Parathyroid Surgery

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1

Philosophical Perspective: Focused vs. Bilateral Approach

- Is it better to err by omission or commission
  - Undertreatment vs. overtreatment
- Primum non nocere (First, do no harm…)
  - But don't fail to cure the patient
- Bayes theorem applied to parathyroidectomy
  - The likelihood of a patient having multi-gland disease can be predicted preoperatively

2

Pathogenesis: Sporadic Primary Hyperparathyroidism

- Sporadic Primary:
  - Single gland ~85% and multi-gland ~15%
- Sporadic (no risk factors):
  - Single adenoma ~90% from somatic mutation
  - Multi-gland disease ~10% (mostly hyperplasia)
- Sporadic / acquired (risk factors)
  - Radiation increases rate of metachronous adenomas
  - Lithium increases rate of MGD ~25-50%

Wilhelm, S et al; AAES Parathyroidectomy Guidelines. *JAMA Surg* 2016

3

Impact of Imaging in Sporadic Primary

- Two concordant localization imaging studies for single adenoma
  - ~95% likely single adenoma
- One localizing and other non-localizing
  - ~90% likely single adenoma
  - Possibility of asymmetric hyperplasia with CT or US localizing small gland w negative Sestamibi

4

Impact of Imaging in Sporadic Primary

- Two discordant studies localizing to opposite sides
  - ~70% single adenoma
  - – Possibility of a false positive?
    - Sestamibi localizing to thyroid nodule
    - CT/US localizing to lymph node or thyroid nodule
- Two non-localizing studies
  - ~50% single adenoma

Philippon, M *et al*: *Eur J Endocrinol* 2014

5

Impact of Biochemistry in Sporadic Primary

- Suspected 'normohormonal' primary
  - – Exclude other causes of hypercalcemia first
    - Consider trial Cinacalcet to confirm primary
  - ~80-90% single adenoma
- Suspected 'normocalcemic' primary
  - – Exclude all secondary causes first
    - Consider Ca/HCTZ challenge to confirm primary
  - ~50% single adenoma

6

When to Plan Bilateral Exploration for Sporadic Primary Hyperparathyroidism

- Non-localized (negative imaging ≥ 2)
- Discordant imaging (opposite sides)
- Concomitant contralateral thyroidectomy
- Normo-calcemic variant?
- Acquired (prior radiation or Lithium)?
- Lack of IOPTH availability?

7

Conversion to Bilateral Exploration

- Insufficient PTH drop after removal of abnormal gland
- Identification of second abnormal gland
- Identification of two normal ipsilateral glands and no abnormal gland
- Recognition of false positive imaging (ie lymph node or thyroid nodule)

8

Pathogenesis: Hereditary

- Hereditary Primary ~85% multi-gland
  - MEN1 (Men1 tumor suppressor mutation)
    - Classically hyperplasia ('nodular')
    - High prevalence of pHPT ~95%
    - High recurrence and failure rate of surgery
  - MEN2a (Ret proto-oncogene 634 and 883)
    - Typically adenomas, may be multi/metachronous
    - Relatively lower prevalence of pHPT ~15-30%
  - HPT JT Syndrome (CDC73 suppressor mutation)
    - Typically multiple adenomas
    - Increased risk of parathyroid carcinoma

9

Pathogenesis: Hereditary

- Other rare causes
  - MEN4
    - 10% of clinically apparent MEN1
      - CDKN tumor suppressor mutation
      - Similar high rate of multi-gland disease
  - Familial Isolated Hyperparathyroidism
    - Need to exclude MEN1(4), FHH, HPT-JT
      - No mutations in MEN1, CDKN, CASR, CDC73
    - ~20% have GCM2 transcription activating mutation
      - Similar high rate of multi-gland disease

10

Pathogenesis: Secondary and Tertiary Renal HyperPTH

- Hyperphosphatemia
- Hypovitamin D (1,25)
- Hypocalcemia
- Typically results in nodular hyperplasia which may be asymmetric

11

Routine Bilateral Parathyroid Exploration

- Hereditary Primary, Secondary and Tertiary
  - Exception may be localized revision surgery
- Extent of resection
  - Total parathyroidectomy with auto-transplant
    - Highest rate of at least transient hypocalcemia
  - Subtotal parathyroidectomy (3 or 3.5 gland)
    - Similar success rate as total w transplant
  - Less than subtotal (<3 gland)
    - Highest rates of persistent/recurrent disease

12

Advantages to Focused Parathyroidectomy

- Lower risk
  - RLN unilateral vs. bilateral risk
  - Hypoparathyroidism doesn't occur unilateral
- "Minimally invasive"
  - Better cosmesis, smaller scar
  - Less pain
- Shorter duration of surgery / anesthesia

13

Requirements for Focused Parathyroidectomy

- Preoperative expectation of single gland disease (play the odds)
- Preoperative imaging suggesting single gland disease (where to start)
- Stopping criteria
  - Intraoperative PTH to r/o persistent hyperPTH
  - Ipsilateral gland check to r/o hyperplasia
  - Intraoperative pathology to confirm abnormal gland
  - Gamma probe to confirm abnormal gland

14

Intraoperative PTH

- Miami criteria: ≥ 50% drop from baseline
- May increase cure rates from 96 to 99%
- Get a second baseline at excision
  - Reduces false negative from manipulation spike
  - Possible earlier termination if already down
- Requiring post-removal levels fall into reference/normal range or <40
  - May reduce false positive but increase false neg

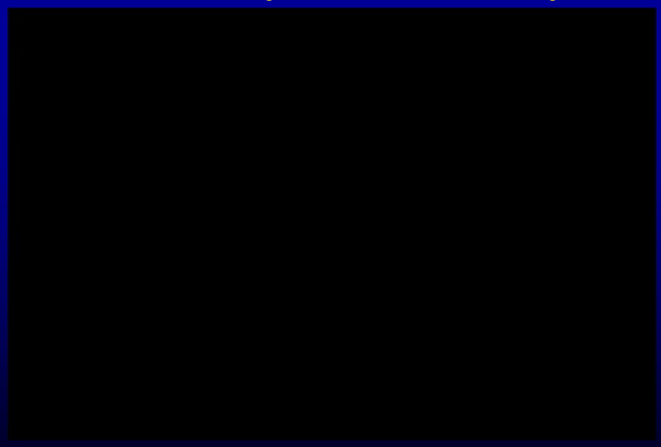
15

Best Candidates for Focused Parathyroidectomy

- Sporadic primary hyperparathyroidism with hypercalcemia
- No risk factors for MGD (fhx, radiation, Li)
- No need for contra/bilateral thyroidectomy
- Preoperative localization to a single gland (1 or 2 modalities)
- Availability of intraoperative PTH

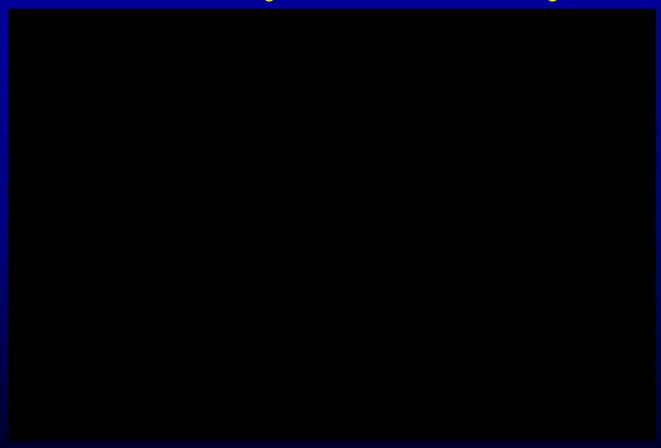
16

Focused Left Superior Parathyroidectomy

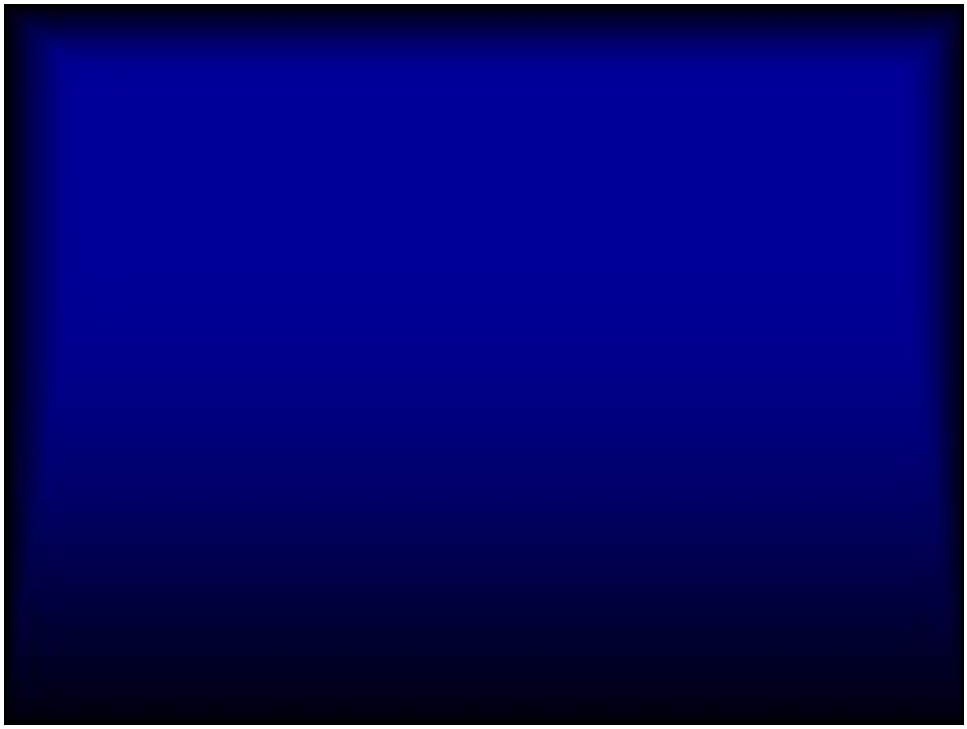


17

Focused Right Inferior Parathyroidectomy



18



19

Pathogenesis: Hereditary, Secondary/Tertiary

- Hereditary syndromes, germline mutations
  - MEN1, MEN2a (634,883), HPT-JT (CDC73)
  - Resultant multi-gland disease
- Secondary / tertiary
  - Hyperphosphatemia
  - Hypo-vitamin D
  - Hypocalcemia
  - Resultant multi-gland disease

20

Potential Candidates for Focused Parathyroidectomy

- Sporadic Normocalcemic Primary HyperPTH
- Sporadic Normohormonal Primary HyperCa
- Sporadic / Acquired Primary HyperPTH
- Non-syndromic Hereditary
- Recurrent Hereditary, Secondary or Tertiary after prior subtotal parathyroidectomy
- Recurrent Sporadic after failed exploration or ipsilateral recurrence

21

Focused Parathyroidectomy Summary

- Patient selection
  - Sporadic primary without risk factors for multi-gland disease
- Preoperative imaging c/w single adenoma
- Intraoperative adjuncts
  - Intraoperative PTH to exclude persistent hyperPTH
  - Ipsilateral gland check to exclude hyperplasia
  - Intraoperative pathology evaluation
    - Larger gland >500mg, rim of normal, lack of fat

22