PARATHYROID GLAND

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OBJECTIVES

- Short introduction about anatomy, histology and physiology of PT glands
- Classify the diseases affect the PT gland according to PT gland function
- Show the gross and microscopical pathological features of different thyroid diseases

CASE

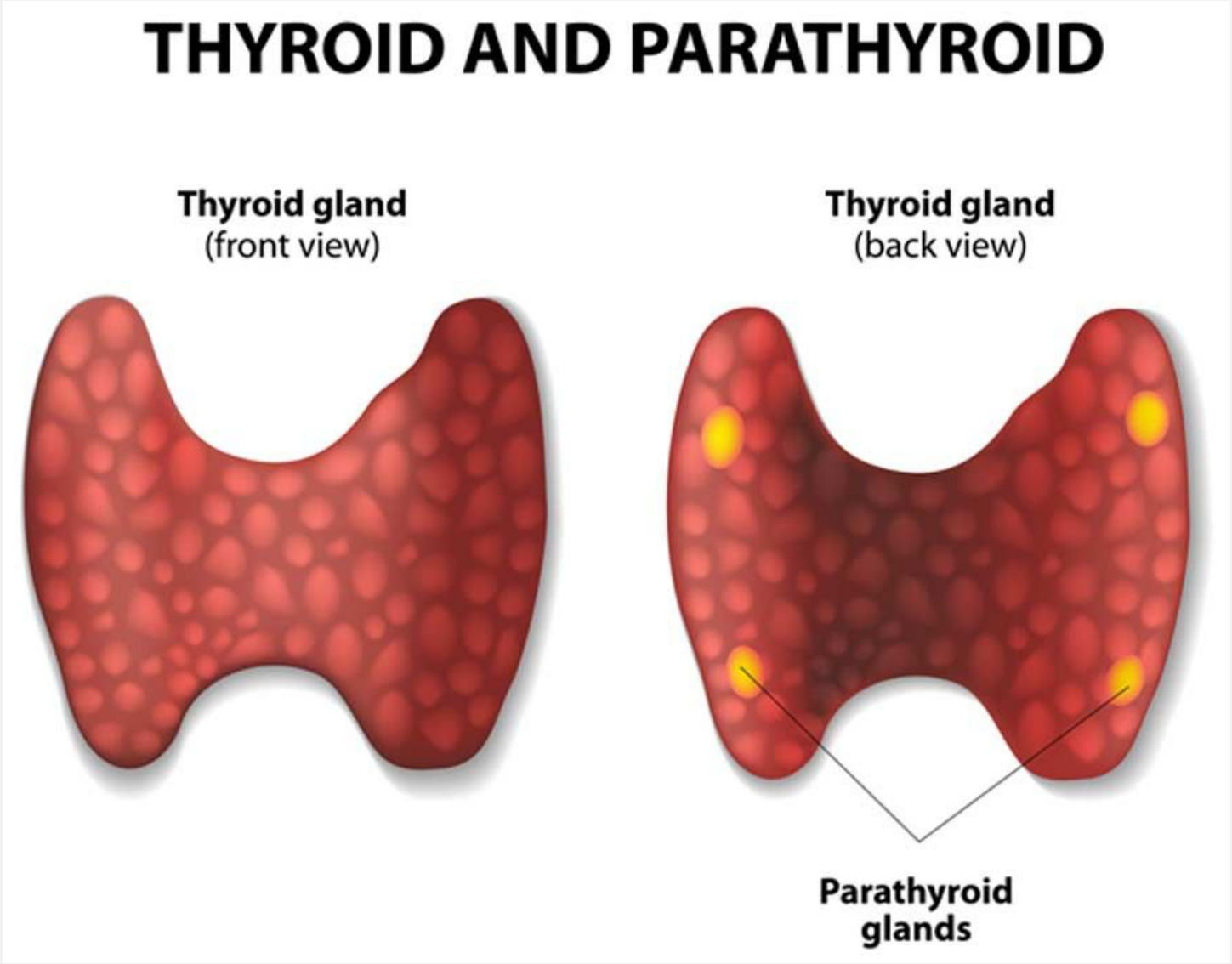
- A 52-year-old woman presents with nausea, fatigue, muscle weak- ness, and intermittent pain in her left flank. Laboratory examination reveals an increased serum calcium and a decreased serum phosphorus. The patient's plasma parathyroid hormone levels are increased, but para- thyroid hormone–related peptide levels are within normal limits. Urinary calcium is increased, and microhematuria is present. Which of the follow- ing is the most likely cause of this patient's signs and symptoms?

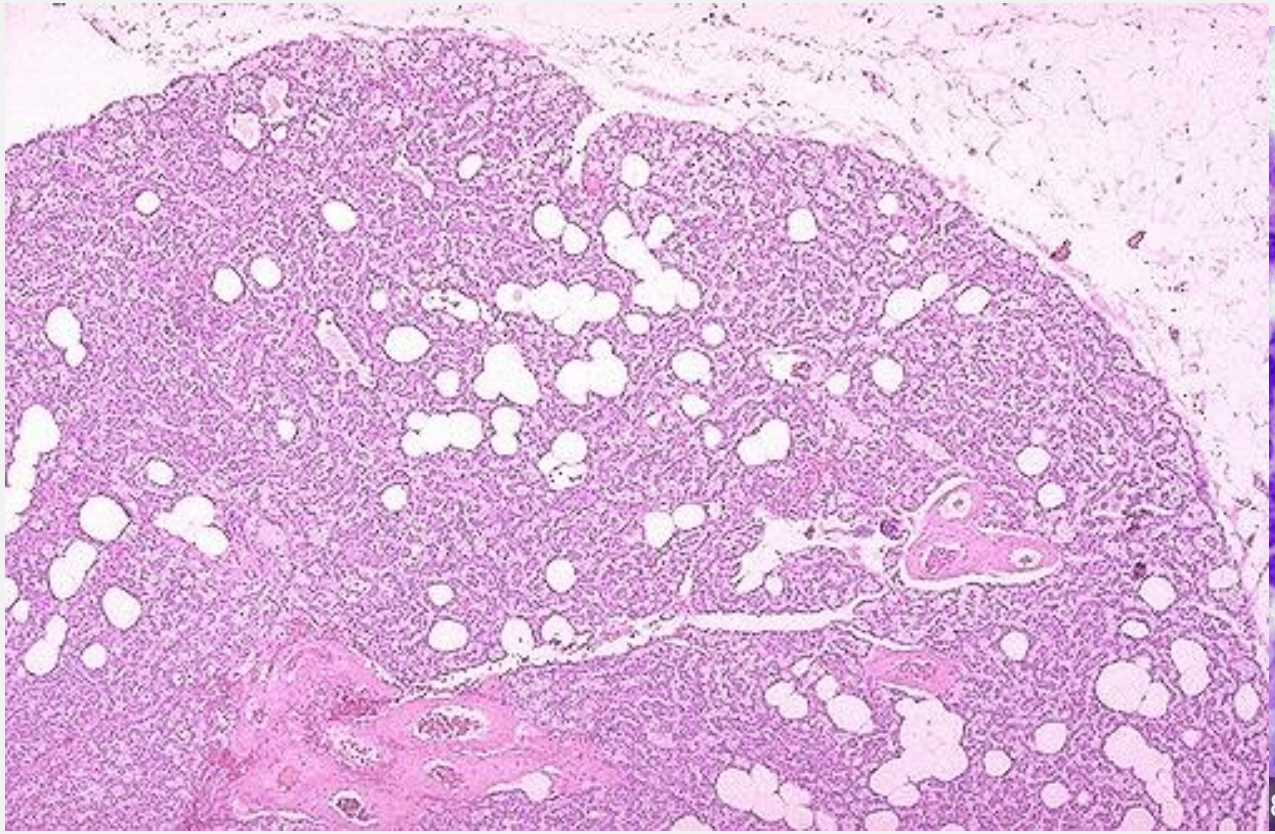
1. Primary hyperparathyroidism
2. Primary hypoparathyroidism
3. Pseudohypoparathyroidism
4. Secondary hyperparathyroidism
5. Secondary hypoparathyroidism

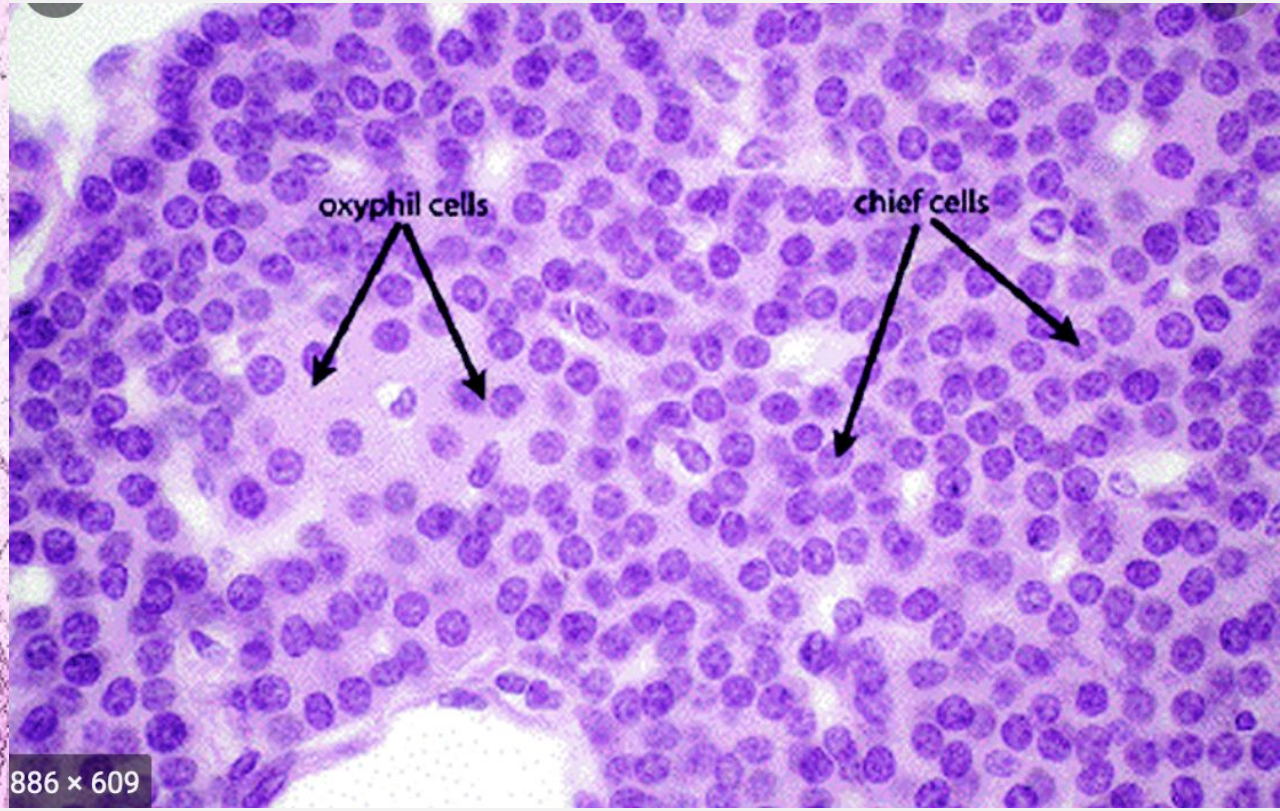
INTRODUCTION

- Normally, there are four oval, resilient parathyroid glands, each averaging 4 × 3 × 1.5 mm. In rare cases, more than four glands are present.
- The parathyroid glands are arranged in two pairs.
- The color varies from reddish brown to light tan to yellow, depending on fat content, which in turn depends on age, nutrition, and activity of the individual.
- The organ is made up of but one basic cell type, the **chief cell,** has a centrally located nucleus and a moderate amount of pale granular cytoplasm
- The **oxyphil cell** has a more abundant cytoplasm, which is deeply acidophilic.

PARATHYROID GLANDS







Here is a normal parathyroid gland for comparison. Adipose tissue cells are mixed with the parathyroid tissue. The amount of fat varies somewhat.

Composed primarily of chief cells and fat with thin fibrous capsule dividing gland into lobules. Chief cells are 6 - 8 microns, polygonal, central round nuclei, contain granules of parathyroid hormone (PTH).

Oxyphil cells Slightly larger than chief cell (12 microns), acidophilic cytoplasm due to mitochondria, No secretory granules

PHYSIOLOGY

Parathyroid activity is controlled by the level of free (ionized) circulating calcium; elevated calcium levels inhibit parathyroid hormone (PTH) synthesis and secretion, whereas hypocalcemia stimulates PTH production. PTH increases calcium levels by:

- Driving osteoclast differentiation (and thereby bone resorption)
- Increasing renal tubular reabsorption of calcium
- Increasing renal vitamin D conversion to the active 1,25-dihydroxylated form
- Increasing urinary phosphate excretion
- Augmenting gastrointestinal calcium absorption

HYPERPARATHYROIDISM

1- Primary Hyperparathyroidism

This is a common endocrine disorder and an important etiology of hypercalcemia; most cases are sporadic, occurring in patients older than 50 years with a 3:1 female predominance. Causes include:

- Adenoma (85% to 95%)
- Primary hyperplasia (5% to 10%)
- Parathyroid carcinoma (1%)

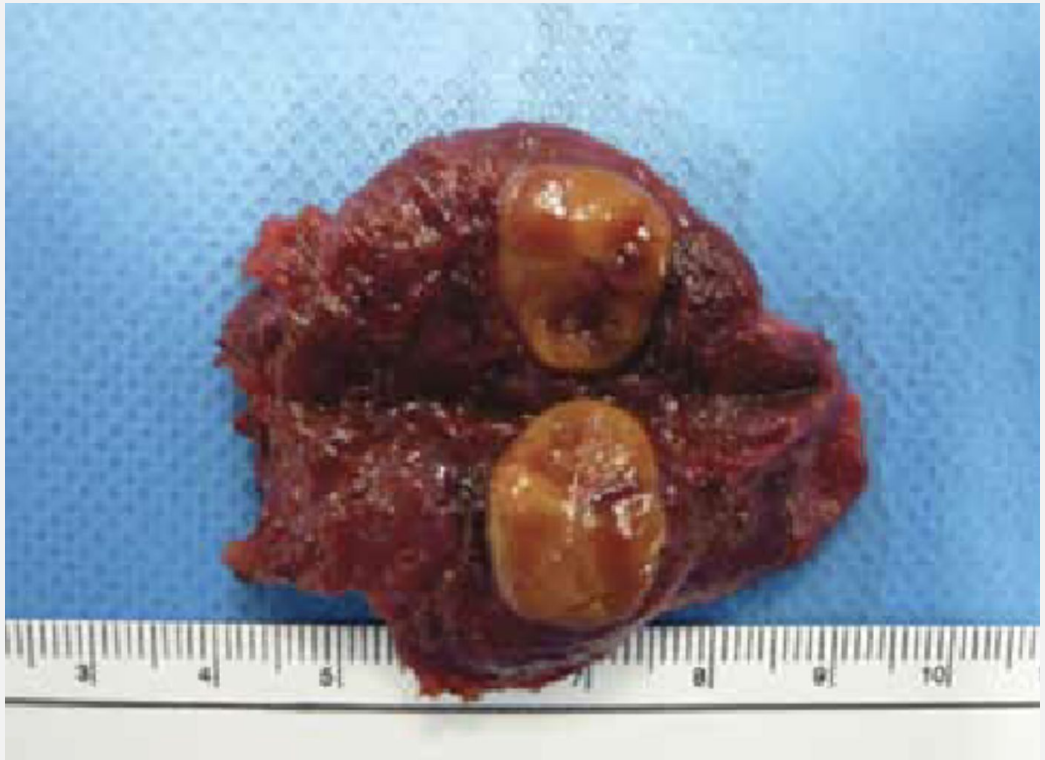
- Sporadic hyperparathyroidism: Most cases of sporadic parathyroid hyperplasia and the vast majority of parathyroid adenomas are monoclonal.
- Familial hyperparathyroidism:
  - MEN-1 syndrome: parathyroid adenomas and hyperplasia
  - MEN-2 syndrome

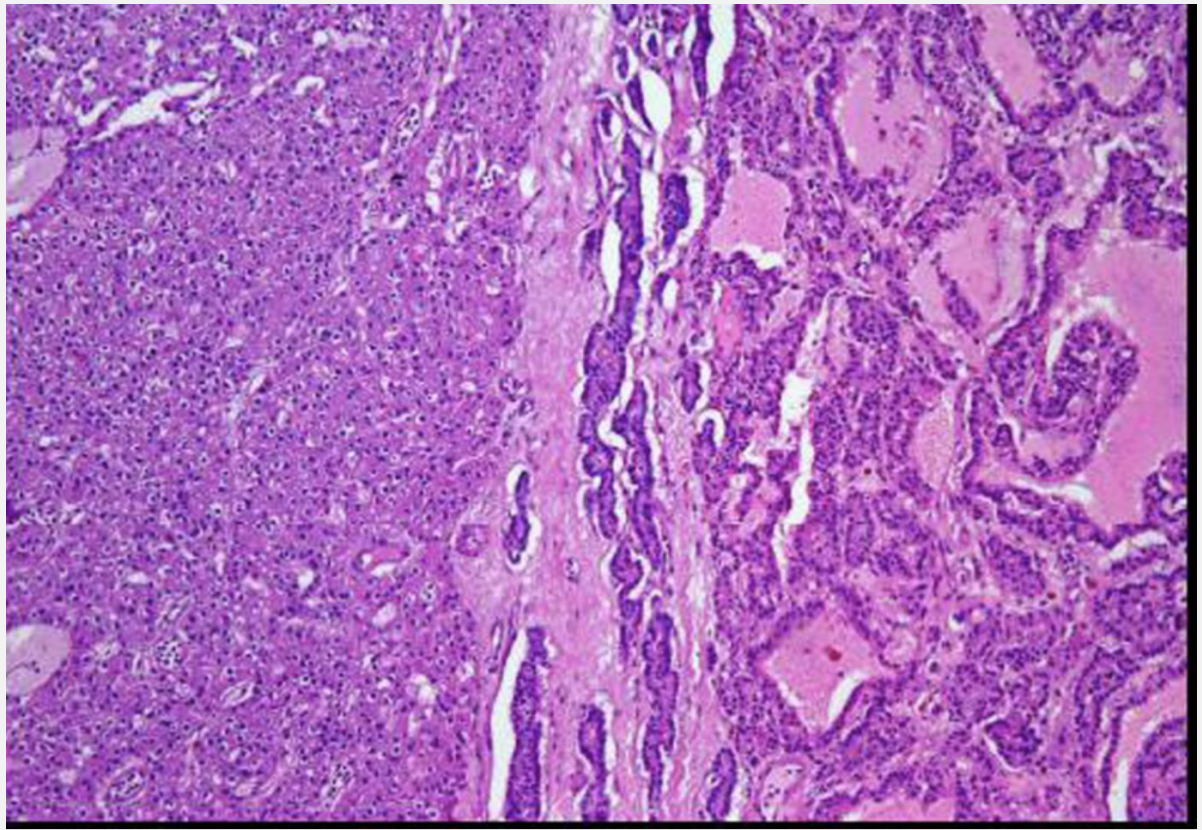
Morphologic changes involve the parathyroid glands as well as all other organs affected by hypercalcemia.

- Parathyroid adenomas:

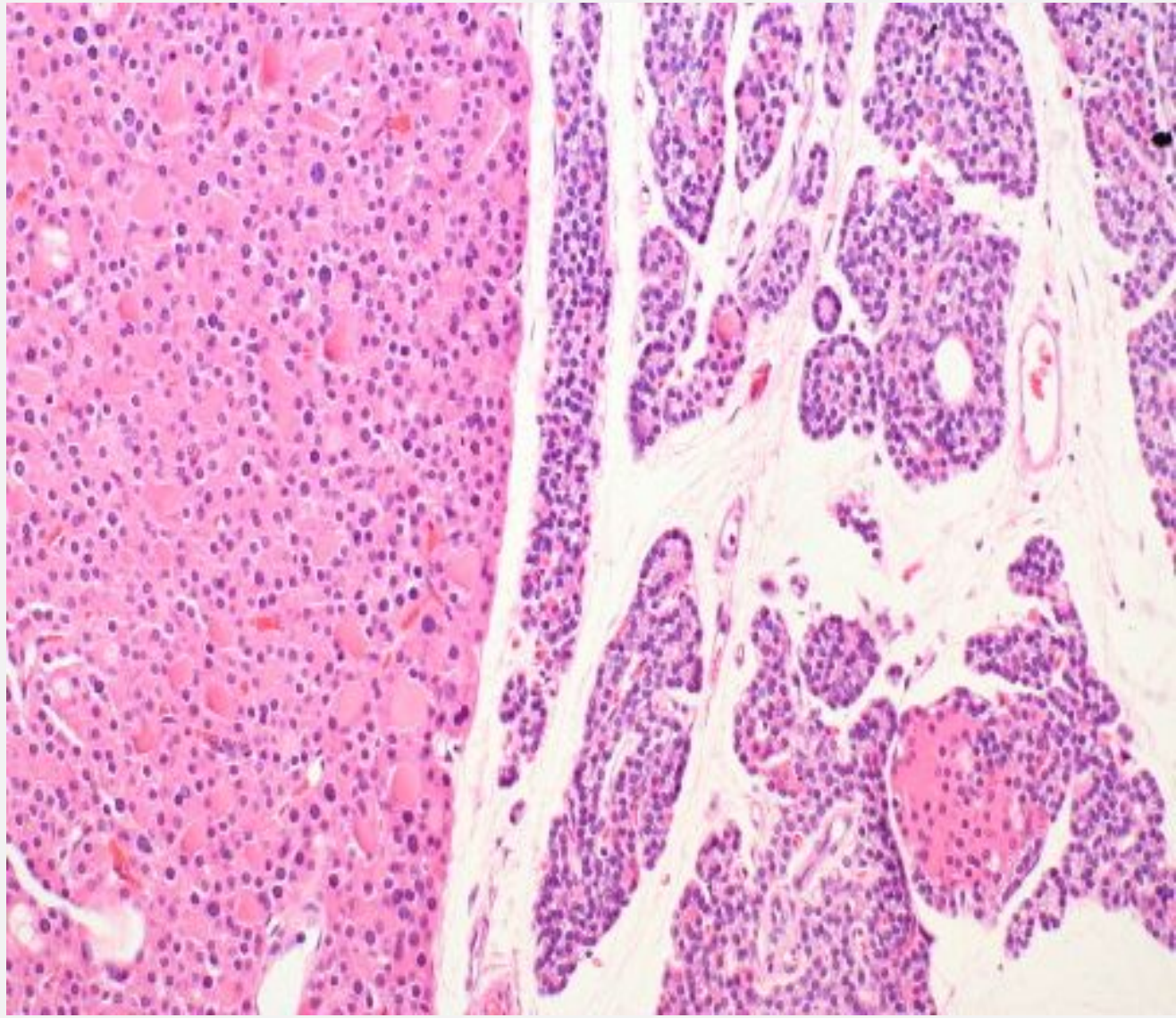
  - Grossly: Tumors are almost all solitary, well-circumscribed, tan- brown nodules that average 0.5 to 5 g; they are surrounded by a delicate capsule; remaining glands are usually normal size or smaller secondary to hypercalcemic feedback inhibition.

  - Microscopically: Lesions are composed predominantly of chief cells arrayed in uniform sheets, trabeculae, or follicles; foci of oxyphil cells may be present, and bizarre atypia is not uncommon. Adipose tissue is inconspicuous.



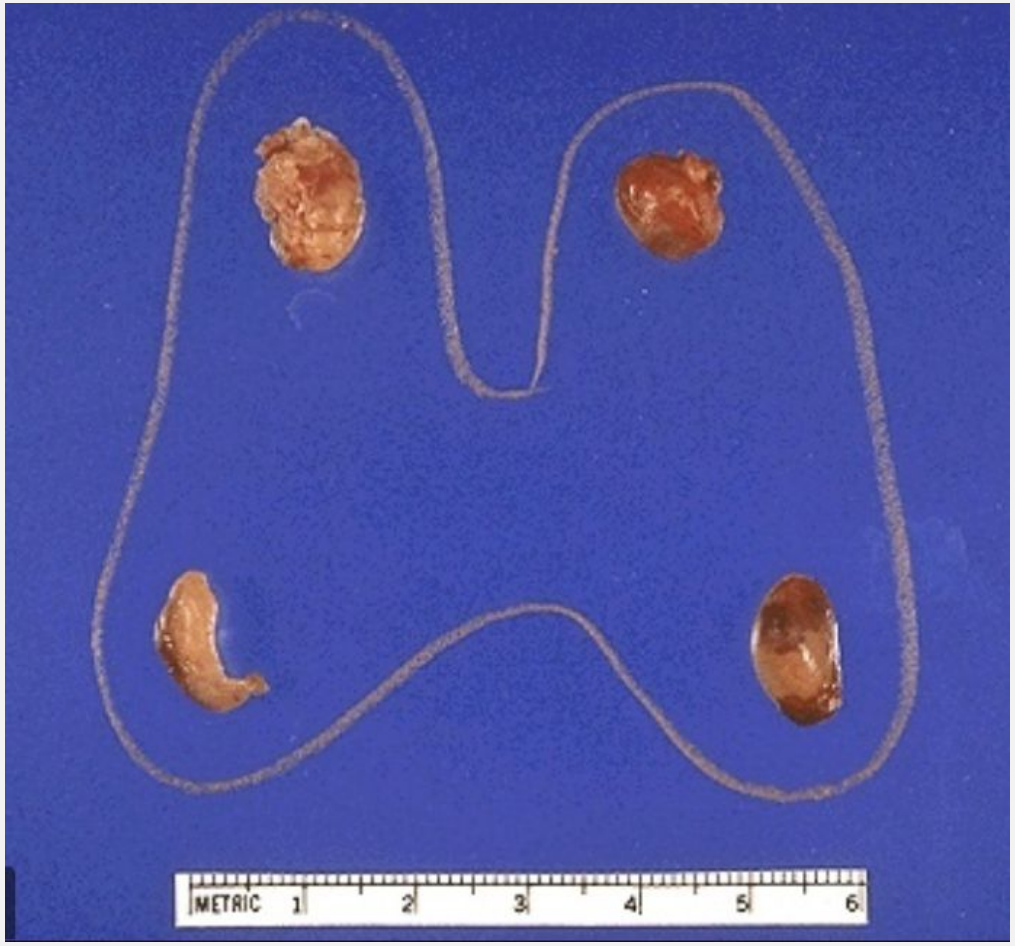


Adjacent to this **parathyroid adenoma** at the left is a **rim of normal parathyroid**. Patients with this form of primary hyperparathyroidism are usually diagnosed with routine chemistry panels in which a high serum calcium is noted, though some may present with renal stones, bone pain, headaches, gallstones, pancreatitis, or gastric ulcers. A parathormone (PTH) assay reveals a high normal to elevated level of PTH.

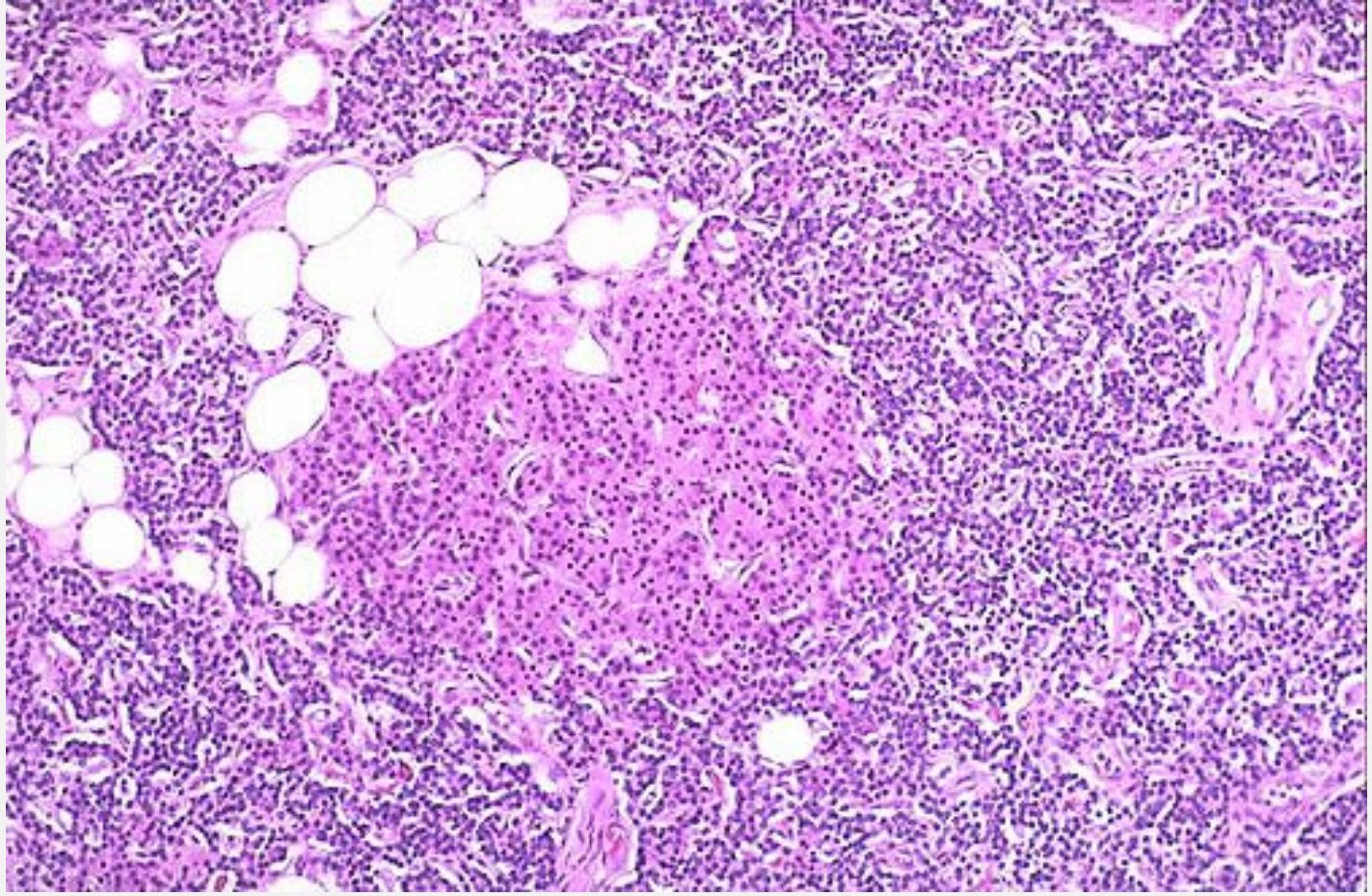


PRIMARY HYPERPLASIA

- Primary hyperplasia:
  - Grossly: All glands are typically involved although not necessarily uniformly; combined weights rarely exceed 1 g.
  - Microscopically: Chief cell hyperplasia typically involves glands in a diffuse or multinodular pattern. Adipose tissue is inconspicuous.



Parathyroid hyperplasia is shown here. Three and one-half glands have been removed (only half the gland at the lower left is present). Parathyroid hyperplasia is the second most common form of primary hyperparathyroidism, with parathyroid carcinoma the least common form.



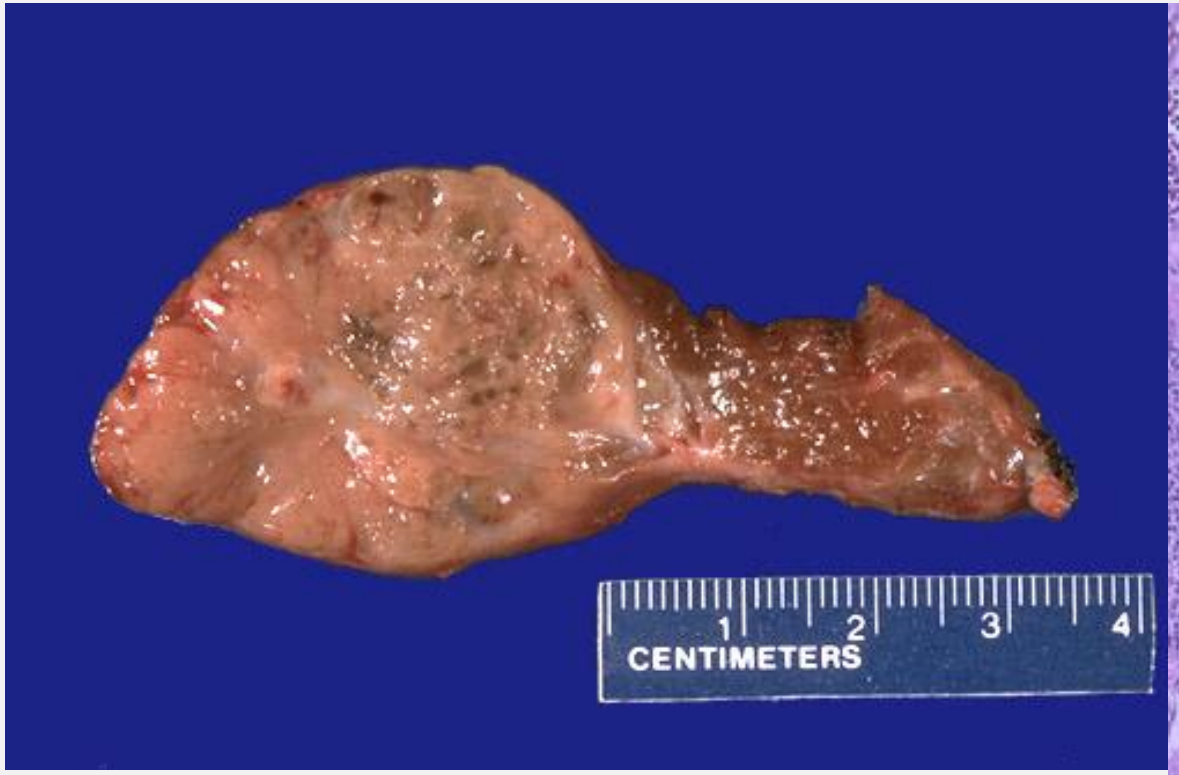
In parathyroid hyperplasia, there is little or no adipose tissue, but any or all cell types normally found in a parathyroid gland are present. Note the pink **oxyphil cells** in the nodule seen here.
This case shown here is "secondary hyperparathyroidism" with all parathyroid glands enlarged as a consequence of chronic renal failure with impaired phosphate excretion. The increased serum phosphate tends to drive serum calcium down, which in turn drives the parathyroids to secrete more parathormone.

Parathyroid carcinoma

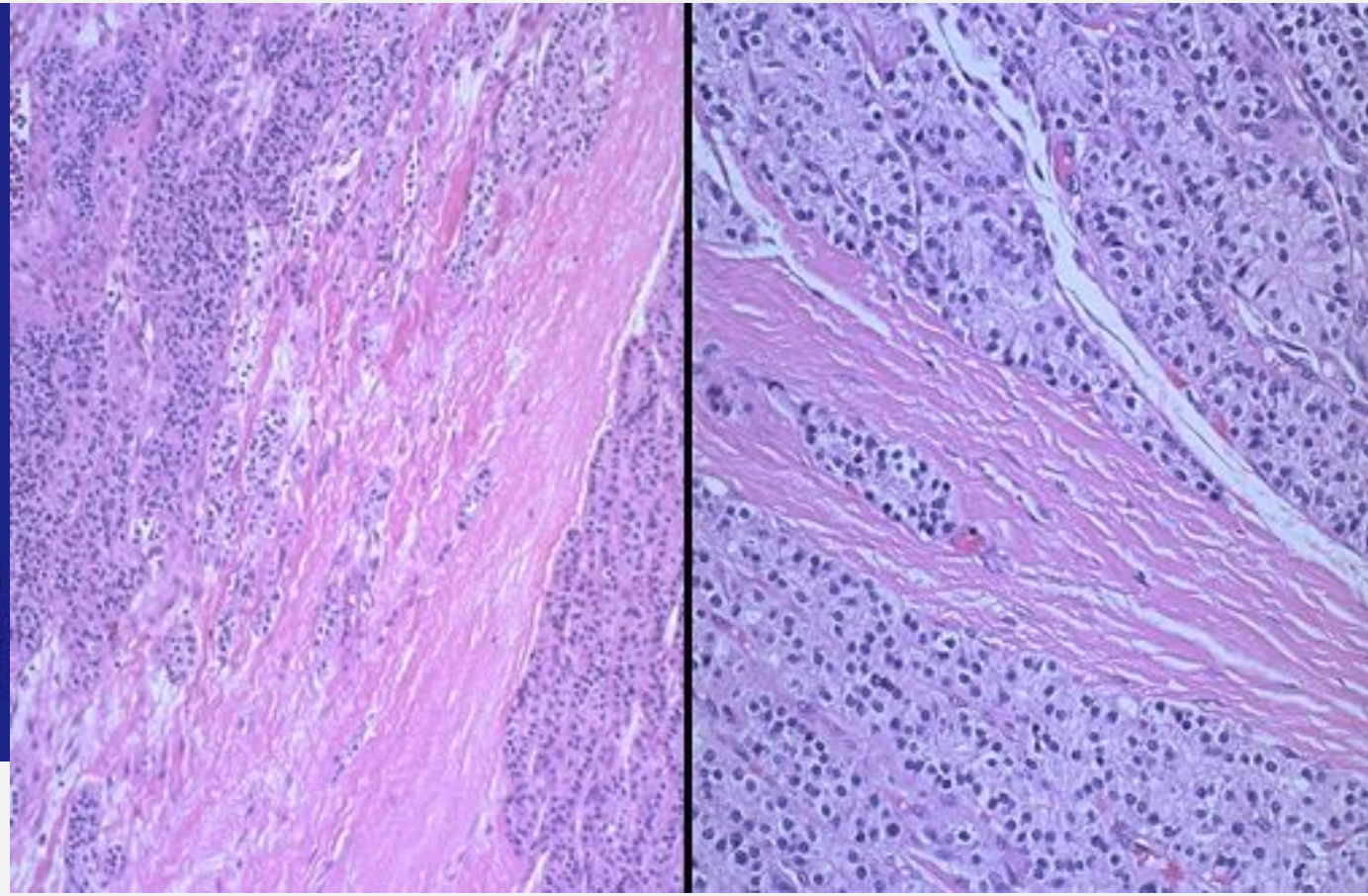
- Parathyroid carcinoma may be grossly and microscopically difficult to distinguish from an adenoma:

Grossly: Typically, one gland is enlarged by a gray-white, irregular mass sometimes exceeding 10 g.

Microscopically: Lesional cells are usually uniform and not too dissimilar from normal parathyroid cells; diagnosis of malignancy is based on the presence of local invasion and/or metastases.



This is the gross appearance of a parathyroid carcinoma. The serum calcium can be quite high. Note the large size and irregular cut surface. These carcinomas have a tendency to invade surrounding tissues in the neck, complicating their removal.



This is a parathyroid carcinoma seen at medium power on the left and higher power on the right. The nests of neoplastic cells that are not very pleomorphic. Note the bands of fibrous tissue between the nests. Parathyroid carcinomas infiltrate surrounding structures in the neck.

CLINICAL COURSE

- ✔ Asymptomatic hyperparathyroidism
- ✔ Symptomatic primary hyperparathyroidism is traditionally associated with a constellation of symptoms: painful bones, renal stones, abdominal groans, and psychic moans:
  - Bone disease and pain with fractures occur secondary to osteoporosis and osteitis fibrosa cystica.
  - Nephrolithiasis (renal stones) occurs in 20% of patients; pain is secondary to obstructive uropathy. Chronic renal insufficiency can cause polyuria and polydipsia.
  - Gastrointestinal disturbances include constipation, nausea, peptic ulcers, pancreatitis, and gallstones.
  - CNS alterations include depression, lethargy, and eventually seizures.
  - Other findings include weakness, fatigue, and cardiac valve calcifications.

SECONDARY HYPERPARATHYROIDISM

Secondary hyperparathyroidism results from any condition associated with chronic hypocalcemia that leads to compensatory parathyroid overactivity

- Renal failure is the most common etiology.
- Renal disease
- Metastatic calcifications cause ischemic damage

HYPOPARATHYROIDISM

- Hypoparathyroidism is much less common than hyperparathyroidism; causes include:

✔ Surgical (e.g., thyroidectomy or treatment of hyperparathyroidism)

✔ Autoimmune hypoparathyroidism associated with autoimmune polyendocrine syndrome, type I

✔ Autosomal dominant hypoparathyroidism

✔ Familial isolated hypoparathyroidism, due either to

❖ primary PTH mutations (autosomal dominant) or

❖ loss-of function mutations in the GCM2 gene responsible for parathyroid development (autosomal recessive)

✔ Congenital absence of all glands (e.g., DiGeorge syndrome)

CLINICAL MANIFESTATION

Manifestations are related to the chronicity and severity of the hypocalcemia:

- Tetany (characterized by neuromuscular irritability) is the hypo- calcemic hallmark: symptoms range from muscle cramps and carpopedal spasms to laryngeal stridor and convulsions
- Mental status changes (e.g., anxiety, depression, or psychosis)
- Intracranial manifestations, including basal ganglia calcifications, parkinsonian-like movement disorders, and elevated intracranial pressure
- Ocular changes with lens calcification and cataract formation
- Cardiac conduction defects, producing a characteristic prolongation of the QT interval
- Dental developmental defects (when hypoparathyroidism is present early in development), including hypoplasia, and defective enamel and root formation