Secondary Hyperparathyroidism

Anita Chiu, MD
SUNY Downstate Medical Center
March 4, 2010
Case Presentation

- CL - 50 year old male known to transplant surgery service with history of progressive chronic fatigue, bone pains and myalgias
- PMH: severe secondary hyperparathyroidism, ESRD on HD since 2002, HTN, HIV
- PSH: R arm AVF creation
- Meds: sensipar, clonidine, ramipril, minoxidil, labetalol, calcium carbonate, HAART therapy
Case Presentation

- Physical Exam:
  - Gen: thin, A&Ox3, no acute distress
  - Lungs: CTA
  - Heart: S1 S2
  - Abdomen: soft, benign
  - Ext: functioning RUE AVF, +thrill, +bruit
Case Presentation

- Preoperative Labs:

5.19  12.8  161
40.1

138  100  33
4.7  26  8.4

10.2  112

PTH 1969
25-hydroxyvitamin D 42ng/mL
Case Presentation

- Imaging:
  - Parathyroid ultrasound obtained
  - Normal thyroid visualized
  - Parathyroids not enlarged and unable to be seen
Case Presentation

Imaging:

- Sestamibi scan obtained
- Focus of persistent slow washout radiotracer uptake at the inferior pole of the left thyroid lobe
Case Presentation

- Scheduled for same day surgery on 12/9/09
- Taken to OR for total parathyroidectomy with left forearm autoimplantation
- Incision made along skin fold
- Bilateral recurrent laryngeal nerves identified and preserved
- All 4 parathyroids identified and removed
- 1 gland autoimplanted into left forearm
- Skin closed over penrose drains
Case Presentation

- Post-op course:
  - POD#1: JP drains removed, profuse bronchial secretions making it difficult to assess the voice
  - POD#6: ENT consult for hoarseness
    - FOE: TVC in the cadaveric position immobile with effort, glottic opening patent -> consistent with bilateral vocal cord paralysis
  - POD#7: Speech & Swallow evaluation – patient not at aspiration risk
Case Presentation

- POD#8 and on: Calcium control, HD, maintenance of renal issues
- 1/28/2010: discharged home on po calcium supplementation with much improved voice (Ca levels 8.8)
- Clinic 2/4/10: Doing well, hoarseness resolved
Case Presentation

Parathyroid Hormone - Intact

pg/ml

[Graph showing the concentration of parathyroid hormone over time with different labels for normal, high, and low values.]
Parathyroid Disease
History

- Discovered by Sir Richard Owen in 1852
- Curator of Natural History Museum
- Dissecting rhinoceros who had died at London Zoo

- 1880: Ivar Sandström, a Swedish medical student, discovered the glands in man
- 1925: Felix Mandl from Vienna credited for first parathyroidectomy for 1° hyperparathyroidism

History

- 1934: Albright discovered the relationship between ESRD and hyperparathyroidism.
- 1960: Stanbury et al. reported on the first elective subtotal parathyroidectomy for 2° hyperparathyroidism.
- 1969: Alveryd reported autografting parathyroid tissue technique.
- 1975: Wells pioneered the above technique.

Physiology

PARATHYROID GLANDS
Sense low serum calcium and increase PTH secretion

Vitamin D

LIVER

Calcidiol (25-OH-D)

KIDNEY

Calcitriol (1,25 (OH)₂D)

Increases calcitriol formation
Decreases excretion of calcium

SMALL INTESTINE

Calcitriol (1,25 (OH)₂D)

Increased absorption of dietary calcium

BONE
Releases calcium and phosphorus

Increased serum calcium
Anatomy

- **Superior glands**
  - 4th branchial pouch
  - Middle third of thyroid
  - At cricothyroid junction
  - Near where RLN passes beneath inferior pharyngeal constrictor to enter larynx

- **Inferior glands**
  - 3rd branchial pouch
  - Near lower lobe of thyroid below thyrothymic ligament
  - Below inferior thyroid artery
  - Anterior to RLN
Anatomy

- Blood supply:
  - Inferior thyroid artery
  - Branch of thyrocervical trunk
Hyperparathyroidism

- **Primary**
  - 80-90% solitary adenoma
  - 10-15% hyperplasia
  - 3-5% double adenoma
  - <2% cancer
- **Secondary**
  - Hyperplasia
- **Tertiary**
  - Autonomous hyperplasia

Symptoms

- Fatigue
- Exhaustion
- Weakness
- Polydypsia
- Polyuria
- Nocturia
- Bone pain
- Constipation
- Depression
- Memory loss
- Joint pain
- Loss of appetite
- Nausea
- Heartburn
- Pruritis
Conditions

- Nephrolithiasis
- Nephrocalcinosis
- Hematuria
- Bone fractures
- Gout
- Pseudogout
- Joint swelling
- Osteopenia
- Osteitis Fibrosa Cystica
- Weight loss
- Duodenal ulcer
- Gastric ulcer
- Pancreatitis
- Hypertension
Diagnosis

- Low to normal calcium level
- Elevated PTH
- Elevated or normal urinary calcium
- Normal to high serum PO4
- Elevated serum Alk Phos
- Bone density abnormalities
Preoperative Localization

- 99m-technetium sestamibi scan
- Ultrasound
- CT scan
- MRI
- Angiography
Sestamibi Scanning

- Hindle et al: preoperative sestamibi in 11 patients referred for first parathyroid surgery
  - 41/45 glands found on scan
  - 91% sensitivity
  - No false positives

- Neumann et al: sestamibi/SPECT in 19 patients with RF and secondary HPT
  - 57/74 hyperplastic glands found at surgery
  - 77% sensitivity


Types of Hyperplasia

- Diffuse
- Nodular
  - Arises from former
  - Usually resistant to medical therapy

Treatment

- Easier to prevent secondary HPT than to treat it
- Vitamin D replacement, phosphorus binders, calcium replacement
- Transplantation


NIH Consensus
Guidelines for Surgery (1990):
Primary Hyperparathyroidism

- Age >50
- Serum calcium >12
- Hypercalcuria >400mg/g creatinine
- Severe manifestations (stones, groans, bones)
- Decrease in bone density <2SD/age
- Progressive renal insufficiency
Indications

- Surgical treatment was traditionally recommended for patients with:
  - bone pain
  - pruritus
  - calcium-phosphate product >70
  - calcium >11 mg/dL with markedly elevated PTH
  - calciphylaxis
  - progressive renal osteodystrophy
  - soft tissue calcification and tumoral calcinosis, despite maximal medical therapy
Parathyroidectomy in ESRD

- Subtotal parathyroidectomy vs total parathyroidectomy with autotransplantation
- Data lacking whether chronic PTH elevations in asymptomatic patients warrant surgical intervention
- Surgery often performed for refractory disease (PTH > 800 pg/ml)

Surgery

- Bilateral neck exploration
  - Identification of all parathyroid glands

- Thymectomy may be warranted in up to 15% of patients
  - Parathyroids may be situated in upper thymus or perithymic fat

Surgery

- Neck extended
- Exploration via 3-4cm incision just caudal to cricoid cartilage
- Strap muscles separated in midline
- Dissection maintained lateral to thyroid for easier identification and to preserve blood supply

Surgery

- If the surgeon identifies 3 glands and cannot identify the 4th gland:
  - Explore retropharyngeal and esophageal spaces
  - Trace RLN into chest
  - Open carotid sheath
  - Thymectomy
  - Consider ipsilateral thyroid lobectomy
  - DO NOT PERFORM MEDIAN STERNOTOMY
Complications

- >95% success with minimal morbidity and mortality with experienced surgeon
- Transient and permanent vocal cord palsy
- Hypoparathyroidism
  - Both permanent if >6 months
  - Risk <1%
- Recurrent hyperparathyroidism

Recurrent Laryngeal Nerve Palsy

- Can be temporary (<6 months) or permanent
- Nerves must be identified in dissection
- Temporary palsies generally attributed to traction injury, injury to extralaryngeal branches

Survival

- Data from United States Renal Database System
- Observational matched cohort study comparing survival of 4,558 HD patients who underwent a first parathyroidectomy with an equal number of control patients who did not undergo surgery
- Short term mortality lower among operative group
  - 30 day postoperative mortality 3%
- Long term survival superior for operative group (median survival 53 months) vs controls (47 months)

Conclusion

- Secondary hyperparathyroidism is a common disease process, reflecting the prevalence of end-stage renal disease.
- Physician judgment plays a significant role regarding the indications and timing of surgery.
- Though the operation can be technically challenging, results are generally quite good, particularly when the patient is well-selected and thoroughly evaluated.
References

- Clinical Practice Guidelines for Bone Metabolism and Disease in Chronic Kidney Disease. Am J Kidney Dis 2003; 42(Suppl 3): S1-M