Hashimoto thyroiditis.

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LEC.3

Hashimoto thyroiditis. (Autoimmune hypothyroidism).

Pathogenesis of Hashimoto thyroiditis.

I. Hashimoto thyroiditis is caused primarily by a ***defect in T cell*** (CD8 cytotoxic) & ***formation of autoantibodies*** (from sensitized B cells).

Types of autoantibodies in Hashimoto thyroiditis.

1. Inhibitory anti- TSH receptor antibodies. That blocks the action of TSH result in hypothyroidism.
2. Ant thyroglobulin & ant thyroid peroxidase antibodies are probably formed as a result of tissue destruction & exposure of normally sequestered thyroid antigens to the immune system.

II. There is a significant genetic component in the disease pathogenesis (explanation):-

1. Increased frequency of disease in first degree relatives of patient.
2. An association with HLA system .

Morphology of Hashimoto disease.

Gross.

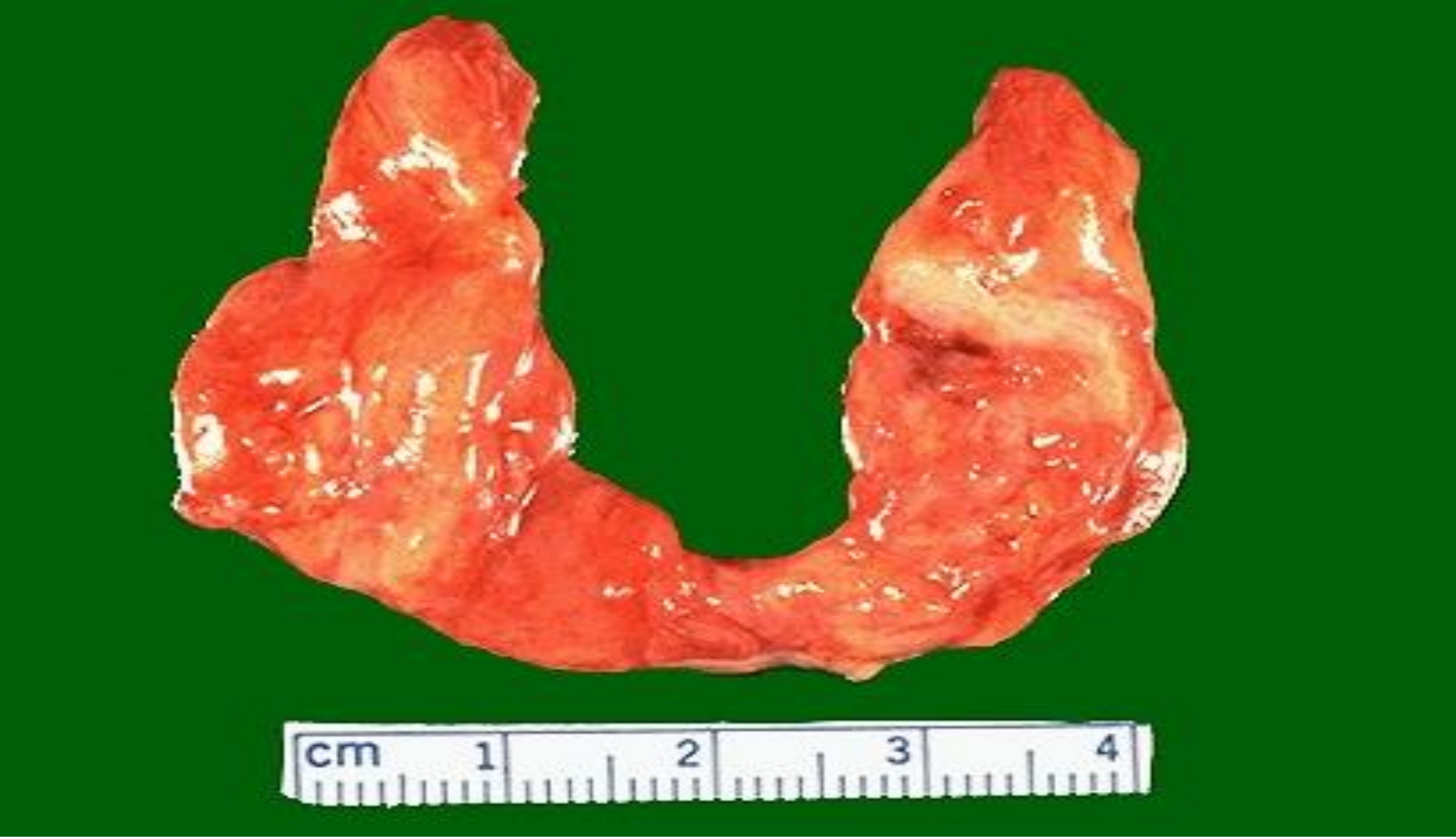
Diffusely & symmetrical enlarged thyroid, with intact capsule.

Mic.

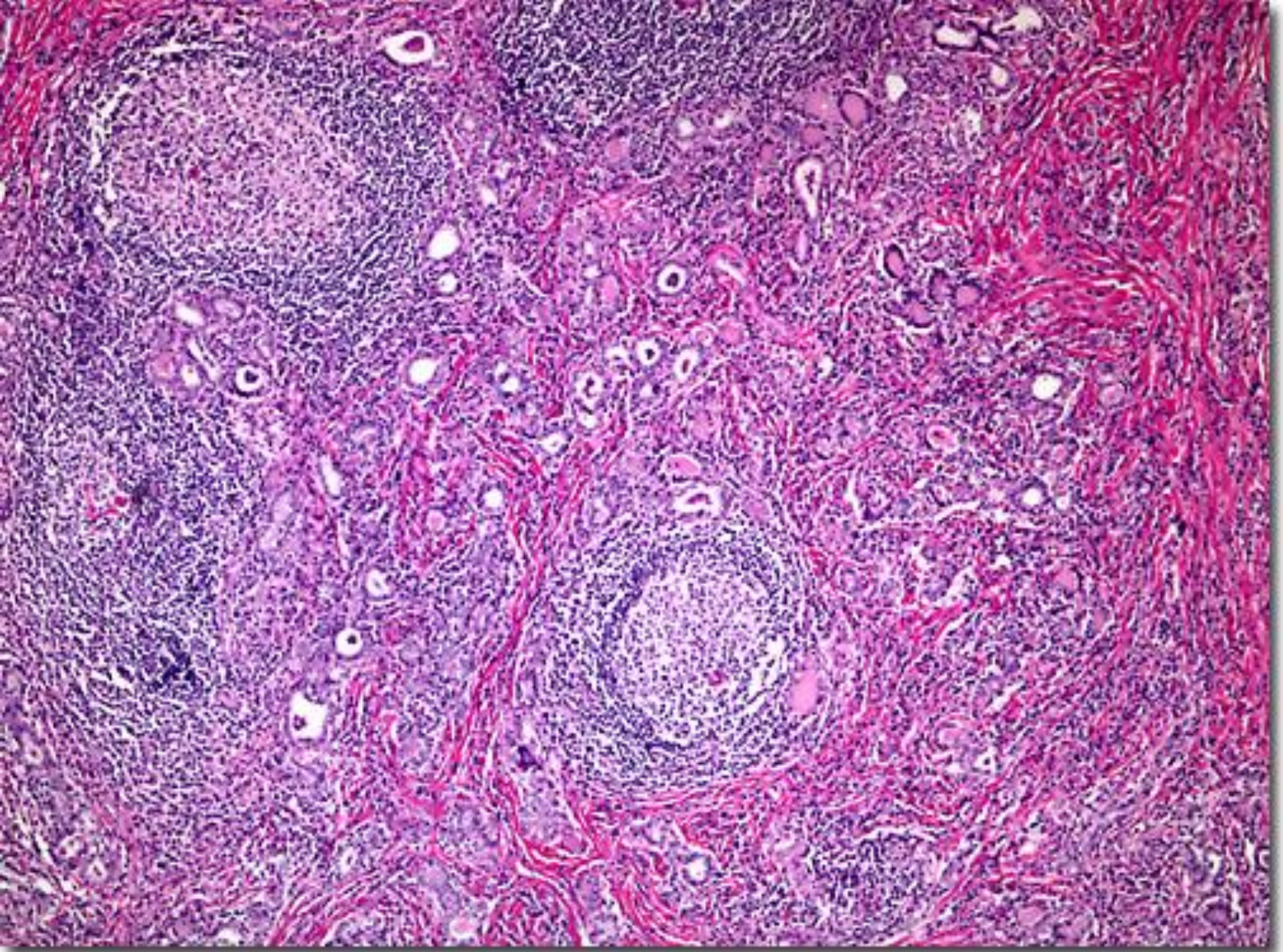
Widespread lymphoid infiltration of thyroid parenchyma by lymphocytes, plasma cells & well developed germinal centers.

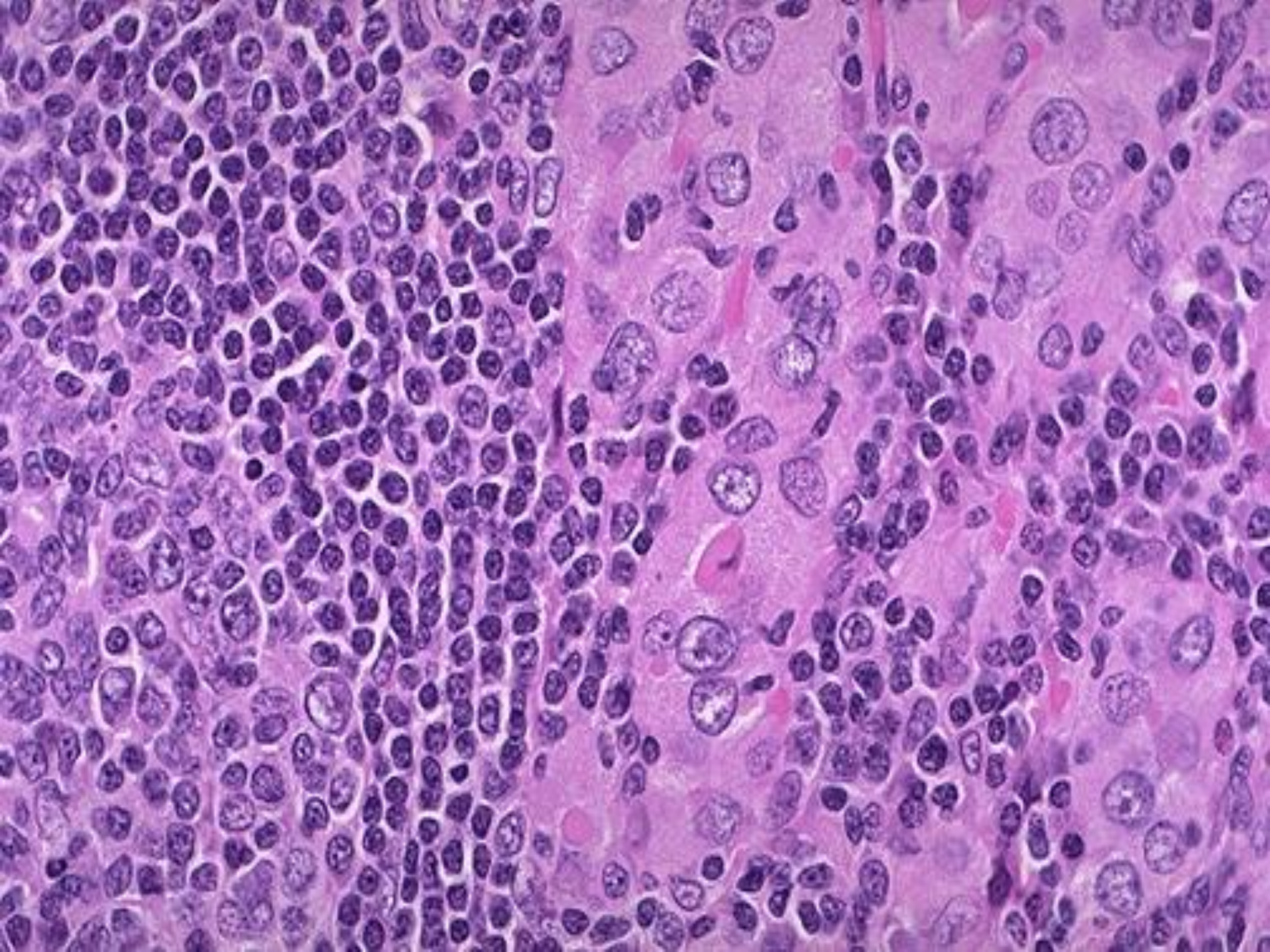
The thyroid follicles are atrophic & are lined by epithelial cells characterized by presence of abundant eosinophilic, granular cytoplasm, termed Hurthle (metaplastic cells) or Oxyphil cells.

Abundant stromal fibrosis does not extend beyond the capsule of the gland.



Hashimoto’s disease





Neoplasms of thyroid gland

Either *benign adenoma or highly anaplastic carcinoma*.

Carcinomas are uncommon, accounting for about 1% of solitary thyroid nodules.

Several clinical criteria provide a clue to the nature of a given solitary thyroid nodule; these criteria are include:-

1. Solitary nodules are more likely to be neoplastic than are multiple nodules.
2. Solid nodules are more likely to be neoplastic than cystic nodules.

3. Nodules in younger patients are more likely to be neoplastic than are those in older patients.

4. Nodules in males are more likely to be neoplastic than are those in females.

5. Cold nodule on thyroid scan tend to be more neoplastic than hot nodule(which are mostly benign).

However fine needle aspiration & histological studies of surgical specimen of thyroid gland give definitive information about the nature of these nodules.

Benign thyroid neoplasms (thyroid adenomas)

Benign neoplasms derived from follicular epithelium.

Characteristics features of thyroid adenomas are:-

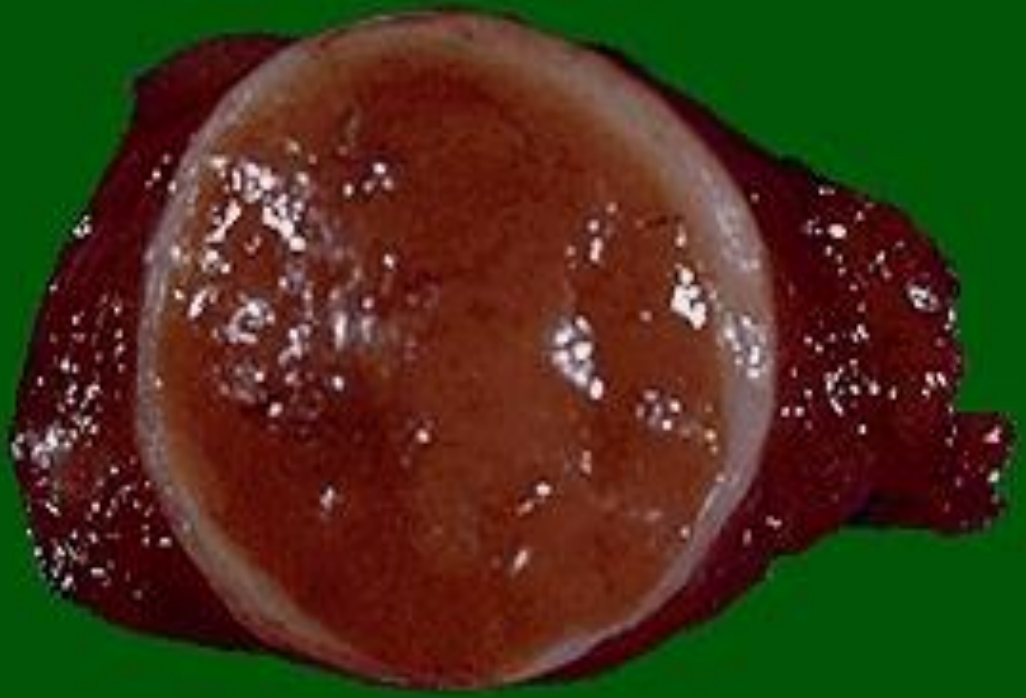
- ✓Solitary, spherical lesion.
- ✓Compresses the surrounding thyroid tissues.
- ✓Well capsulated.

Microscopically adenoma composed of uniform follicles that contain colloid, occasionally, contain oxyphil or Hurthle cell changes.

Occasionally, exhibit pleomorphism & atypia.

Small proportion of adenoma becomes toxic adenomas & cause clinically thyrotoxicosis.

Most of adenomas are cold nodules on thyroid scan while toxic adenomas are warm or hot, (Up to 10% of cold thyroid nodules are proved to be malignant).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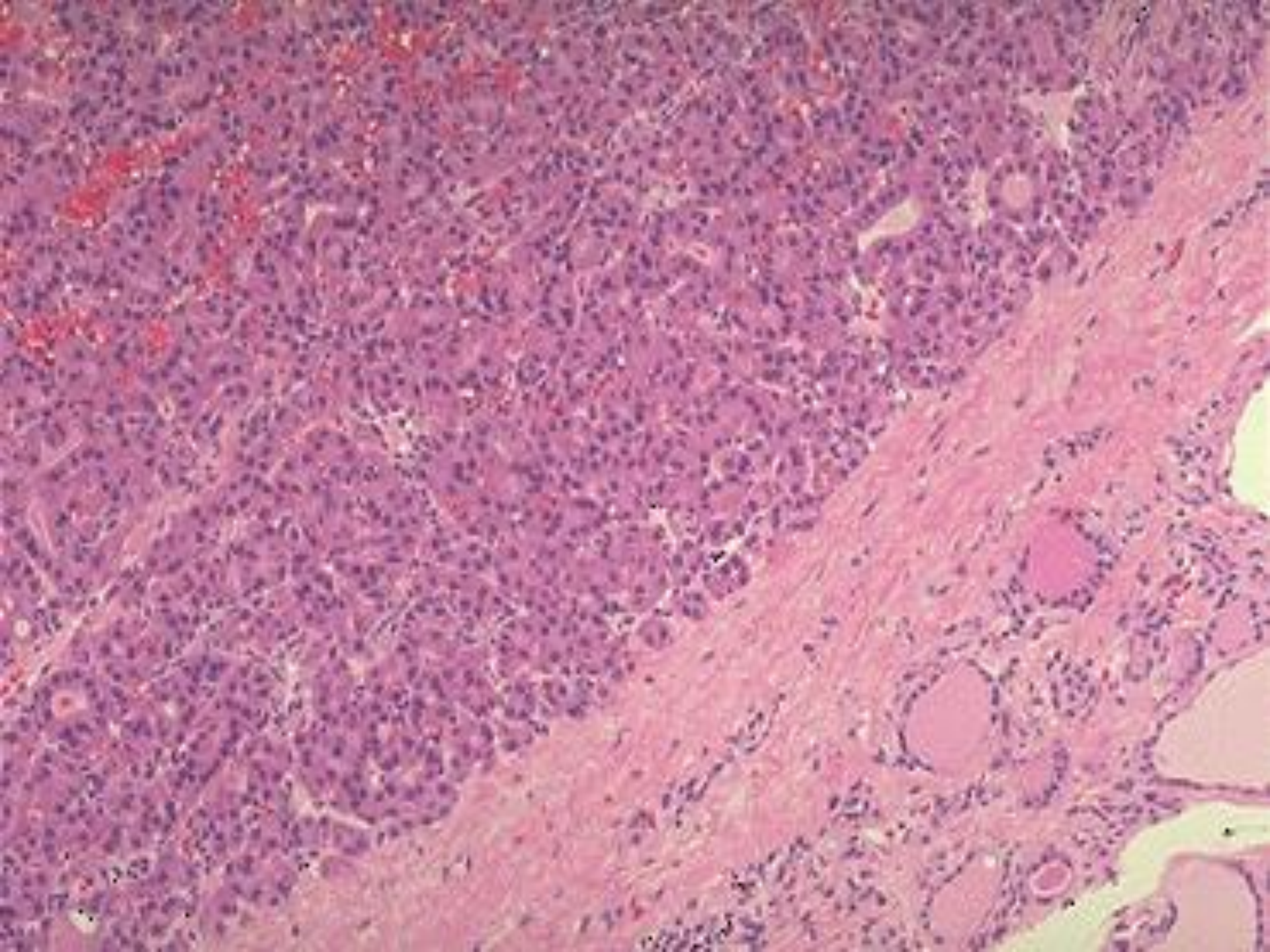
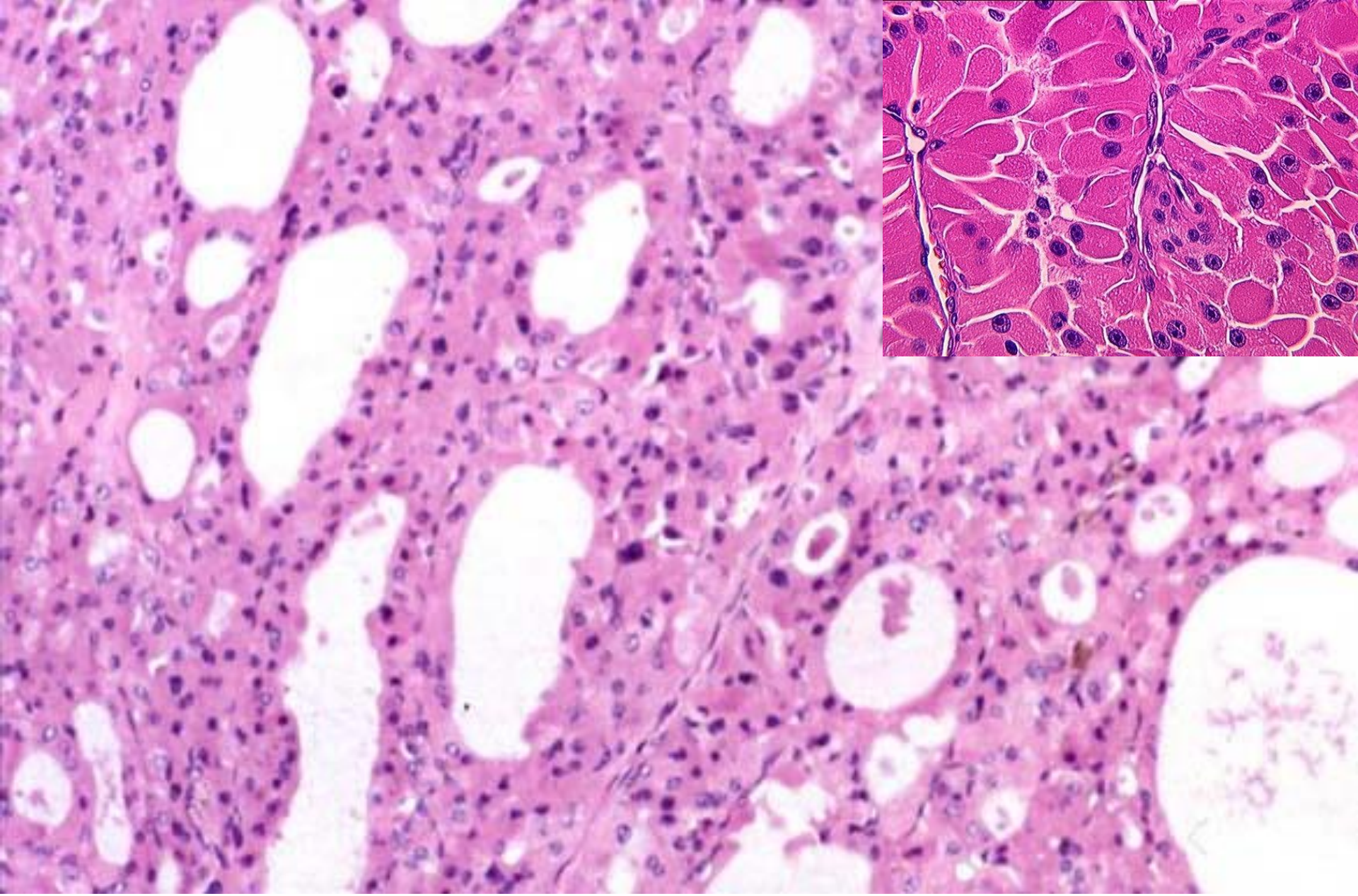




HÜRTHLE CELL ADENOMA, note “atypia”

Carcinomas of thyroid.

Age: Mostly in adult (in childhood mostly is papillary carcinoma).

Sex: Female predominance in all types of thyroid cancers.

Origin: All types of cancers are derived from follicular epithelium, except for medullary carcinomas which are derived from Para follicular or C cells.

The major subtypes of thyroid carcinomas are:

1. Papillary carcinomas (75%-85% of cases).
2. Follicular carcinoma (10%- 20% of cases).
3. Medullary carcinoma (5% of cases).
4. Anaplastic carcinoma (< 5% of cases).

Etiology

1. Genetic factors: by following explanation:

I. Clustering of tumors in families.

II. Familial medullary carcinomas occur in multiple endocrine neoplasia type 2 (disorder associated with gene mutation).

Familial papillary carcinomas have been recently proved to be associated with gene mutation (RET proto-oncogene).

Other genes abnormalities include PTEN, APC, p53, PTC).

2. Ionizing Radiation: by following facts

- Exposure to ionizing radiation, during the first 2 decades of life…… development of thyroid cancer.
- 9% of those receive radiotherapy in childhood for reactive tonsillar enlargement, tinea capitis…… development of cancer.
- Most of post radiotherapy thyroid cancers are papillary carcinomas.

3. Preexisting thyroid diseases.

- Long standing multinodular goiter in areas with iodine deficiency have higher incidence of follicular carcinomas.
- There is little evidence that follicular adenomas progress to carcinomas.

Papillary carcinomas(80% of thyroid cancers):

Most of cases are presented as nonfunctioning, painless mass within the thyroid or as metastases in the cervical lymph nodes.

Can occur at any age, even at childhood.

Morphology of papillary carcinomas.

Gross

Either (solitary or multifocal), (well demarcated & even encapsulated or infiltrative).

May contain areas of fibrosis, calcifications & cysts.

MIC

Definitive microscopic diagnosis of papillary carcinoma depends on:

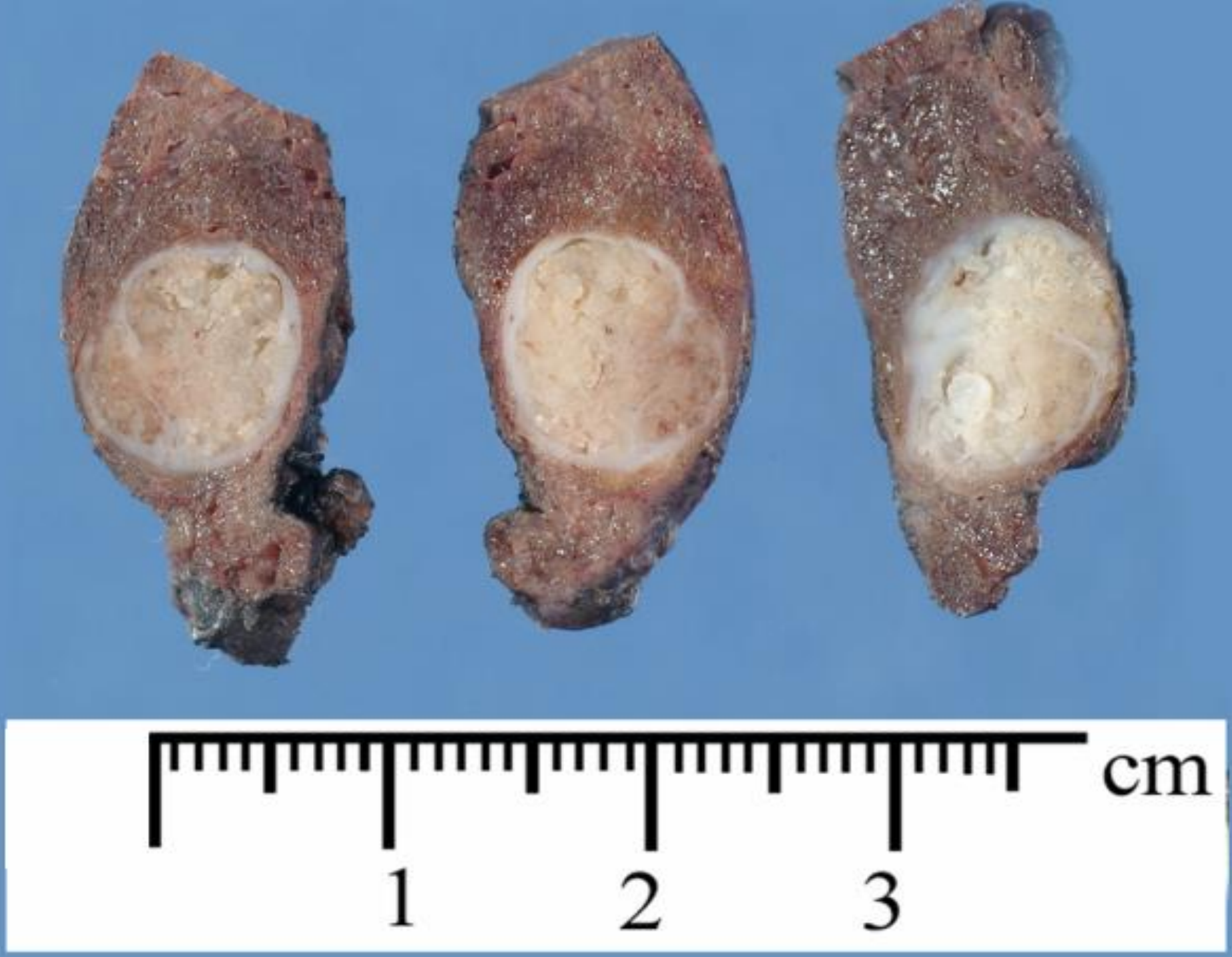
Nuclear features of neoplastic cells.

- Optically clear nuclei (ground glass or Orphan Annie nuclei).
- Intranuclear inclusions which are due to cytoplasmic invaginations (also are called nuclear pseudo-inclusions).

Papillary architecture.

- These papillae can present in some of benign conditions like hyperplastic nodules.
- Papillae of carcinoma differ from those of benign conditions by presences of dense fibro vascular cores.
- Psammoma bodies are often present within the papillae.

Lymphatic invasions are often present while blood invasion are uncommon.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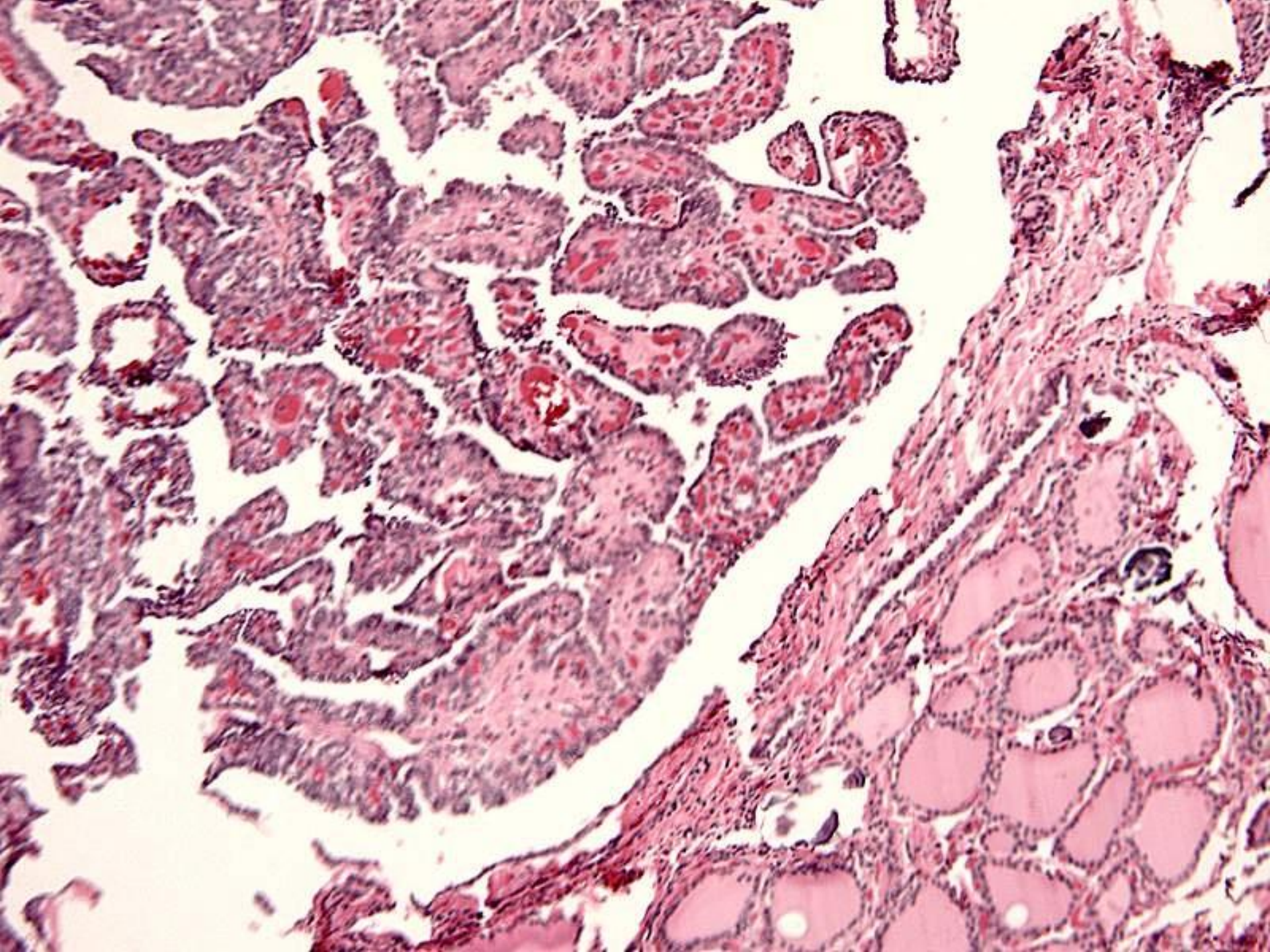


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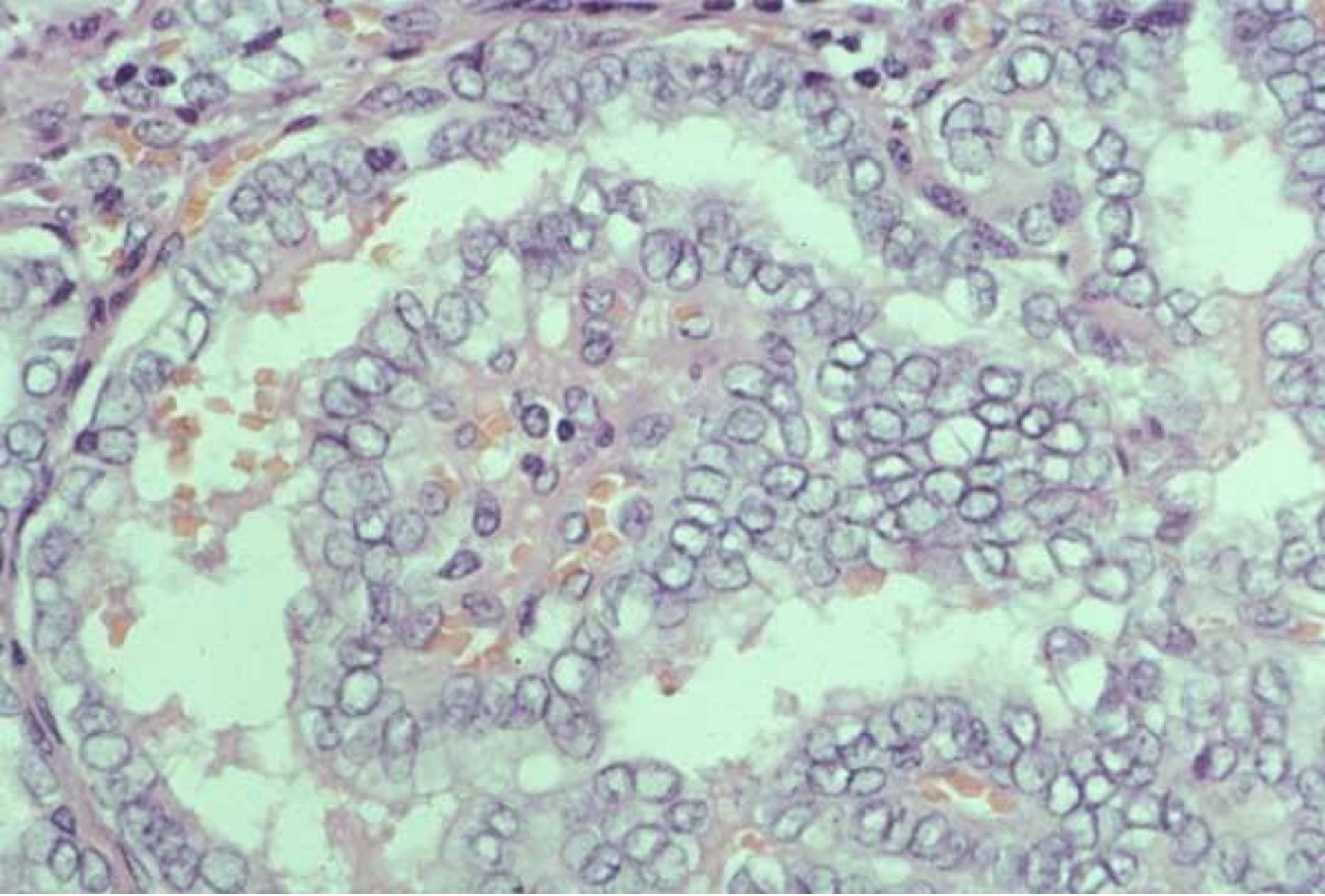


ORPHAN ANNIE CELLS in PAPILLARY CARCINOMA

***Follicular carcinoma*:**

They usually present at older age than the papillary carcinomas.

The incidence of follicular carcinomas is increased in areas of dietary iodine deficiency (may have relation to the nodular goiter).

There is no evidence that follicular carcinomas are aroused from preexisting adenomas.

Clinically follicular carcinomas present most frequently as solitary "cold" thyroid nodules.

In rare cases, they may be presented as hyper functional nodules.

These neoplasms tend to metastasize through the bloodstream to the lung, bone & liver.

Regional lymph nodes metastases are uncommon.

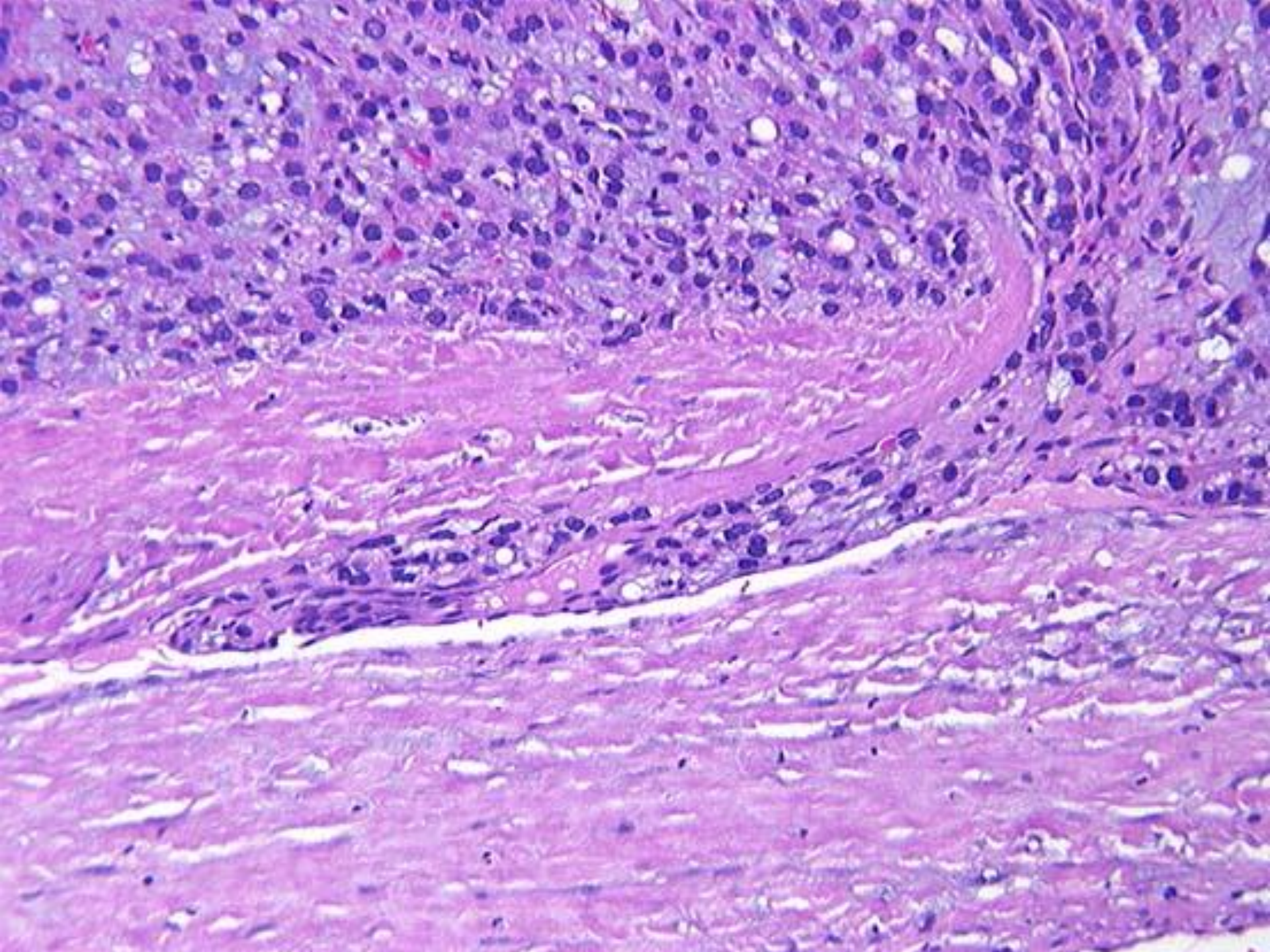
Morphology of follicular carcinoma:

Gross

Either well demarcated lesions (encapsulated) or infiltrative lesions.

Mic

On microscopic level it is difficult to distinguish between follicular adenoma & follicular carcinomas, so the diagnosis of carcinoma are depending on presence of capsular & / or vascular invasion .



Medullary Carcinoma of thyroid:

Arise from **Para follicular** cells (C cells) of thyroid.

Secretes **Calcitonin.**

80% of cases are sporadic, while 20% are familial, (mutation in RET gene).

Most of cases are in adult.

Morphology of medullary carcinoma:

Gross

Either **solitary lesion ,or multicentric** (more with familial cases).

Large tumors show areas of hemorrhage,

Mic.

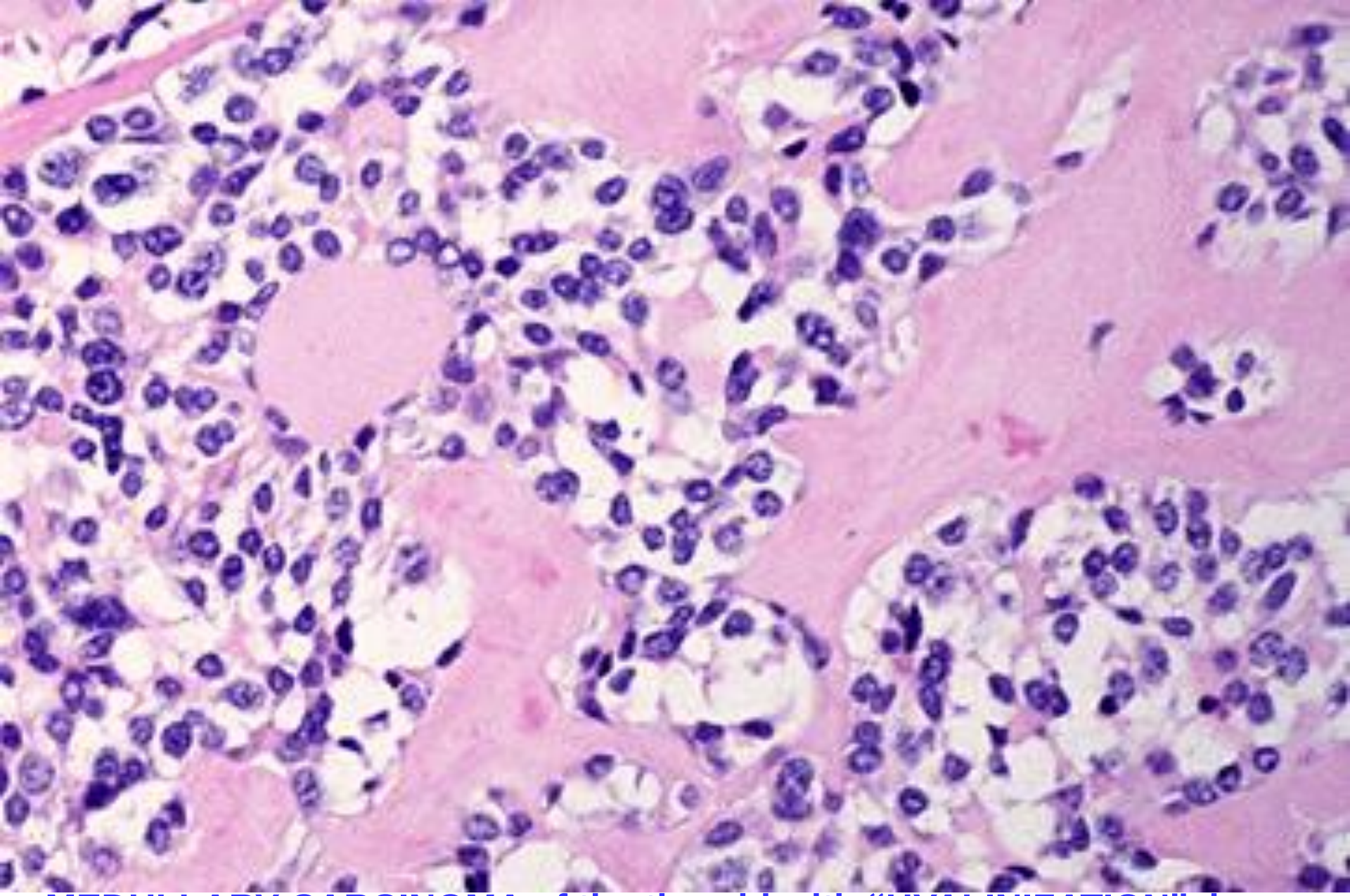
Tumor consists of polygonal to spindle cells, arrange in nests, trabeculae & even follicles.

Amyloid deposits are characteristic of these tumors.

Clinical features of medullary carcinoma.

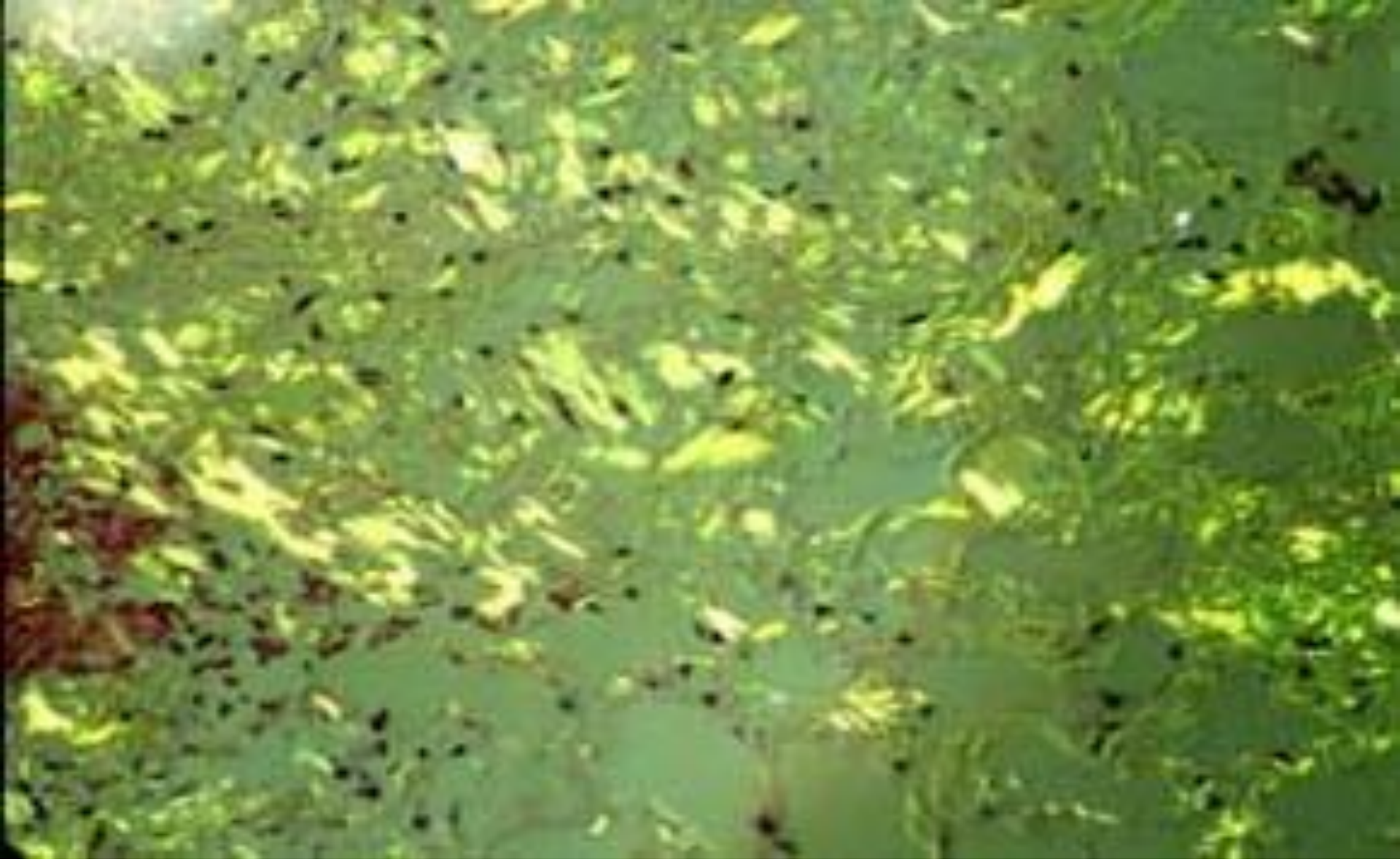
Most of cases are presented as ***mass in the neck.***

Diarrhea due to secretion of VIP substances by the tumor.



MEDULLARY CARCINOMA of the thyroid with "HYALINIZATION", i.e.,

AMYLOID!!!



HYALINIZATION showing APPLE GREEN birefringence in CONGO RED stain, i.e., AMYLOID

Anaplastic carcinoma of thyroid :

Mostly in old patient, aggressive tumors.

Common in areas of endemic goiter.

In most of cases deaths occurs in less than one year as a result of aggressive local growth & compress the vital structures in the neck.

Morphology of anaplastic carcinoma:

Gross

Presented as bulky masses that are usually grow beyond the capsule of the gland.

Mic.

Neoplasms are composed of highly anaplastic cells, exhibiting three distinctive morphologic patterns (Giant cells, Spindle cells & Squamoid like cells).

Simple goiter (Multinodular goiter):

- Is the most common thyroid disease.
- **Either endemic or sporadic** (both indicate the presence of goiter due to impaired synthesis of thyroid hormones……. Elevated level of TSH).

Endemic multinodular goiter:

- Occur in areas where iodine supplement by soil, water & food is poor.
- **Called endemic when 10% of population at theses areas have goiter.**
- With iodine supplementation, the frequency & severity of endemic goiter is declined significantly.

Sporadic multinodular goiter:

- Less common than endemic goiter.
- In female more than male.
- Common in puberty or young adult (increased demands).
- Could be due to ingestion of substances interfering with synthesis of thyroid hormones (e.g. cauliflower).
- Or could be due to hereditary enzymatic defect (decreased synthesis of thyroid hormones).

Pathogenesis of multinodular goiter:

There is hypertrophy & hyperplasia of thyroid follicular cells by elevated level of TSH.

At early stage….. Diffuse enlargement of thyroid gland which is called (diffuse nontoxic goiter), in this stage the follicles are lined by crowded columnar cells

(Sometimes result in formation of Papillae).

If dietary iodine is increased……. Colloid goiter (dilated follicles lined by flat cells).

Colloid grossly appears brown, glassy & transparent.

With time, repeated attacks of stimulation & involution will result in formation of irregular enlargement or called nodular or multinodular goiter.

Gross:

- Asymmetrical enlargement of thyroid, may reach massive size.
- On cut section nodular surface with variable amount of colloid.
- Areas of fibrosis, hemorrhage, calcification & cystic change.

Mic:

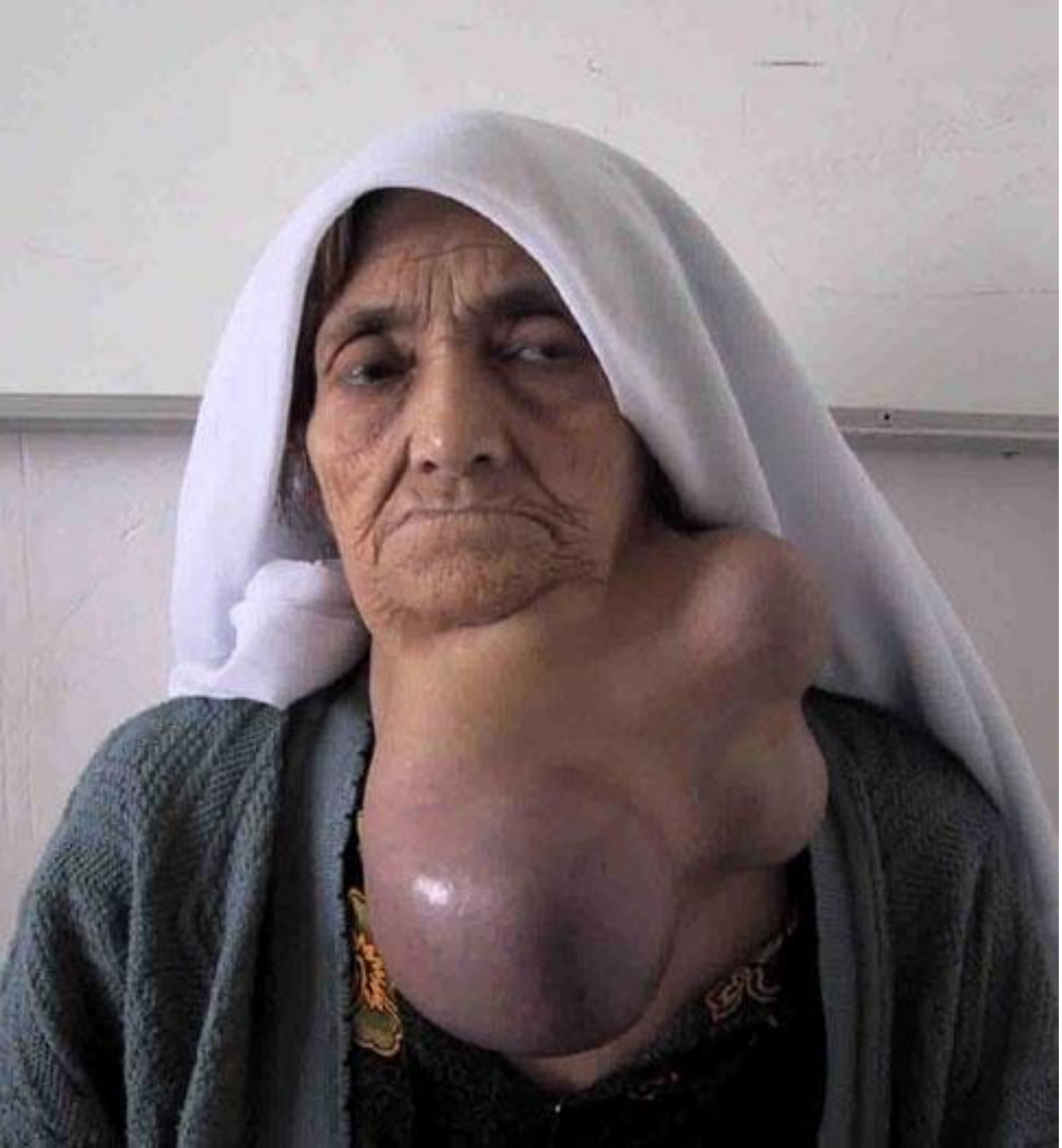
Colloid rich follicles lined by flat epithelium, with many areas of hypertrophy & hyperplasia.

Clinical features:

Mass in the neck, compress on airways, dysphagia, compress the veins of neck.

Complications:

1. Toxic multinodular with hyperthyroidism (cardiac symptoms without ophthalmopathy & dermatopathy of graves disease).
2. Long stand multinodular goiter may result in anaplastic carcinoma.
3. Sometimes result in hypothyroidism.



GOITER

Thank you