Challenges and Pearls in Parathyroid Surgery

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Outline

- History
- Asymptomatic hyperparathyroidism
- Hyperparathyroidism with normal PTH
- Ultrasound localization
- Use of rapid PTH
- Venous sampling
- Unusual cases

Disclosures:
None

History

- 1852 Sir Richard Owen (London) – Autopsy on rhinoceros
- 1880 Sandström: parathyroid in human
- 1904 Ashkanazy: osteitis fibrosa cystica
- 1925 Felix Mandl first parathyroidectomy in Vienna
- 1926 First parathyroidectomy in US
- 1934 Albright: assoc. of parathyroid dis. & renal failure
Capt. Charles Martell

Mediastinal Parathyroid Adenoma

Charles Martell
Intraop diagram
Histology

Evolution of Presenting Symptoms

Asymptomatic Hyperparathyroidism
Surgical Guidelines for “Asymptomatic” Hyperparathyroidism (2009) (Consensus Recommendations)

JCEM 2009;94(2):335-9

Age <50
Creatinine clearance <60 ml/min
Ca 1 mg/dl > normal range
T score < -2.5 any site and/or previous fracture

HYPERPARATHYROIDISM
INDICATIONS FOR SURGERY

<table>
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<tr>
<th>Parameter</th>
<th>1990</th>
<th>2002</th>
<th>2009</th>
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<tr>
<td>S Ca**</td>
<td>1.1-1.6 mg/dl</td>
<td>1.0 mg/dl</td>
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<td>24 hour U Ca**</td>
<td>&gt; 400 mg</td>
<td>&gt; 400 mg</td>
<td>NI</td>
</tr>
<tr>
<td>CrCl</td>
<td>Reduced by 30%</td>
<td>Reduced by 30%</td>
<td>Reduced &lt; 60 ml/min</td>
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<tr>
<td>BMD</td>
<td>Z &lt; -2</td>
<td>T &lt; -2.5</td>
<td>T &lt; -2.5</td>
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<tr>
<td>Age</td>
<td>&lt; 50 yrs</td>
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<td>&lt; 50 yrs</td>
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Patient desire also indication for surgery!

Surveillance of Patients Observed with Hyperparathyroidism (2009)

- Serum Calcium Annual
- Serum creatinine Annual
- Bone density 1-2 yrs
  - Measure all three sites
- 24 hour urine excretion No
- Creatinine clearance No
- Abdominal radiography No

Findings of 15-Year Study

- 37% of asymptomatic patients had disease progression over 15 years
- Lumbar spine BMD stable ( cancellous)
- Femoral neck and radius BMD declined before 10 years (cortical)
- Surgery restored normal biochemical indices
- Surgical treatment restored BMD and effect sustained for 15 years

The Natural History of Primary Hyperparathyroidism with or without Parathyroid Surgery after 15 Years

Surgery in 59 patients (51%) 49 with asymptomatic disease 9 with symptomatic disease
No surgery in 57 patients (49%) 49 with asymptomatic disease 20 with surgical criteria 8 without surgical criteria

Normalization of biochemical values and increased bone density in 15 patients (130% of symptomatic and asymptomatic patients)

Disease progression in 22 patients 16 with asymptomatic disease 7 with surgical criteria 17 without surgical criteria
(37% of asymptomatic patients) 8 with symptomatic disease (130% of symptomatic patients)

Stable disease in 31 patients 21 with asymptomatic disease 10 with surgical criteria 25 without surgical criteria
(50% of asymptomatic patients)

J Clin Endocrinol Metab 93: 3462–3470, 2008

Outcome of Operated Patients
Parathyroidectomy improves functional capacity in “asymptomatic” older patients with primary hyperparathyroidism; a randomized control trial
• 18 (>50 years) asymptomatic PHPT
• Assigned to surgery or control group
• 6 minute walk distance increased 184 ft in surgery group (Approx. 10% increase)
• Improved functional ADLs

Medical Management of PHPT
Khan A et al. J Clin Endocrinol Metab 2009;94(2):373-81
Medical management of asymptomatic primary hyperparathyroidism: proceedings of the third international workshop
• Bisphosphonates and hormones decrease bone turnover and improve BMD (no fracture data) Do not lower Ca or PTH
• Cinacalcet reduces Ca and PTH and raises Phosphorous. Does not decrease bone turnover or improve BMD

Medical Management
25% progression of disease in 10 yrs (more likely in pts < 50yrs)
• Bisphosphonates – studies show increased bone density
• Ca/Vit D – help reduce bone loss
• Calcimimetics (Cinacalcet) – currently in use for parathyroid ca and secondary HPT
• SERMs – tamoxifen or raloxifene
Monitor bone density every year and Ca level every 6 months
Elevated PTH and Normal Calcium

- 20% (34/178) in series by Maruani
- Check ionized calcium, may be high
- Up to 15-20% of PHPT cases
- Consider renal leak
- If thiazides given, Ca will increase


Elevated PTH, Normal Ca

Anatomic Localization of Parathyroid Glands

Parathyroid Identification

- Superior Parathyroid (IV)
  - 80% within 2 cm. circle centered 1 cm. Above intersection of RLN and inf. thyroid artery.
  - Glands lie in paratracheal tissue surrounding thyroid, but may be adherent, or within capsule
  - Gland dorsal (superior and lateral) to RLN
  - Ectopic locations: 80% retroesophageal, <20% superior to sup. pole thyroid gland, 1% within thyroid gland
Parathyroid Identification

- Inferior parathyroid gland
  - Normal: 60-70% within 1-2 cm. semicircle below lower pole of thyroid
  - Often in soft tissue adjacent to inferior pole of thyroid
  - Abnormal glands most commonly in thymus
  - Ectopic glands: ant. mediastinum 10%, intracapsular (inf. pole+) <5%, level of hyoid, carotid sheath, or intrathoracic

Location of Superior Parathyroid Glands

- Location of inferior Parathyroid Glands (From Wang)
**Locations of Ectopic Parathyroid Glands**
(From Wang)

- Inferior parathyroid descends with thymus
- Can overshoot and extend into mediastinum
- Arrested descent can produce ectopic parathyroid glands

**Undescended Parathymus**

- 7 cases undescended “Parathymus”

**Systematic Exploration for Hidden Parathyroid Gland**

1. Mobilize thyroid gland
   Commonly find gland on post. edge of gland
2. Mobilize upper end of thymus
3. Paratracheal and retropharyngeal dissection
4. Incise carotid sheath
5. Thyroid lobectomy (not at first surg)
6. Mediastinotomy
   Repeat sestamibi scan before this step
Recurrent Hyperparathyroidism (1)

- 79 y.o. Female with elevated calcium and PTH
- R Superior parathyroid adenoma by experienced endocrine surgeon
  - IOPTH drop to normal range
- Developed recurrent hyperparathyroidism
- Repeat exploration left side, normal gland ID’d, and Left lobe removed

Recurrent Hyperparathyroidism (1)

- Persistent hyperparathyroidism
  - Calcium 13-14
  - PTH over 700
  - Required cinacalcet to control calcium
- Ultrasound performed
- Old operative note reviewed
  - Fibrous texture to adenoma
Recurrent Hyperparathyroidism (1)

Diagnosis:
Parathyroid carcinoma
Parathyroid Carcinoma

• Rare-
  – <1% hyperparathyroidism
  – 0.005% all cancers
• Most common in 49-59 yr. age group
  – Roughly 1 decade younger than PHPTH
• >90% hormonally functional
• Sporadic and part of genetic syndrome
  – HPTH-Jaw Tumor Syndrome (in 15% of cases)
  – MEN1, MEN2a, Isolated familial HPTH

Parathyroid Carcinoma

• Often profound hypercalcemia
• Often renal and skeletal manifestations
  – Polyuria, renal colic, nephrocalcinosis, nephrolithiasis
  – Bone pain, osteopenia, pathologic fractures
  – Nausea, abdominal pain, ulcers, pancreatitis
  – Depression, fatigue

Parathyroid Carcinoma

• Hypercalcemic crisis
• Nonfunctional tumors present with infiltrative symptoms (e.g. hoarseness)
• Palpable mass 40-70%
• Lymph node metastasis 15-30%
• 1/3 have distant metastases (lungs, liver, bone)
• Brown tumors may mimic metastases

Parathyroid Carcinoma

• FNA
  – Not diagnostic
  – Concern about seeding
• Tumor firm, gray to white
  – May invade surrounding structures
• Surgical complete resection
  – Local recurrence common
  – Radiation therapy ineffective
  – Chemotherapy ineffective
• Ablation of mets (ETOH, RFA, embolization)
Parathyroid Carcinoma

- Mean time to recurrence 2.5-4.8 years
- Persistent or recurrent disease in 50%
- Up to 25% distant metastases
- Mortality due to complications of hypercalcemia, e.g. renal failure

Recurrent Hyperparathyroidism (2)

- 42 y.o. female treated for T1N0 SCCA Tongue
- Noted to have elevated Ca (10.3) and PTH
- At age 26 had nephrolithiasis, dx. PHPTH
- Underwent removal parathyroid adenoma
- Gradual increase in Ca last few years
- Ca 10.2, P0₄ 2.8, Cr 0.7, PTH 101
- Recent kidney stone

Recurrent
Hyperparathyroidism (2)

- Ultrasound: possible mass behind left lobe thyroid
- MRI: Several possible right paratracheal masses
Recurrent Hyperparathyroidism (2)

• Parathyroid exploration
• Bilateral IJV sampling
  – R IJV PTH 566
  – L IJV PTH 373
• Extensive dissection both sides of neck
  – Bilat paratracheal, pretracheal, sup. mediastinum
• Found focus of parathyroid on lateral aspect thyroid gland in atypical position

Recurrent Hyperparathyroidism (2)

• PTH dropped to 44, then 3
• Reimplantation ½ gland L forearm
Multiple nodules of parathyroid tissue in right neck soft tissue

Higher magnification of one of the nodules

**Recurrent Hyperparathyroidism (2)**
- Diagnosis: Parathyromatosis
- Rare cause of recurrent HPTH

**Parathyromatosis**
- Rare cause of recurrent HPTH
- First reported 1975
- 2012 review found 35 patients English Literature
- Theory of spillage at time of excision or preexisting parathyroid rests
- Association of rupture and spillage
Parathyromatosis

- Review 35 cases
- 21 female, 14 male
- 22/35 ESRD
- Mean time to reoperation:
  - Healthy 6 years (1.5-23 yr)
  - ESRD 3 years (0.3-29 yr)
- Rupture and spillage documented 9/35

Coexisting Thyroid Pathology

Attich. H&N 1993;15(1)20-23

948 Parathyroidectomies
242 (26%) thyroid pathology
211 (20%) benign pathology
31 (6%) Non-medullary cancer

Lessons:
- Consent for thyroid lobectomy
- Ultrasound before surgery

Intraoperative PTH Assay

Surgical Findings in Primary Hyperparathyroidism

- Single adenoma 80-90%
- Hyperplasia 10-20%
  - “double adenoma” 6-10%
  - Hyperplasia 3%
Intraoperative PTH assay

- Immunochemiluminometric assay
- Double antibody labeling
- Multiple vendors
- Record PTH level pre-op, just before resecting, and 10 min. after removal
- 50% decrease from highest level 10 min. after excision and value in normal range has 98% success rate

Intraoperative PTH assay

- If multiple enlarged glands,
  - Remove enlarged glands (4 gland exploration)
  - check PTH level after last gland excised
- If <10, implant ½ gland in arm

Examples of Intraoperative Assay

LH: 69 y.o. male with Elevated Calcium and PTH

- Nephrolithiasis
- Intraoperative PTH (Immulyte Turbo)
  - Pre incision: 141
  - Pre excision: 200
  - Early post exc. (10 min): 34
  - Late post exc. (60 min): 18
Rapid PTH: Practical Considerations

- Site of sampling - IJV values higher than peripheral blood
- Discard 10cc blood from IV line before drawing sample
- Surgical manipulation increases PTH
  - minimal manipulation after excision of adenoma
- Obtain two baseline samples
  - Manipulation will increase PTH value
  - Sampling after disrupt blood supply will result in falsely low peak pre-excision value
- Very high PTH will not drop to normal in 10 min.

Radioguided Parathyroid Surgery

- Pre-op sestamibi injection to aid localization
  - Characterization of adenoma vs. hyperplasia in *ex vivo* specimens
  - Learning curve
  - Faster turnover (no waiting for results)

Video Assisted Parathyroidectomy

- Endoscopic assisted technique
- Operate off monitor
- Small incision
- High magnification
- Must re-orient to anatomy
- Must learn to operate off monitor
- Need steady assistant to hold scope
- Modified instrumentation
- Must have accurate localization

M.C. 64 y.o. Hispanic Female

- Elevated Ca on screening labs.
- PTH and urine calcium excretion elevated
- Sestamibi scan showed right lesion
- Ultrasound performed
Ultrasound

Minimally Invasive Surgery Definition?

My incision is smaller than your incision
Endoscopic Parathyroidectomy

Robotic Parathyroidectomy

- Maximally invasive approach for maximal cosmetic benefit
- Select population wanting to avoid neck incision
- A long run for a short slide?

Intraoperative Use of OCT in Endocrine Surgery

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Normal Thyroid

Follicles

Normal Parathyroid

Fat

Hypercellular Parathyroid

Loss of fat with increased cellularity

Parathyroid vs. Fat

Parathyroid

Fat
Summary

• Diagnostic imaging improving
  – Ultrasound in the office
  – New imaging modalities (e.g. 4D-CT)
• Rapid assays allow intraoperative feedback
• Surgery becoming more focused and less invasive
• Potential shift in indications for surgery
  – Bone loss favoring surgery
  – Medical parathyroidectomy
• Surgery more predictable in many cases, but still can be challenging cases