PARATHYROID GLAND

Anatomy and Embryology

.4 parathyroid glands situated posterior to the thyroid.

.Superior glands:

Found just superior to the intersection of the inferior thyroid artery and the recurrent laryngeal nerve.

Derived from the fourth pharyngeal pouch.

Occasionally found within the substance of the thyroid gland.

.Inferior glands

Derived from the third pharyngeal pouch.

Embryologic association with the thymus, the inferior glands are often found adjacent to or within the thymus.

Usually located near the inferior pole of the thyroid.

Physiology

.Parathyroid Hormone:

Primarily responsible for maintaining extracellular calcium concentrations.

Secretion is regulated directly by the plasma conc. of ionized calcium.

.Effects of parathyroid hormone

Increase the concentration of plasma calcium by-

- Increasing the release of calcium and phosphate from bone matrix.
- Increasing calcium reabsorption by the kidney.
- And increasing renal production of 1,25-dihydroxyvitamin D-3 (calcitriol), which increases intestinal absorption of calcium.

Also causes phosphaturia, thereby decreasing serum phosphate levels.

Primary Hyperparathyroidism

.Unregulated overproduction of parathyroid hormone (PTH) resulting in abnormal calcium homeostasis.

.Etiology:

Hyperplasia Or Adenoma

- 85% of cases- a single adenoma.
- 15% of cases- multiple glands are involved (ie, either multiple adenomas or hyperplasia)

Rarely- parathyroid carcinoma.

Primary Hyperparathyroidism

- Most cases- sporadic.
- Familial cases can occur either as part of-
  - Multiple endocrine neoplasia syndromes (MEN 1 or MEN 2a).
  - Hyperparathyroid-jaw tumor (HPT-JT) syndrome.
  - Familial isolated hyperparathyroidism (FIHPT).

Pathophysiology

- In primary hyperparathyroidism
  - Adenomas- the normal feedback on parathyroid hormone production by extracellular calcium seems to be lost.
  - In parathyroid hyperplasia- an increase in the cell numbers is probably the cause.
- The chronic excessive resorption of calcium from bone-
  - Result in osteopenia/ osteoporosis.

Pathophysiology….

- In severe cases-

  May result in Osteitis Fibrosa Cystica.

  - Subperiosteal resorption of the distal phalanges.
  - Tapering of the distal clavicles.
  - Salt-and-pepper appearance of the skull.
  - And brown tumors of the long bones.

  The chronically increased excretion of calcium in the urine-

  - Can predispose to the formation of renal stones.

Pathophysiology….

- Other symptoms due to the hypercalcemia itself-

  Muscle weakness, fatigue.

  Volume depletion, nausea and vomiting.

  And in severe cases- coma and death.

  Neuropsychiatric manifestations are particularly common and may include depression.

  Can increase gastric acid secretion-

  - may have a higher prevalence of peptic ulcer disease.

  Pancreatitis.

Symptoms

.The clinical syndrome of primary hyperparathyroidism:

"Bones, stones, abdominal groans, and psychic moans."

.Skeletal manifestations include-

Bone and joint pain, pseudogout, and chondrocalcinosis.

Osteitis fibrosa cystica.

.Renal manifestations include-

Polyuria, kidney stones, hypercalciuria and rarely nephrocalcinosis.

Symptoms....

.Gastrointestinal manifestations include-

Anorexia, nausea, vomiting.

Abdominal pain, constipation, peptic ulcer disease.

And acute pancreatitis.

.Neuromuscular and psychologic manifestations include-

Proximal myopathy, weakness and easy fatigability.

Depression, inability to concentrate, and memory problems.

.Cardiovascular manifestations include-

Hypertension, bradycardia, and left ventricular hypertrophy

Examination

- Physical examination findings- usually noncontributory.
- Examination may reveal- muscle weakness and depression.
- A palpable neck mass-
  - not usually expected with hyperparathyroidism
  - in rare cases, it may indicate parathyroid cancer.

Workup

Blood

- Total serum calcium and albumin levels or ionized calcium levels.
  - Hypercalcemia should be documented on more than one occasion before a diagnostic workup is undertaken.
- An elevated intact parathyroid hormone level with an elevated ionized serum calcium level-
  - Diagnostic of primary hyperparathyroidism.
- A 24-hour urine calcium measurement- is necessary to rule out FHH.
- Mild hyperchloremic acidosis, hypophosphatemia, and mild-to-moderate increase in urinary calcium excretion rate.

Imaging

- Imaging studies are used to guide the surgeon once surgical therapy has been decided.
- Nuclear medicine scanning with Radiolabeled Sestamibi-
  - A widely used technique.
  - Radionuclide concentrated in thyroid and parathyroid tissue-
    - Usually washes out of normal thyroid tissue in under an hour.
    - Persists in abnormal parathyroid tissue.
    - Therefore, on delayed images, an abnormal parathyroid is seen as a persistent focus of activity.

Imaging....

- Ultrasonography of the neck-
  - May be equivalent or superior to sestamibi scanning.
- CT scanning and MRI-
  - Now been largely replaced by sestamibi scanning and ultrasound.
- Dual-energy X-ray absorptiometry (DXA)-
  - A useful tool to demonstrate the skeletal involvement in primary hyperparathyroidism.

Treatment

Hypercalcemic Crisis

- Intravascular volume expansion with sodium chloride.
- Loop diuretics such as furosemide once the intravascular volume is restored.
- Drugs such as calcitonin and IV bisphosphonate have been used as a temporary measure prior to surgical treatment.

Medical Treatment

- Monitoring:

  Patients who do not meet the guidelines for surgical intervention can be monitored safely.

- Annual assessment:

  For overt signs and symptoms of primary hyperparathyroidism.

  Serum creatinine level

  And 3-site dual-energy x-ray absorptiometry (DXA) study.

- Serum calcium should be checked every 6 months.

Medical Treatment….

- Diet and lifestyle:

  Patients should maintain a moderate daily elemental calcium intake of 800-1000 mg and a vitamin D intake appropriate for their age and sex.

  Maintaining good hydration.

  Participation in regular exercise activity.

  And avoidance of certain medications (such as thiazides, diuretics, and lithium) are desirable.

Medical Treatment….

- Pharmacotherapy:

  Estrogen therapy.

  Selective estrogen receptor modulators-

  - such as raloxifene.

  Bisphosphonates-

  - Alendronate.

  Calcimimetic drugs-

  - such as cinacalcet.

Medical Treatment....

- Other treatments:

  Percutaneous alcohol injection and other percutaneous ablation techniques

  - Have been suggested as an alternative treatment in patients who cannot or will not undergo surgery.

  Percutaneous techniques have high complication rates in small numbers of patients

  - Their routine use cannot yet be supported.

Surgery

- Indications for surgery-

  1.0 mg/dL above the upper limit of the reference range for serum calcium.

  24-hour urinary calcium excretion greater than 400 mg.

  A 30% reduction in creatinine clearance.

  Bone mineral density T-score below -2.5 at any site.

  Age younger than 50 years.

Surgery....

- Standard operative approach:

  Complete neck exploration with identification of all parathyroid glands.

  OR

  Removal of all abnormal glands with autotransplantation.

  In the case of 4-gland hyperplasia-

  - 3.5-gland parathyroidectomy is performed.

  A nonabsorbable suture is left as a tag to identify the gland.

Secondry Hyperparathyroidism

Secondry Hyperparathyroidism

.Secondary hyperparathyroidism:

Overproduction of parathyroid hormone

Secondary to a chronic abnormal stimulus for its production.

.Typically, this is due to chronic renal failure.

.Another common cause is vitamin D deficiency.

Etiology

.In chronic kidney disease-

Overproduction of parathyroid hormone occurs in response to hyperphosphatemia, hypocalcemia.

And impaired 1,25-dihydroxyvitamin D production by the diseased kidneys.

.Hyperphosphatemia-

Directly stimulate parathyroid hormone synthesis and parathyroid hyperplasia.

And indirectly promotes secondary hyperparathyroidism by decreasing free calcium level.

Clinical Features

- Virtually all patients with renal failure have
  - Hyperparathyroidism to some degree
  - Clinical presentation is often that of renal failure.
- In secondary hyperparathyroidism due to vitamin D deficiency
  - Symptoms are mainly due to the vitamin deficiency
  - E.g.- osteomalacia with increased fracture risk, myopathy.
- In advanced cases- some patients may have bone pain.

Workup

- Serum level of parathyroid hormone, calcium, phosphorus, and 25-hydroxyvitamin D should be measured.
- Patients with secondary hyperparathyroidism usually have
  - A low-normal calcium and elevated parathyroid hormone.
- The phosphate level may vary based on the etiology-
  - High values in renal insufficiency
  - And low values in vitamin D deficiency.

Treatment

- Medical management is the mainstay of treatment for secondary hyperparathyroidism.

- Correcting vitamin D deficiency can be achieved using-
  - 50,000-IU capsule of vitamin D-2 once a week for 8 weeks
  - and repeating the course for another 8 weeks if needed to achieve vitamin D sufficiency.

Treatment

- Current nonsurgical treatment options for management of secondary hyperparathyroidism in chronic kidney disease:

  Dietary phosphate restriction .

  Phosphate binders can be used if hyperphosphatemia persists despite dietary phosphate restriction.
  - Calcium-based phosphate binders such as calcium carbonate or calcium acetate
  - Non-calcium-based phosphate binders such as sevelamer hydrochloride or lanthanum carbonate

  Calcium supplementation should be limited to less than 2 g/d.

  Vitamin D and its analogs.

  Treatment with calcimimetics such as cinacalcet.

Treatment

- Indications for surgery include-

  Bone pain or fracture

  Pruritus, calciphylaxis

  And extraskeletal nonvascular calcifications with elevated PTH levels despite appropriate medical therapy.

Tertiary Hyperparathyroidism

Tertiary Hyperparathyroidism

.Tertiary disease is characterized by-

Development of autonomous hypersecretion of parathyroid hormone causing hypercalcemia.

.Etiology is unknown.

. but may be due to monoclonal expansion of parathyroid cells (nodule formation within hyperplastic glands).

. A change may occur in the set point of the calcium-sensing mechanism to hypercalcemic levels.

. Four-gland involvement occurs in most patients.

PATHOPHYSIOLOGY

Observed most commonly in-

- Patients with chronic secondary hyperparathyroidism and often after renal transplantation.

Hypertrophied parathyroid glands fail to return to normal-

- Continue to over secrete parathyroid hormone, despite serum calcium levels that are within the reference range or even elevated.
- Hypertrophied glands become autonomic and cause hypercalcemia, even after withdrawal of calcium and calcitriol therapy.

This type of tertiary disease is particularly dangerous because the phosphate level is often elevated.

TREATMENT

- Total parathyroidectomy with autotransplantation

- Subtotal parathyroidectomy.