The mystery of the hidden parathyroid adenoma

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Case #1

Primary Hyperparathyroidism

Case of missed adenoma

• 55 year old woman with hypercalcemia for 5 years.
• Calcium 10.9–11.4, PTH 59–93, vitamin D 18, creatinine 0.8.
• Osteopenia (T -2.0 femur).

Imaging

• Ultrasound & Sestamibi negative for a parathyroid adenoma
• 7 mm benign appearing thyroid nodule noted on ultrasound

Case of missed adenoma

• Four gland exploration
• Single left upper adenoma, retroesophageal
• 500 mg parathyroid adenoma
• Intraoperative PTH 101 to 14.6

Ultrasound false negatives

• May occur due to body habitus, gland morphology, small glands
• Deep glands may be obscured by the trachea or esophagus
• Large multinodular goiter may obscure glands
• Ectopic glands outside the scanned field (e.g. mediastinum)

Chien, Oto Clin N America 2010
Primary Hyperparathyroidism

**Ultrasound false positives**
- Posterior, exophytic thyroid nodules
- Central compartment lymph nodes
  - Hashimoto thyroiditis
  - Thyroid cancer

**Sestamibi false positives**
- Thyroid adenomas (follicular and Hürthle cell neoplasms, rich in mitochondria)
- Thyroid carcinomas
- Cervical lymphadenopathy (inflammatory, Hashimoto, metastases)
- Potentially reduce false positives with subtraction imaging

**False negative sestamibi scan**
In one series, 32% of patients had a negative sestamibi
- Single adenoma in 92%

<table>
<thead>
<tr>
<th>Predominant cell type</th>
<th>False negative</th>
<th>True positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chief cell rich</td>
<td>72%</td>
<td>91%</td>
</tr>
<tr>
<td>Oxyphil cell rich</td>
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</tbody>
</table>

Mean weight
- 517 mg
- 1180 mg

**Sestamibi false negatives**
- Submandibular glands may obscure an ectopic gland
- Double adenoma, four gland hyperplasia
- Early washout of a parathyroid adenoma
  - look at early images
- Smaller glands may be missed
  - up to 80% < 300 mg, 25% >1250 mg

Early washout

**U/S + Sestamibi**
- Concordant 50-70%
- Increased sensitivity: 70 to 90%
- Correlate findings, to discern sestamibi ...
  - false positive (thyroid nodule) and
  - false negative (early washout of parathyroid adenoma)

Early
- Delayed

**Case #2**
Case #2

- 67 year old man with primary HPT for 8 years: calcium 11.1, PTH 85, creatinine 0.8, vit D 30
- History of nephrolithiasis, osteopenia (T -1.5 forearm) traumatic radius fracture, memory loss, recent CAGB for MI
- Family history of PHPT (father and sister)

Imaging

- Imaging of choice?
- 4DCT with ultrasound was performed

Intraoperative findings

- Intraoperative ultrasound used for direct approach, left upper
- Left upper excised
- Inadequate drop in PTH (118 to 93 at 10 min)
- Converted to four gland exploration
- Four gland hyperplasia
- 3.5 glands excised (each approximately 170 mg)
- Intraoperative PTH 118 to 10

Case of an ectopic gland

- 53 year old woman with hypercalcemia for 3 years.
- Calcium 11-11.5, PTH 60-92, vitamin D 35, creatinine 0.79.
- Ultrasound & sestamibi negative for a parathyroid adenoma.
- Traumatic right wrist fracture 30 years ago.
- Fatigue, depression, memory loss and joint pain.
- 4D CT revealed...
Primary Hyperparathyroidism

**Ectopic left lower gland**

Undescended left lower at level of hyoid bone

**Case of an ectopic gland**

- Approach?
  - Intraoperative ultrasound used for direct approach
- 690 mg parathyroid adenoma
- Intraoperative PTH 65 to 12.8

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**4DCT**

- First described by Rodgers in 2006 (MDACC) at AAE5
- Three dimensional CT
- 4th dimension: changes in perfusion of contrast over time
- Rapid uptake and washout of hyperfunctioning parathyroid glands (functional information)
- Improved lateralization – vs sestamibi or ultrasound

- Left lower parathyroid adenoma

**4D CT**

- Pre-contrast
- Post-bolus (30s); arterial phase
- Post-contrast image (60s); venous phase
- Delayed image (90s)

- Left superior parathyroid adenoma with rapid uptake and washout

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**4D CT**

- Lymph node 60 HU at 30 sec
- Left upper parathyroid 160 HU at 30 sec (faster uptake of contrast)

**4D CT**

- Detailed anatomic correlation
- Ectopic & supernumerary glands
- Good for reoperative cases or discordant imaging
- Some use it as first line imaging

- Undescended left lower gland
- Posterior to hyoid bone
- Above carotid bifurcation

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*Kilburn, Ann Surg Onc 2011*
*Kilburn, Surgery 2006*
*Stsrker, Ann Surg Onc 2011*
*Rodgers, Surgery 2006*
*Mahajan, WJS 2012*
*Lee, Seminars in Roent 2013*
*Kunstman, JCEM 2013*
*Libutz, Surgery 2010*
Primary Hyperparathyroidism

4DCT

Left lower parathyroid adenoma

Modified 4D CT

- Pre and post-contrast CT only, with ultrasound
- Half the radiation of standard 4DCT

Primary Hyperparathyroidism

Right upper gland

Primary Hyperparathyroidism

4D CT (two phase)

- Two phase:
  - Arterial (at 18-22 seconds)
  - Venous (immediately after)
- Similar efficacy as 4 phase
- 80% lateralized correctly
- Improved detection if ...
  - Gland > 1 g
  - Ca > 11
  - BMI < 30
  - No Hashimoto thyroiditis

Primary Hyperparathyroidism

Modified 4D CT

- A (arterial phase)
- B (venous phase)

Left inferior adenoma
Early uptake & washout

Primary Hyperparathyroidism

Sensitivity & specificity of 4D CT

- Will identify 50-80% of glands missed on ultrasound & sestamibi

Yale, 2013, n=87

<table>
<thead>
<tr>
<th>Lateraled to correct side of neck</th>
<th>4DCT</th>
<th>Ultrasound</th>
<th>Sestamibi/SPECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>94%</td>
<td>71%</td>
<td>62%</td>
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</table>

<table>
<thead>
<tr>
<th>Correct quadrant</th>
<th>86%</th>
<th>48%</th>
<th>40%</th>
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</thead>
<tbody>
<tr>
<td>Double adenoma or MGH</td>
<td>86%</td>
<td>0</td>
<td>0</td>
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Primary Hyperparathyroidism

4DCT radiation exposure

<table>
<thead>
<tr>
<th>Radiation dose (mSv)</th>
<th>Cost</th>
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<tbody>
<tr>
<td>4DCT (4 phase)</td>
<td>10</td>
</tr>
<tr>
<td>Modified 4DCT (2 phase)</td>
<td>5</td>
</tr>
<tr>
<td>Sestamibi (planar imaging)</td>
<td>6</td>
</tr>
<tr>
<td>Sestamibi with SPECT/CT</td>
<td>9</td>
</tr>
<tr>
<td>Transatlantic flight</td>
<td>0.1</td>
</tr>
<tr>
<td>CXR</td>
<td>0.1</td>
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<tr>
<td>Mammogram</td>
<td>0.4</td>
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<tr>
<td>Abdomen/pelvis CT</td>
<td>10-14</td>
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<tr>
<td>Annual radiation exposure</td>
<td>3</td>
</tr>
</tbody>
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**Conclusions**

- PHPT is underdiagnosed
- Imaging is not used for diagnosis; purpose is to facilitate a focused operation
- 4DCT is increasing in popularity
- Imaging is *suggestive*; the ultimate localization occurs in the OR
- Most patients are cured by safe surgery—a surgeon is best suited to explain the risks and benefits of surgery

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