Atypical Parathyroid Adenoma with Findings of Severe Hypercalcemia and Hyperparathyroidism

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None
Objectives

1) Evaluation of patients with thyroid and parathyroid masses
2) Evaluation of patients with hypercalcemia
3) Evaluation of patients with hyperparathyroidism
Reminder!

It is easy to criticize in hindsight.
The best way to look at an error is through root cause analysis. We are not doing that today as the point of this lecture is not to focus on morbidity and mortality but to use this case as a learning point for assessing a patient with elevated calcium and parathyroid levels.
We are here to learn!
Case presentation

67 yo Asian F presented to ENT clinic for anorexia, fatigue, weakness, rib pain, constipation, malaise, a documented weight loss of 30 lbs over 7 months, and a large left neck mass.

Prior history from PCP:
12/08/14- serum Calcium elevated 10.6 (8.6-10.2). TSH normal
12/09/15- Routine health maintenance. Osteoporosis noted. Ca 11.6 (8.7-10.3)
5/02/16- US for Lt thyroid mass: right lobe 1.6 cm and left lobe 3.3 cm. Left lobe had a 3 cm dominate, solid mass
Case presentation (cont)

PCP timeline (cont)

5/16/16- US guided FNA: lymphocytic thyroiditis
4/27/16- Swollen glands, no mention in PE, given Biaxin 500 mg BIDx 7 days
7/27/16- Constipation, given Linzess and colonoscopy ordered
8/31/16- normal colonoscopy
12/16/16- Documented weightloss of 22 lbs in 5 months. No mention of thyroid mass in PE but mention in assessment. Ca 16.0 (8.5-10.1)
Referral to ENT
Case presentation (cont)

12/19/16 Repeat calcium 15.0 (8.5-10.1)
12/20/16 Sees ENT. Visibly enlarged left thyroid that is mobile anterior-posteriorly but not superior-inferiorly. Non-tender. Nasolaryngeal endoscopy performed which was normal. Repeat labs ordered and a left thyroid lobectomy recommended. FNA repeated as well.
TSH was normal at 0.426 mIU/L. Free T4 normal at 1.02 ng/dL
Calcium 11.6 mg/dL. Repeat calcium 3 days later 15.0 mg/dL
Alkaline phosphatase 223 U/L. Repeat 3 days later 233 U/L
Hypercalcemia

Multiple causes

- Primary hyperparathyroidism
- Inherited: MEN, Familial isolated hyperparathyroidism, Hyperparathyroidism-jaw tumor syndrome
- Familial hypocalciuric hypercalcemia
- Renal failure
- Malignancy
- Vitamin D intoxication
- Chronic granulomatous disorders
- Medications
- Pituitary or adrenal cause
- Immobilization
- Nutrition
- Milk-alkali syndrome
Work-up algorithm for hypercalcemia

**Evaluation of Patients with Hypercalcemia**

- **Hypercalcemia**
  - Key historical considerations:
    - Confirm if $\text{Ca}^{2+}$ chronic
    - Clues from history and physical findings
  - **Acute (or unknown) duration**
    - PTH high:
      - $1^{st}$ Hyperparathyroidism
      - Consider malignancy
      - PTHrP assay
      - Clinical evaluation
  - PTH low:
    - Screen negative
    - **Chronic duration (months)**
      - PTH low:
        - Other causes:
          - Granulomatous disease
          - FHH
          - Milk-alkali syndrome
          - Medications (lithium, thiazides)
          - Immobilization
          - Vit D or Vit A intoxication
          - Adrenal insufficiency
          - Hyperthyroidism
      - PTH high:
        - Hyperparathyroidism: $1^{st}, 2^{nd}, 3^{rd}$
        - Consider MEN syndromes

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Back to our case

Repeat Calcium 16.0 mg/dL

iPTH 1311 pg/mL

Creatinine normal

According to algorithm, DDx: primary hyperparathyroidism, MEN syndromes
Primary Hyperparathyroidism

• “Stones, bones, groans with psychiatric overtones”

• Symptoms not necessarily due to hypercalcemia
  • Anorexia
  • Nausea
  • Constipation
  • Polydipsia
  • Polyuria

• Nephrolithiasis most common complication of primary hyperparathyroidism (15-20% of newly diagnosed patients)

• Patients with primary hyperparathyroidism and vitamin D deficiency have more significant disease with larger adenomas, increased PTH concentrations, increased bone turnover, and more frequent fractures

Diagnosis
- Serum calcium
- Serum PTH

Decision for or against surgery
- Serum 25(OH)D
- Bone densitometry (DXA)
- Urinary calcium excretion and creatinine clearance

Surgical

Preoperative localization (if indicated)
- Parathyroid ultrasound
- Sestamibi imaging

Postoperative follow-up
- Serum calcium and PTH levels at 2 weeks, 6 months and 12 months
- DXA at 12 months

Medical

- Hydration and mobilization
- Moderate calcium intake
- Bisphosphonate treatment in case of documented osteoporosis

Follow-up in patients who do not undergo surgery
- Serum calcium every 6 months
- Urinary calcium excretion and creatinine clearance every 6 months
- DXA every 12 months
Primary Hyperparathyroidism DDx

Parathyroid adenoma
Parathyroid carcinoma
Atypical parathyroid adenoma
Familial hypocalciuric hypercalcemia
Drugs: thiazides and lithium
Differences between benign adenoma and parathyroid carcinoma

Benign adenoma
- Modest Ca elevation
  - <15
- Non-palpable neck mass
- PTH <3x upper limit of normal

Carcinoma
- Ca >15
- PTH >3x upper limit of normal
- Palpable neck mass
- Symptoms more profound
What now?

FNA
- Can use to determine origin of the mass- in our sample case, the mass was found to be parathyroid tissue with positive test for parathyroid hormone and negative tests for TTF1, calcitonin, and thyroglobulin
- Pathology could not determine if mass was malignant or benign in this case

MRI- r/o MEN
- Patient had 2 x 4 mm area of hypoenhancement along right pituitary which was read as volume averaging or cystic microadenoma
- Abdominal MRI negative for any pathology
Treatment options

Medical

– Asymptomatic
– Non-surgical candidate
  • Avoid thiazides or lithium, eat low calcium diet, maintain exercise, stay hydrated, moderate calcium and vitamin D intake
  • Medications can include cinacalcet or bisphosphonates
  • Estrogen-progestin therapy- raloxifene
  • Denosumab- investigational
Treatment options

Surgery

- Who is a surgical candidate when asymptomatic?
  - Serum Ca 1.0 mg/dL or more above upper limit of normal
  - Skeletal indications
    - Bone density at the hip, lumbar spine, and/or distal radius T-score <-2.5
  - Renal indications
  - Age <50 years old
Case surgery

Pre-op PTH >2000 pg/mL
Mass was mildly adherent to SCM and firm attachment to the left thyroid lobe
Mass was 7.2 x 4.0 x 3.5 cm and was 42.2 gms
No metastasis to lymph nodes
15 minutes after removal, PTH was 213 pg/mL
Parathyroid hormone level remained >100 pg/mL months after surgery
Histology

Hypercellular tissue with mild pleomorphism and solid to glandular architecture. Thick acellular fibrous bands throughout the parathyroid tissue and abundant hemorrhage. No necrosis, lymphovascular invasion, or surrounding tissue invasion noted. Tissue positive for pnaacytokeratin. TTF-1 and chromogranin negative.
Gross specimen
Fibrous bands with hemorrhage and thick acellular fibrous bands
Solid pattern
Pseudofollicular pattern and thick fibrous capsule
What to make of this?

Labs had features of carcinoma
Presentation had features of carcinoma
Surgery had features of benign adenoma due to there being a thick fibrous capsule and relative non-adherence to surrounding tissue
Size consistent with carcinoma
Histology has a mixed picture but does not meet the pathologic diagnosis of carcinoma
Final diagnosis

Atypical parathyroid adenoma
Patient's PTH remained elevated and she desired medical management with endocrinology versus more surgery.
Patient lost to follow-up
References


