
  - Patchy staining
  - Expression decreases with increased activity

- Neuroendocrine markers
  - CGA+ (expression decreases with increased activity)
  - Synaptophysin +

- Cytokeratins
  - CK8,18,19+

- Negative
  - Thyreoglobulin, CEA, TTF1
  - Calcitonin (hyperplastic parathyroid may be +)

- Mib1
  - Not useful for DD adenoma/carcinoma
  - >5% → closer and longer follow up
GATA3 is sensitive and relatively specific for parathyroid differentiation (paragangliomas 78% +)
Frozen Section

In the past:
Hyperplasia
Adenoma
Carcinoma

Today:
Is it a parathyroid?
### Frozen Section

<table>
<thead>
<tr>
<th></th>
<th>Abundant</th>
<th>Frequent</th>
<th>Rare</th>
<th>Absent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Thyroid</strong></td>
<td>10</td>
<td>41</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td><strong>Parathyroid</strong></td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>45</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abundant</td>
<td>&gt;50 crystals/100x</td>
</tr>
<tr>
<td>Frequent</td>
<td>6-50 crystals/100x</td>
</tr>
<tr>
<td>Rare</td>
<td>&lt;6 crystals/100x</td>
</tr>
</tbody>
</table>

Primary hyperparathyroidism (pHPT)
Secondary hyperparathyroidism (sHPT)
Tertiary hyperparathyroidism (tHPT)

→ Hypercalcemia
# Primary Hyperparathyroidism

<table>
<thead>
<tr>
<th>Condition</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chief cell adenoma</td>
<td>80-85%</td>
</tr>
<tr>
<td>Chief cell hyperplasia</td>
<td>15% (20% fam.)</td>
</tr>
<tr>
<td>Carcinoma</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Inflammation</td>
<td>very rare</td>
</tr>
</tbody>
</table>

**Familial syndromes**

- MEN 1, MEN 2A,
- familial hypocalciuric hypercalcemia,
- familial isolated HPT
- HPT-Jaw-Tumor-Syndrome,
- neonatal HPT

---

Hypercalcemia due to oversecretion of PTH secretion independent of the needs of the organism **stones, bones, groans, and psychiatric overtones**
Chief Cell Adenoma

Encapsulated solid tumor. No lobulation. No fat cells.

Hyperplastic chief cells. Suppressed parathyroid tissue.
Primary Hyperparathyroidism

- a Clear cell adenoma
- b Adenoma of oxyphilic cells
  - Def. >90% oxyphilic cells
- c Lipoadenoma
- d Chief cell hyperplasia
  - 20% MEN 1 or MEN 2A
Atypical Adenoma

Atypical features but no clearcut criteria of malignancy (no capsular/vascular invasion) Close and prolonged follow up indicated. Mostly benign course of R0 resected lesions.
<table>
<thead>
<tr>
<th></th>
<th>Adenoma</th>
<th>Hyperplasia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight</td>
<td>1g on average</td>
<td>&lt;1g</td>
</tr>
<tr>
<td>Cell type</td>
<td>One cell type</td>
<td>Mixture</td>
</tr>
<tr>
<td>Nuclei</td>
<td>Pleomorphous</td>
<td>Monomorphous</td>
</tr>
<tr>
<td>Suppressed tissue</td>
<td>50%</td>
<td>Absent</td>
</tr>
<tr>
<td>Stromal fat</td>
<td>Reduced to absent</td>
<td>Present</td>
</tr>
<tr>
<td>Connective tissue</td>
<td>Reduced to absent</td>
<td>Broader septae</td>
</tr>
<tr>
<td>Capsule</td>
<td>Present</td>
<td>Absent</td>
</tr>
</tbody>
</table>
Secondary Hyperparathyroidism

- Chronic renal failure
- Vitamin D shortage
- Malnutrition/malabsorption/maldigestion

Regulative disturbance of calcium homeostasis: bone symptoms but no hypercalcemia
Secondary Hyperparathyroidism

Diffuse → nodular hyperplasia

Chief cell hyperplasia
Tertiary Hyperparathyroidism

- patients with chronic renal failure/malabsorption
- long-term secondary hyperparathyroidism
- asymmetric nodular hyperplasia

hypercalcemia with loss of response to serum calcium levels → subtotal parathyroidectomy or total parathyroidectomy with autotransplantation
Tertiary Hyperparathyroidism
Carcinoma of the Parathyroid

• Criteria of malignancy (min. 1)
  – Invasion of adjacent tissue like thyroid, esophagus, nerves, cervical soft tissue
  – Lymph node or distant metastases (histologically proved)
Carcinoma of the Parathyroid

• Criteria associated with malignancy (min. 2-3)
  – Penetration of the capsule (60%)
  – Vascular invasion (10-15%)
  – >5 mitoses/10 HPF
  – Broad intratumoral fibrous septae
  – Coagulation necrosis
  – High nuclear:cytoplasmic ratio
  – Diffuse cellular atypia
  – Macronucleoli
Carcinoma of the Parathyroid

No grading
No TNM classification

Broad fibrous septae
Muscle invasion
Invasion of the capsule
## Neoplasias

<table>
<thead>
<tr>
<th></th>
<th>Adenoma</th>
<th>Atypical Adenoma</th>
<th>Carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>capsule</td>
<td>Thin, complete</td>
<td>variable</td>
<td>thick fibrous capsule</td>
</tr>
<tr>
<td>suppressed tissue</td>
<td>present in 50%</td>
<td>variable</td>
<td>rare</td>
</tr>
<tr>
<td>macroscopy</td>
<td>red-brown</td>
<td>variable</td>
<td>grey-white,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>lobulated, nodular</td>
</tr>
<tr>
<td>stromal fat</td>
<td>reduced to lacking</td>
<td>reduced to lacking</td>
<td>lacking</td>
</tr>
<tr>
<td>mitoses</td>
<td>≤ 1/10 HPF</td>
<td>&gt;1/10 HPF</td>
<td>&gt;1/10 HPF</td>
</tr>
<tr>
<td>capsule/vascular</td>
<td>no</td>
<td>+/-</td>
<td>CI: 2/3</td>
</tr>
<tr>
<td>invasion</td>
<td></td>
<td></td>
<td>V1: 10-15%</td>
</tr>
<tr>
<td>prognosis</td>
<td>very good</td>
<td>variable</td>
<td>Recurrences, distant</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>metastases in 1/3</td>
</tr>
</tbody>
</table>
Failed Parathyroid Surgery

• Persistent disease:
  – Ectopic position
  – Double gland disease
  – Unsuspected hyperplasia
  – More than four glands
  – Inexperienced surgeon

• Recurrent disease (> 6 months)
  – Subtotal parathyroidectomy for hyperplasia
  – Recurrent or metastatic parathyroid cancer
  – Parathyromatosis

Ectopic locations of parathyroid