Lecture 5
thyroid and parathyroid

2.Follicular Carcinoma

- It account for 5% to 15% of primary thyroid cancers.
- They are more common in women (occurring

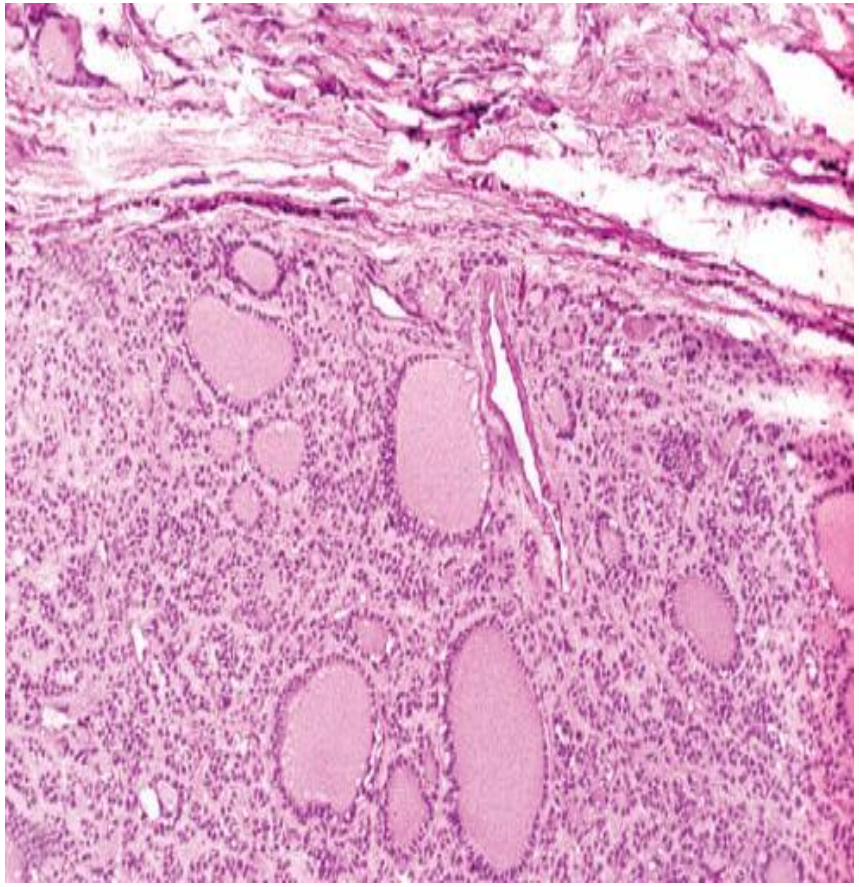
  in a ratio of 3 : 1) and manifest at an older age than papillary carcinomas,
- The a peak incidence between 40 and 60years of age.
- Is more frequent in areas with dietary iodine deficiency (accounting for 25%–40% of thyroid cancers)

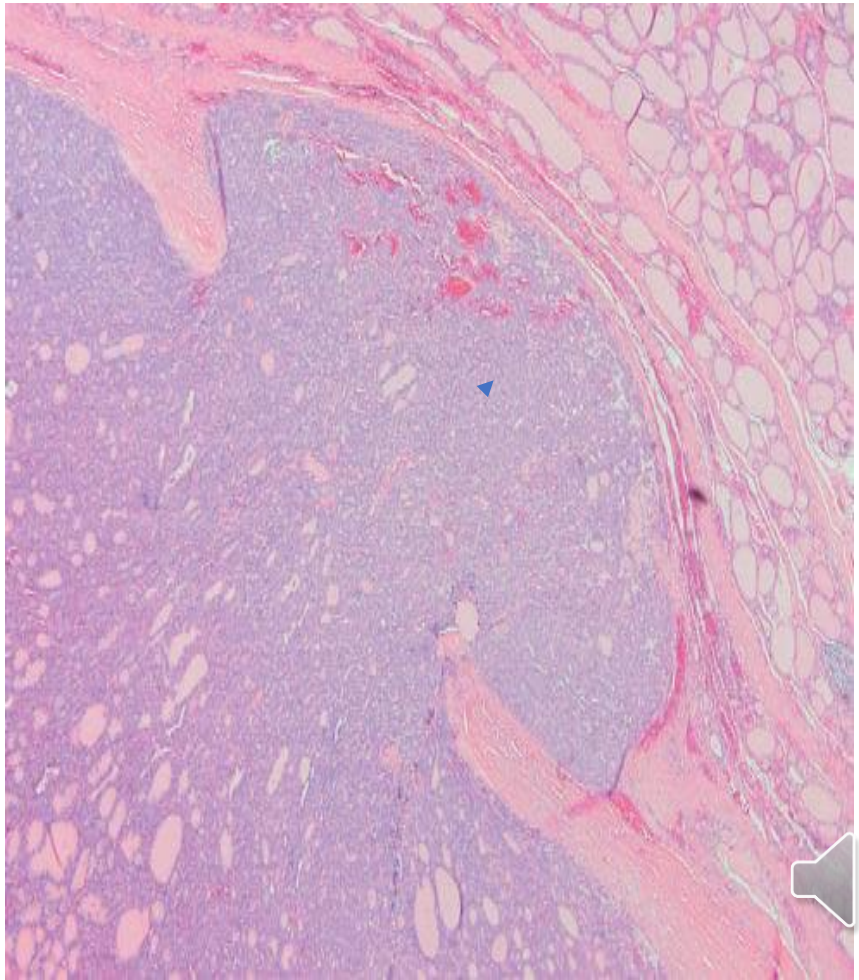
Morphology

- On microscopic examination, most follicular carcinomas are composed of uniform cells forming small follicles, similar to normal thyroid
- Follicular carcinomas may be

a. widely invasive, infiltrating the thyroid parenchyma and extrathyroidal soft tissues, or

b. minimally invasive type which are sharply demarcated lesions that may be impossible to distinguish from follicular adenomas on gross examination.





Clinical Features

- Follicular carcinomas manifest as solitary cold thyroid nodules
- In rare cases, they may b*e* hyperfunctional
- Tend to metastasize through the **bloodstream (hematogenous dissemination*)*** to the lungs, bone, and liver.
- Regional nodal metastases are uncommon.
- One-half of patients with widely invasive carcinomas succumb die within 10 years,
- Less than 10% of patients with minimally invasive follicular carcinomas die within the same period

3.Anaplastic Carcinoma

- Anaplastic carcinomas are undifferentiated tumors of the thyroid follicular epithelium, accounting for less than 5%of thyroid tumors.

- They are aggressive, with a mortality rate approaching 100%
- Patients are older than those with other types of thyroid cancer, with a mean age of 65 years.

Morphology

- Anaplastic carcinomas manifest as bulky masses that grow rapidly beyond the thyroid capsule into adjacent neck structures.
- On microscopic examination, these neoplasms are composed of highly anaplastic cells, which may be large and pleomorphic

.

Clinical Features

- Anaplastic carcinomas have poor prognosis despite despite therapy.
- Metastases to distant sites are common, but in most cases death occurs in less than 1 year as a result of aggressive local growth and compromise of vital structures

4.Medullary Carcinoma

- Are neuroendocrine tumors derived from the parafollicular cells, or C cells, of the thyroid.
- Like normal C cells, medullary carcinomas

  secrete calcitonin, measurement of which plays an important role in the diagnosis and postoperative follow-up of patients..
- Medullary carcinomas arise sporadically in about 70% of cases

- The remaining 30% are familial, occurring

A. in the setting of multiple endocrine neoplasia (MEN) syndrome 2A or 2B,

B. or familial medullary thyroid carcinoma without an associated MEN syndrome,

- Sporadic medullary carcinomas, and familial cases without an associated MEN syndrome, occur in adults,.

- Cases associated with MEN-2A or MEN-2B occur in younger patients, including children

Morphology

- Medullary carcinomas may arise as a solitary nodule or may manifest as multiple lesions involving both lobes of the thyroid.
- Multicentricity is common in familial cases.
- Calcitonin is readily demonstrable both within the cytoplasm of the tumor cells and in the stroma

Clinical Features

- Medullary carcinoma manifests as a mass in the neck, sometimes associated with compression effects such as dysphagia or hoarseness.
- In some instances the initial manifestations are caused by the secretion of a peptide hormone (e.g., diarrhea caused by the secretion of vasoactive intestinal peptide).

Screening of the patient's relatives for elevated calcitonin levels and or *RET* mutations permits early detection of tumors in familial cases.

- All members of MEN-2 kindreds carrying *RET mutations are offered prophylactic* thyroidectomies to preempt the development of medullary carcinomas;

Parathyroid diseases

I.HYPERPARATHYROIDISM

- Hyperparathyroidism may occur

a. Primary form

b. S*econdary Form,*

c. and, less commonly, as tertiary Form.

- The first condition represents an autonomous,

  spontaneous overproduction of PTH

-The latter two conditions typically occur as secondary phenomena in patients with chronic renal insufficiency

Primary Hyperparathyroidism

- Is a common endocrine disorder and an important cause of hypercalcemia.
- There was a dramatic increase in the detection of cases mainly due to routine performance of serum calcium assays in hospitalized patients.

- The frequency of occurrence of the various parathyroid lesions underlying primary hyperparathyroidism

1. Adenoma 85% to 95%
2. Primary hyperplasia (diffuse or nodular)5% to 10%
3. Parathyroid carcinoma 1%

MORPHOLOGY

- The morphologic changes in primary hyperparathyroidism include

1. Those in the parathyroid glands
2. In other organs affected by hypercalcemia.

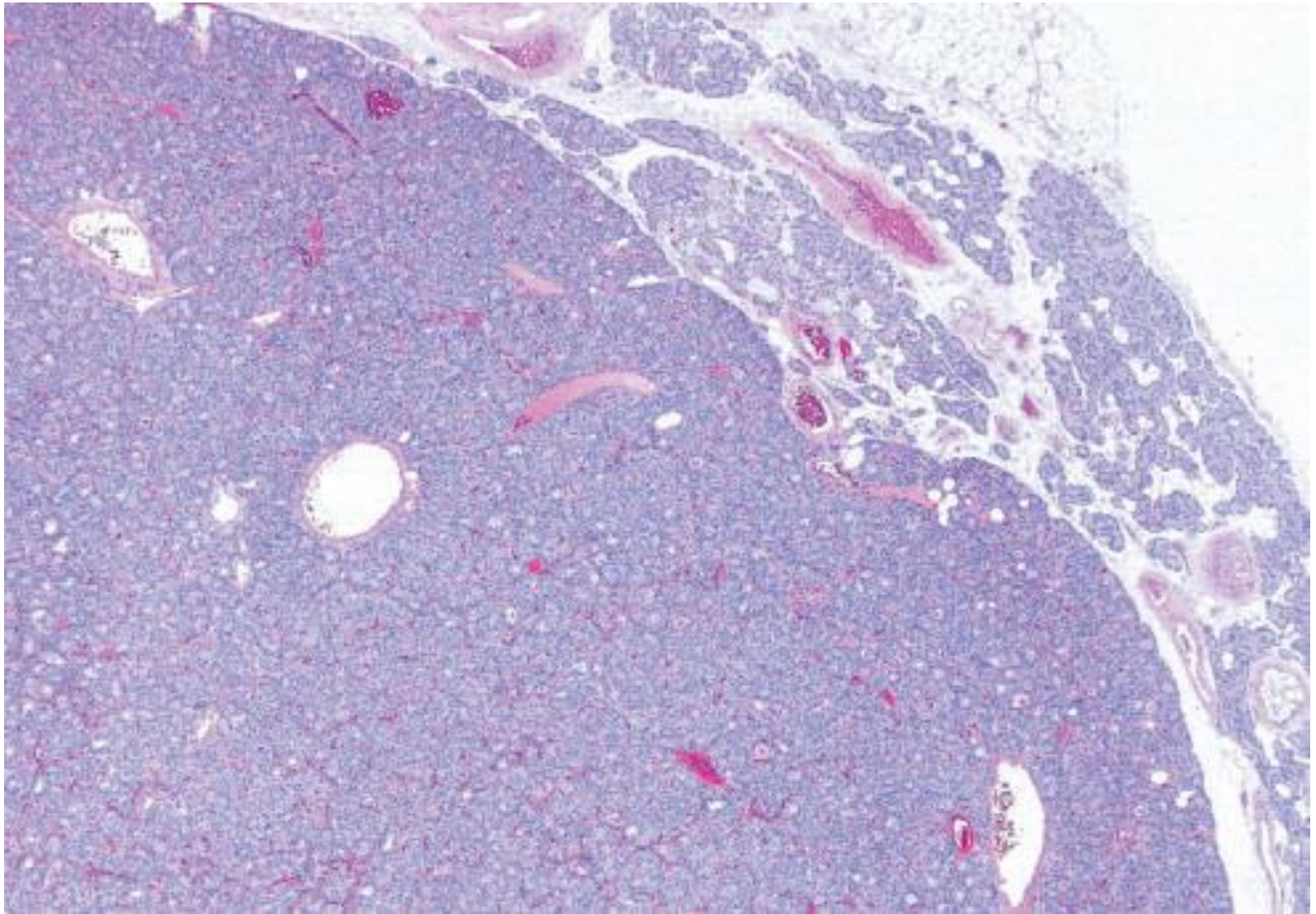
- In 85-95% of cases, one of the parathyroid glands harbors a solitary adenoma.

-The typical parathyroid adenoma

a. Is a well-circumscribed,
b. Soft, tan nodule
c. Invested by a delicate capsule.
d. Parathyroid adenomas are confined to a single gland
e. The other glands are normal in size or somewhat shrunken, as a result of feedback inhibition by elevated serum calcium.
f. Most parathyroid adenomas weigh between 0.5 and 5 g.

- On microscopic examination,

a. Parathyroid adenomas are composed predominantly of chief cells
b. A rim of compressed, non-neoplastic parathyroid tissue, generally separated by a fibrous capsule, often is visible at the edge of the adenoma.
c. Mitotic figures are rare.
d. In contrast with the normal parathyroid parenchyma, adipose tissue is inconspicuous within adenomas.



Parathyroid hyperplasia

- Is typically a multiglandular process.
- In some cases, enlargement may be grossly apparent in only one or two glands, complicating the distinction between hyperplasia and adenoma.

Parathyroid carcinomas

- May be circumscribed lesions that are difficult to distinguish from adenomas,
- Or they may be clearly invasive neoplasms.
- These tumors enlarge one parathyroid gland
- Sometimes exceed 10 g in weight.
- The tumor mass is usually enclosed by a dense, fibrous capsule.
- The diagnosis is not based on cytologic detail unreliable

Note:

- Invasion of surrounding tissues and metastasis are the only definitive criteria.
- Local recurrence occurs in one third

  of cases, and more distant dissemination occurs in another one third

Morphologic changes in other organs:

I. **Skeletal changes**

1. **Ostitis fibrosa cystica**

- High PTH Increases osteoclastic activity, which results in erosion of bone and mobilization of calcium salts, affecting the metaphyses of long bones.
- Bone resorption is accompanied by increased osteoblastic activity and the formation of new bone

- In more severe cases, the cortex is grossly thinned and the bone marrow contains increased amounts of fibrous tissue accompanied by foci of hemorrhage and cysts **2.Brown tumors** of hyperparathyroidism
- Aggregates of osteoclasts, reactive giant cells, and hemorrhagic debris form masses that may be mistaken for neoplasms

II. Renal changes.

1.Nephrolithiasis

- PTH-induced hypercalcemia favors formation of urinary tract stones calcium contain stones

2. And (nephrocalcinosis)

- Calcification of the renal interstitium and tubules

III .Metastatic calcification

- Calcication secondary to hypercalcemia also may be seen in other sites, including the stomach, lungs, myocardium, and blood vessels.

Clinical Features

- Primary hyperparathyroidism usually affects adults
- Is much more common in women than in men
- *The most common manifestation is an increase in serum calcium*
- *Primary hyperparathyroidism is the most*

  common cause of *clinically silent hypercalcemia*.
- The most common cause of clinically apparent hypercalcemia in adults is cancer, which can cause hypercalcemia through a variety of mechanisms, including

a. secretion of PTH-like polypeptides from cancers of other organs, such as lung adenocarcinoma and this is Called paraneoplastic syndrome

b. osteolytic bone metastases

Other laboratory findings

a. hypophosphatemia

b. increased urinary excretion of Calcium and phosphate

Clinical Manifestations

- Pain, secondary to

a. fractures of bones weakened by osteoporosis or ostitis fibrosa cystica
b. and resulting from renal stones was at one time a prominent manifestation of primary hyperparathyroidism.

NOTE:

- Because serum calcium is now routinely assessed in most patients who need blood tests for unrelated conditions hyperparathyroidism is usually detected early in its course

- Additional signs and symptoms that may be encountered in some cases include the following:

1. G*astrointestinal disturbances, including constipation,* nausea, peptic ulcers, pancreatitis, and gallstones
2. *Central nervous system alterations, including depression,* lethargy, and seizures
3. *Neuromuscular abnormalities, including weakness and* hypotonia
4. *Polyuria and secondary polydipsia*

Secondary Hyperparathyroidism

- Secondary hyperparathyroidism is caused by chronic depression of serum calcium levels most often as a result of renal failure leading to compensatory overactivity of the parathyroids.
- The mechanisms by which chronic renal failure induces secondary hyperparathyroidism are complex

1. Chronic renal insufficiency is associated with decreased phosphate excretion, which results in hyperphosphatemia.

- The elevated serum phosphate levels directly depress serum calcium levels.

2.Loss of renal α1-hydroxylase activity, which is required for the synthesis of the active form of vitamin D, reduces the intestinal absorption of calcium

- These alterations cause chronic hypocalcemia,

  which stimulates the activity of the parathyroid glands

2.HYPOPARATHYROIDISM

- Is less common than hyperparathyroidism.

The major causes include the following:

1. *Surgical ablation: The most common cause is inadvertent* removal of parathyroids during thyroidectomy or other surgical neck dissections.
2. *Congenital absence: This occurs in conjunction with thymic* aplasia (Di George syndrome) and cardiac defects, secondary to deletions on chromosome 22

3. A*utoimmune hypoparathyroidism:*

- *This is a hereditary* polyglandular deficiency syndrome arising from autoantibodies to multiple endocrine organs (parathyroid, thyroid, adrenals, and pancreas).
- This condition is caused by mutations in the *autoimmune regulator gene AIRE*

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