Parathyroid Disease & Surgery

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Case Presentation

- HPI: 65yo male with ESRD and hyperparathyroidism complaining of pain of the back and extremities. PTH level was 1835.

- PMHx: ESRD, Hyperparathyroidism, Hypertension, Prostate cancer s/p prostatectomy and radiation

Case Presentation

- Social Hx: denies alcohol abuse, cigarettes, or illicit drug use
- Allergies: Iodine
- Medications: Metoprolol, Simvastatin
- Labs: PTH 1835, Ca 8.8, Mag 2.0, Phos 2.8
Case Presentation

• Imaging:
  – CT scan
  – Sestamibi scan
    • 2 foci of increased uptake at thoracic inlet
Case Presentation

• Operation: Total Parathyroidectomy with autotransplantation
  – Positioning – cervical spine extension
  – Kocher’s incision approximately 2 fingerbreadths above sternal notch
  – Division of Platysma
  – Creation of subplatysmal flaps
  – Vertical incision between strap muscles
  – Lateral mobilization of the thyroid gland
  – Identification of the RLN
  – Identification and excision of each parathyroid gland
    • Right superior – expected
    • Right inferior – expected
    • Left superior – expected
    • Left inferior – substernal, aortic arch
  – Autotransplantation
  – Post-operative PTH 1835 → 190
Case Presentation

• Post-operative Course
  – PO Calcium QID
  – IV Calcium Glucagon taper
  – PO Vitamin D

• Serial exams
  – Chvostek’s sign
  – Perioral numbness/tingling

• Discharged home POD#8 with PO calcium QID
Case Presentation

• Questions about the case?
Parathyroid Disease & Surgery

- History of parathyroid gland & surgery
- Anatomy & Physiology
- Hyperparathyroidism – types
- Pre-operative work-up
- Parathyroidectomy
- Post-operative management
- Surgical complication and considerations
History

• 1852 – Sir Richard Owen
  – Rhinoceros autopsy at the London Zoo
  – Dinosauria – Darwinism

• 1880 – Ivar Sandstrom, MS
  – Human glands

• 1891 – F.D. von Recklinghausen
  – Osteitis fibrosa cystica
**History**

- 1925 – Felix Mendl
  - Credited for first parathyroidectomy
- ?1917 – Sir John Bland-Sutton
- 1926 – EJ Lewis
  - First in the States – Cook County Hospital, Chicago
Anatomy

- Embryology
  - Superior glands – 4th branchial pouches
  - Inferior glands – 3rd branchial pouches
- Blood supply
  - Inferior thyroid artery
  - Superior thyroid artery 20%
- Venous drainage
  - Superior thyroid vein
  - Middle thyroid vein
  - Inferior thyroid vein
Anatomy

• Superior glands
  – Dorsal to RLN crossing with ITA
  – Posterior aspect of upper/middle thyroid
  – Level of cricoid cartilage

• Inferior glands
  – Anteromedial to RLN crossing with ITA
Physiology

- Calcium
- Parathyroid hormone
- Vitamin D
- Calcitonin
Physiology – Calcium

• Normal calcium level
  – Total calcium 8.5-10.5mg/dL
  – Ionized calcium 4.4-5.2mg/dL

• Storage
  – Extracellular 10,000x > intracellular
  – 50% ionized/active form
  – 40% bound to albumin, phosphate, or citrate

• Function
  – Excitation-contraction coupling in muscle
  – Synaptic transmission
  – Coagulation
  – Hormone secretion
  – Second messenger regulation
  – Motility
  – Membrane trafficking
Physiology – Parathyroid Hormone

- 2-4 minute half-life
- Metabolic activation
  - Low serum calcium
  - Low 1,25 vitamin D
  - Catecholamines
  - Hypomagnesemia
- Function – calcium regulation
  - Bone
    - Osteoclast stimulation → calcium and phosphate secretion
  - Small bowel
    - Increases calcium absorption in small bowel via vitamin D
  - Kidney
    - Limits calcium excretion in distal tubule
    - Inhibits phosphate reabsorption
Physiology – Vitamin D

• Metabolic activation
  – 7-dehydrocholesterol in skin → Calcidiol in liver → Calcitriol in kidney

• Functions
  – Stimulates absorption of calcium and phosphate from gut
  – Stimulates osteoclasts → calcium resorption from bone
Physiology – Calcitonin

• Source
  – Thyroid C cells

• Metabolic activation
  – Calcium
  – Pentagastrin
  – Catecholamines
  – CCK
  – Glucagon

• Functions
  – Inhibits osteoclast-mediated bone resorption
  – Inhibits P reabsorption in kidneys
Hyperparathyroidism

- Primary
- Secondary
- Tertiary
Hyperparathyroidism

- Primary
- Secondary
- Tertiary
Hyperparathyroidism

• Primary

• Secondary

• Tertiary
Hyperparathyroidism

- Primary
- Secondary
- Tertiary
Primary Hyperparathyroidism

- 1% of adults in US
- Females are 2-3 times more likely than males
- Most common cause of hypercalcemia after excessive PO intake
Primary Hyperparathyroidism

• Causes of PHPT
  – Single adenoma 80-85%
  – Multiglandular hyperplasia 10%
  – Double adenoma 4%
  – Carcinoma 1%

• Associations
  – 100% of MEN1 patients
  – 25% of MEN2A patients
Primary Hyperparathyroidism

- **Bones**
  - Bone pain, osteopenia, osteoporosis and bone fractures
- **Stones**
  - Kidney stones
  - Renal dysfunction
  - Urinary frequency/incontinence
- **Moans**
  - Nausea/vomiting
  - Fatigue and proximal muscle weakness
- **Psychiatric overtones**
  - Poor concentration and depression
  - Delirium and coma
- **Cardiovascular disease**
  - Hypertension, MI, atherosclerosis
Primary Hyperparathyroidism

• Most patients are asymptomatic
  – 23-62% develop symptoms over 10 years if left untreated

• Surgical indications for asymptomatic PHPT
  – Age <50yo
  – BMD >-2.5SD
  – Calcium >1 over normal
  – Creatinine clearance <60
  – Previous bone fracture/fragility
Primary Hyperparathyroidism

- Treatment –
  - Parathyroidectomy
    - Single gland excision if solitary tumor
    - Bilateral neck exploration if multiglandular disease or MEN syndrome
Primary Hyperparathyroidism

- **Pre-operative Work-up**
  - Rule out Familial Hypercalcemia Hypocalceuria
    - 24h urine collection and creatinine
  - Ultrasound
    - Evaluates parathyroid and thyroid
  - Sestamibi scan
    - Tc99 uptake with relation to mitochondrial activity
    - Less accurate with multiglandular disease and larger tumors
  - 4D CT scan – more rapid tumor uptake
  - MRI
  - Selective venous sampling
    - Rarely performed
    - 2-fold gradient from contralateral side

- Sestamibi + US = 94-99% sensitivity
Primary Hyperparathyroidism

• PTH levels
  – Immediately pre-operatively
  – Send 5 and 10 minutes after removal of gland
  – Should decrease by 50%
Secondary Hyperparathyroidism

- Normal but hyperplastic parathyroid tissue

- Causes
  - Chronic renal insufficiency*
  - Poor calcium intake or absorption
  - Vitamin D deficiency
  - Hyperphosphatemia
Secondary Hyperparathyroidism

- Clinical presentation
  - Renal osteodystrophy
  - Periarticular calcium deposits
  - Nephrocalcinosis
  - Increased cardiovascular mortality
  - Calciphylaxis – 80% mortality
Secondary Hyperparathyroidism

• Treatment
  – Medical management
  – Surgical management
Secondary Hyperparathyroidism

• Treatment
  – Medical management
  – Surgical management

  • Calcium supplements
  • Calcimimetics – Calcinet – calcium-sensing receptor protein to calcium
  • Vitamin D analogs
    – Lowers PTH
    – Elevates Calcium
    – Elevates Phos
  • Phosphate-binders
  • Low phosphate diet
  • Dialysis

• Monitor Ca, P, Vitamin D, and PTH (150-300 pg/ml)
Secondary Hyperparathyroidism

- **Treatment**
  - Medical management
  - Surgical management

- Parathyroidectomy

- Renal transplant – 95% successful

- Address underlying cause
Secondary Hyperparathyroidism

- Indications for parathyroidectomy
  - Failed medical management
  - Refractory symptoms
  - Intractable rapid turnover bone disease
  - Calciphylaxis – emergency

- Relative contraindication – imminent renal transplant
Secondary Hyperparathyroidism

• Pre-operative workup
  – Thyroid US
    • Assess Parathyroid and Thyroid
  – No localization studies needed – except if
    • Concern for ectopic or supernumerary parathyroid glands
    • Concerning ultrasound
Tertiary Hyperparathyroidism

- Chronically stimulated parathyroid gland → autonomous
Tertiary Hyperparathyroidism

• Treatment
  – Calcinet – lowers calcium and PTH
  – Parathyroidectomy
    • Post-transplant parathyroidectomy
    • Pre-transplant parathyroidectomy
Parathyroidectomy

• Ectopic parathyroid gland

• Subtotal versus total parathyroidectomy

• Autotransplantation

• Alternative approaches
Parathyroidectomy – Ectopic Gland

- Captain Charles Martell
  - Parathyroid adenoma
  - 8 fractures
  - Chronic joint pain
  - Shrank from 6’1” to 5’6”

- 6 neck explorations at MGH and in New York
  - All negative

- Studied anatomy textbooks himself and insisted on chest exploration

- Operation #7
  - 3cm adenoma found in mediastinum → partial excision

- Post-operatively
  - Tetany
  - Nephrolithiasis causing ureteral obstruction
  - OR → laryngospasm → expired
Parathyroidectomy – Ectopic Gland

- 5-40% ectopic location
- Superior glands
  - Typically found 2cm radius of RLN-ITA junction
  - Tracheoesophageal groove
  - Retroesophageal groove
  - Posterosuperior mediastinal
  - Intrathyroidal
  - Carotid sheath
  - Paraesophageal
- Inferior glands – more variable
  - Typically found anteromedial to RLN-ITA junction
  - Intrathymic*
  - Anterior superior mediastinal
  - Intrathyroidal
  - Thyrothymic ligament
  - Submandibular
Parathyroidectomy – Ectopic Gland

• Intra-operative tools
  – Parathyroid levels
  – Ultrasound
  – Frozen section
  – Gamma probe with Tc99
Parathyroidectomy – Ectopic Gland

- Focused parathyroidectomy
- → Bilateral extended cervical exploration
- → Consider Cervical thymectomy
- → Hemithyroidectomy on side of localization studies
- • Median sternotomy
  - Wait!
Meta-analysis of 13 studies

1589 patients with secondary hyperparathyroidism
- s/p subtotal parathyroidectomy
- s/p total parathyroidectomy with autotransplantation

End-points
- Rate of symptomatic improvement
- Radiological success
- Recurrence or persistence
- Need for re-operation

No significant difference between subtotal and total with autotransplantation
Parathyroidectomy — Autotransplantation

- Autotransplantation
  - Mincing of most normal appearing gland
  - Sites
    - Sternocleidomastoid muscle
    - Brachioradialis muscle
    - Chest wall soft tissue

- Cryopreservation
  - Cryopreservation — 60% successful; MEN or high risk patients
  - Immediate implantation — 90% successful
Open parathyroidectomy

Focused minimally invasive parathyroidectomy (MIP)
  - Unilateral neck exploration

Minimally invasive endoscopic (MIEP)
  - Via neck or axilla
  - Requires 5 incisions if bilateral
  - 10% conversion rate

Minimally invasive videoscopically-assisted (MIVAP)
  - Gasless dissection
  - Higher complication rate

Minimally invasive radio-guided (MIRP)
  - Tc99 injection pre-operatively
  - Gamma probe
Post-operative Management

- Hungry bone syndrome
- Recurrent laryngeal nerve injury
- Expanding hematoma
- Persistent or recurrent hyperparathyroidism
Post-operative Management

• Hungry bone syndrome
• Recurrent laryngeal nerve injury
• Expanding hematoma
• Persistent or recurrent hyperparathyroidism

• Rapid drop in PTH → boney absorption of serum calcium
• Nadir at 2-4 days post-op

• Presentation
  – Tetany
  – Seizures
  – Heart failure
Post-operative Management

- Hungry bone syndrome
- Monitor calcium levels
- Serial exams
  - Chvostek’s sign
  - Trousseau’s sign
- Medications
  - PO Calcium supplementation – 4-6g/day
  - IV Calcium Gluconate
  - Dialysis patients can have increasing dialysate bath calcium concentration
  - Vitamin D – Calcitriol
    - Preoperative vitamin D deficiency
    - Persistent despite calcium supplementation
  - Treat hypomagnesia
Post-operative Management

• Hungry bone syndrome
• Recurrent laryngeal nerve injury
• Expanding hematoma
• Persistent or recurrent hyperparathyroidism

• If persistent hypocalcemia
  – Failed autotransplantation
  – Remnant parathyroid tissue
Post-operative Management

- Hungry bone syndrome
- Recurrent laryngeal nerve injury
- Expanding hematoma
- Persistent or recurrent hyperparathyroidism
- Unilateral – hoarseness or breathiness
- Bilateral
  - Respiratory failure
  - Immediately after extubation
Post-operative Management

- Hungry bone syndrome
- Recurrent laryngeal nerve injury
- Expanding hematoma
- Persistent or recurrent hyperparathyroidism

- Remove staples/sutures to release pressure
- Intubate if necessary
Post-operative Management

- Hungry bone syndrome
- Recurrent laryngeal nerve injury
- Expanding hematoma
- Persistent or recurrent hyperparathyroidism

- Persistent – no resolution
  - Inadequate resection
  - 80% of re-operations

- Recurrent – >6m postop
  - Return of tumor/tissue
  - 20% of re-operations
Summary

• Most common sites of superior and inferior parathyroid glands are superolateral and anteromedial to crossing of ITA and RLN, respectively.
• Ideal localization studies include Sestamibi scan with or without ultrasound.
• Ectopic parathyroid adenomas can be found along their embryologic origin.
• Consider cervical thymectomy and hemithyroidectomy if still cannot find a ectopic parathyroid adenoma.
• Do not perform sternotomy on the first surgery.
• Hungry bone syndrome can be prevented by post-operative calcium and close monitoring.
Thank you!

• “It hardly seems credible that the loss of bodies so tiny as the parathyroids should be followed by a result so disastrous.”

— Halsted
A 45yo perimenopausal woman is referred for possible parathyroidectomy. Her serum calcium has been 9-9.5mg/dL over the past year. Cl 100, Phos 3.4, PTH 90 (N 30-55). Bone density scan confirms osteopenia of the femoral neck. Sestamibi scan is not conclusive. Which of the following would you recommend?

- A. Parathyroidectomy
- B. Hormone replacement therapy
- C. Cincalcet
- D. Bisphosphonates
- E. Measure Vitamin D levels
During a neck exploration for primary hyperparathyroidism, only 3 parathyroid glands were identified and all appear normal in size. What is the best next step in management?

- A. Thymectomy
- B. Remove all 3 glands and re-implant 1 into the forearm.
- C. Remove 2.5 glands and close.
- D. Perform median sternotomy
- E. Obtain biopsy samples of all 3 glands and close.