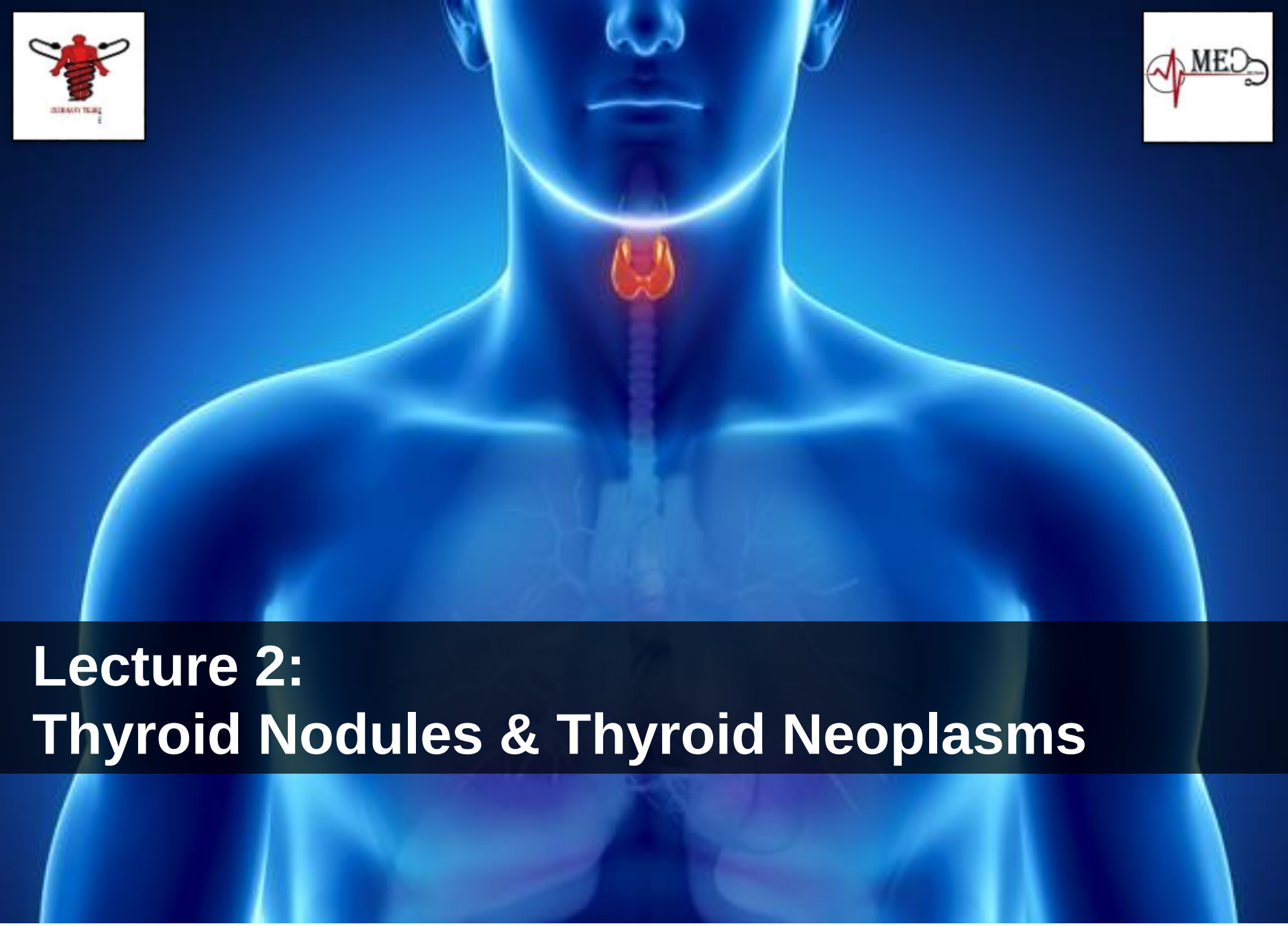


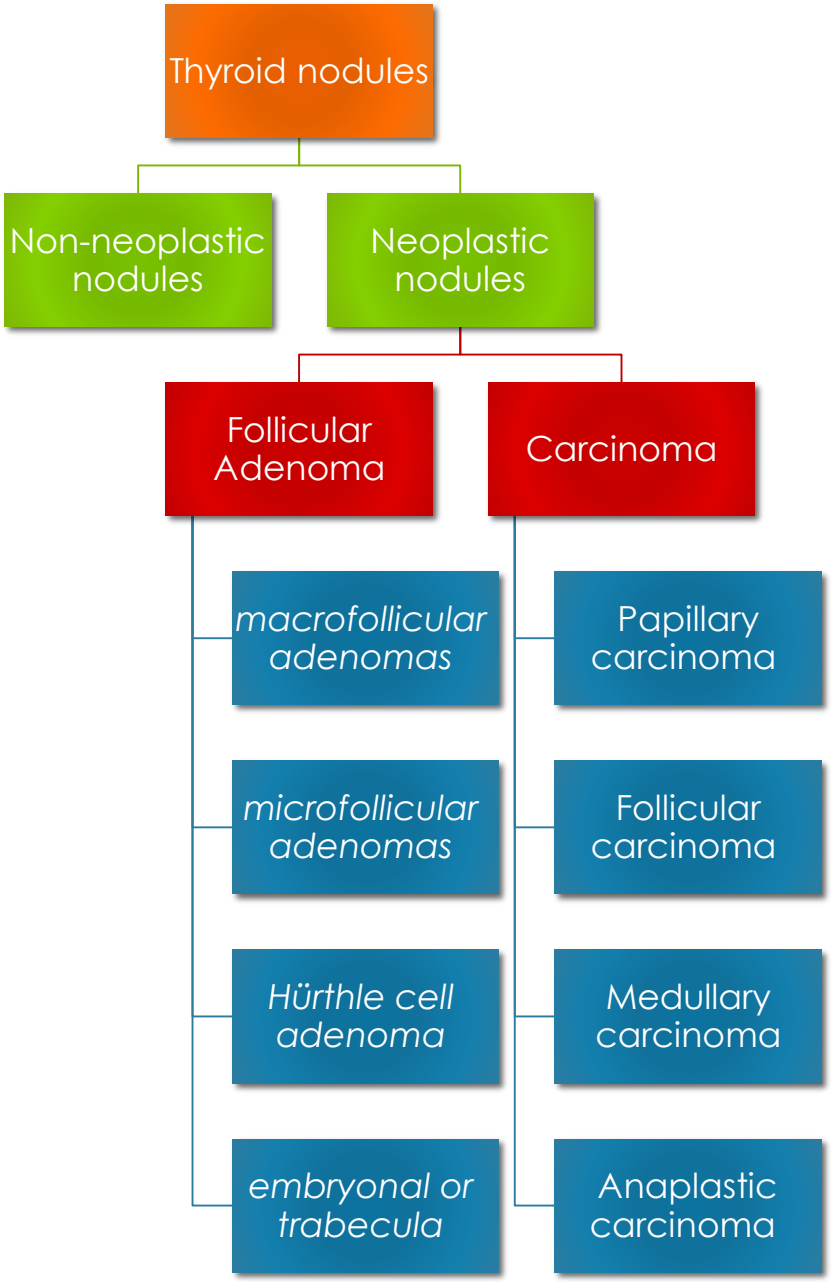
Lecture 2:
Thyroid Nodules & Thyroid Neoplasms

▫ Important ▫ Notes ▫ Explanation

Objectives

The student should :

- ✓ Know the definition of a solitary nodule in the thyroid.
- ✓ Recognize the differential diagnosis of a solitary thyroid nodule.
- ✓ Pathology of thyroid neoplasms including : follicular adenomas, papillary carcinoma, follicular, anaplastic and medullary carcinomas.


Thyroid nodules
Non-neoplastic nodules
Neoplastic nodules
Follicular Adenoma
Carcinoma
macrofollicular adenomas
microfollicular adenomas
Hürthle cell adenoma
embryonal or trabecula
Papillary carcinoma
Follicular carcinoma
Medullary carcinoma
Anaplastic carcinoma

Solitary Thyroid Nodule

Definition: Palpably discrete swelling within an otherwise apparently normal thyroid gland.

Incidence increases throughout life and occurs more in females than males 4/1

Majority: localized, non-neoplastic of nodular goiter conditions or benign neoplasms and less likely carcinoma.

Neoplasms: benign neoplasms are more common than malignant carcinomas (Ratio **10**/1)

The first thing we do is ultrasound, to check if it's **cystic** or **solid** (worry more).

Differentiation: (Dr. Hala emphasized on this 4 times)

1. Non-neoplastic: **cystic** nodule of nodular goiter or **solid** hyperplastic nodule of nodular goiter.
2. Neoplastic: **cystic** benign neoplasm or **solid** malignant neoplasm (adenoma or carcinoma).

Thyroid Neoplasms

Neoplastic nodules either benign or malignant tend to*(not must) have these characteristics :

- to be solitary nodule (not multiple nodules)
- in younger patients (not older ones)
- affecting males more than females
- history of radiation
- Nodules uptaking radioactive iodine (hot nodules): benign

- they may affect elderlies, females and patients with no history of radiation.

Differentiation, cont.:

- Hot Nodule: excess uptake of Iodine-131, hyper-functioning thyroid tissue.
- Cold Nodule: no uptake of Iodine-131, hypo-functioning thyroid tissue. **(usually solid)**

Adenomas (*follicular adenomas)*

Features: Adenomas of the thyroid are typically discrete, solitary masses.

Types: classified on the basis of degree of follicle formation and the colloid content of the follicles into:

1) *Simple colloid adenomas (macrofollicular adenomas).*
2) *Hürthle cell adenoma*
3) *fetal or microfollicular*
4) *embryonal or trabecular*

Toxic adenoma :

a small proportion of adenomas produce thyroid hormones and cause clinically apparent thyrotoxicosis and they are called "toxic adenomas"

Adenoma and Carcinoma :

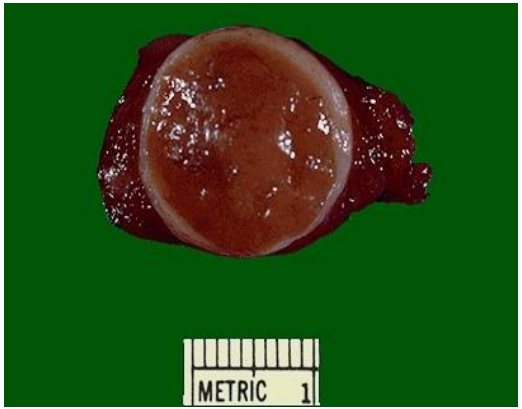
To distinguish** follicular adenomas from follicular carcinomas ,Careful evaluation of the integrity of the capsule is needed.

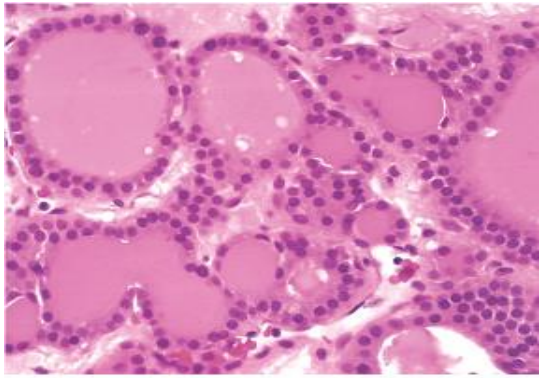
In Follicular carcinoma there will be capsular and/or vascular invasion. (one of the two is enough)

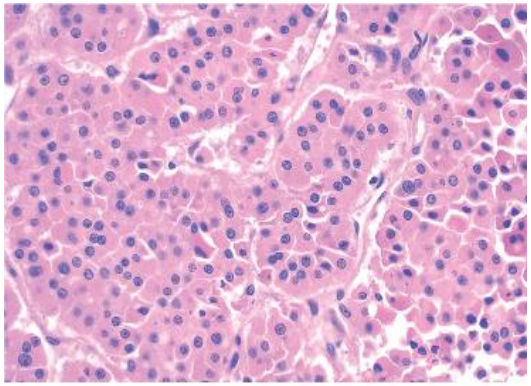
**Many times follicular adenoma and follicular carcinoma look same as the normal tissue

Important:

- Follicular adenomas: **encapsulated** mass lesion. (not infiltrating)
- Follicular carcinomas: invasion of capsule or blood vessels.





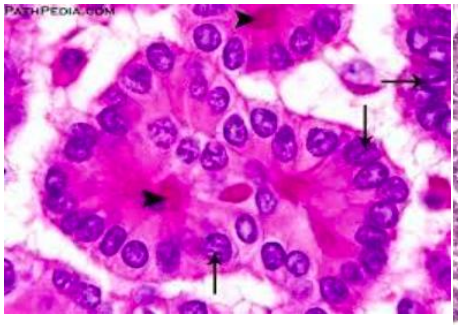


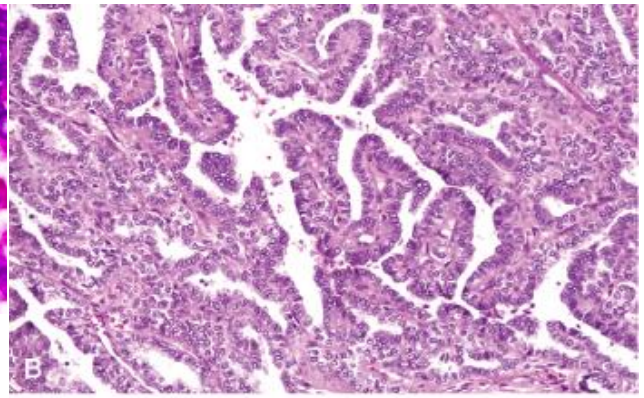
Carcinomas

- Carcinomas of the thyroid account for about 1.5% of all cancers.
- Majority of thyroid carcinomas associated with previous exposure to ionizing radiation (especially papillary type).
- There are four types:
  1. Papillary carcinoma
  2. Follicular carcinoma
  3. Medullary carcinoma
  4. Anaplastic carcinoma
- All thyroid carcinomas (except medullary carcinoma) are derived from the thyroid follicular epithelium.

carcinoma	Papillary carcinoma	Follicular carcinoma	Medullary carcinoma	Anaplastic carcinoma
	85% of cases	5% to 15% of cases	5% of cases	Less than 5% of cases
Age	25 to 50 Most often in last 30s	40 to 60 years	40 to 60 years	Older age group >65 year
Mutations	rearrangements of the tyrosine kinase receptors RET or NTRK1 or activating point mutations in BRAF	RAS family of oncogenes	occur in multiple endocrine neoplasia type 2 (MEN-2) RET protooncogene mutation	**p53** tumor suppressor gene
Notes	Has Good prognosis in general	More common in women (3 : 1)	70%sporadic 30% familial	Very poor prognosis

1. Papillary carcinoma:

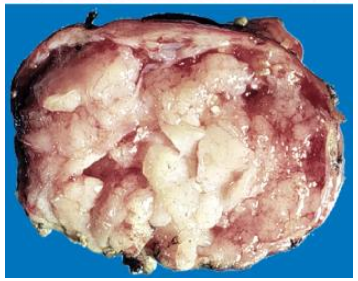




Morphology

- **Papillary structures**
- **Orphan Annie nuclei** (clear nuclei)
- Psammoma bodies
- Pseudoinclusions
- Grooved nuclei (arrows)

In papillary carcinoma we'll see follicular cells forming papillary carcinoma and/or orphan annie nuclei. (one of the two is enough to confirm)



Variants*

- Tall cell variant
- Hyalinizingtrabecular tumors (ret/PTC gene rearrangement)
- Follicular **
- Encapsulated
- Diffuse sclerosing

We can differentiate between the variants of papillary carcinoma & follicular carcinoma by nuclear features.

Clinical Course

- Most present as asymptomatic thyroid nodules.
- The first manifestation may be a mass in a cervical lymph node.
- Prognosis of PTC is dependent on several factors including age (in general, the prognosis is less favorable among patients older than 40 years), the presence of extra-thyroidal extension, and presence of distant metastases (stage).
- Good prognosis.
- **this neoplasm tend to metastasize through lymph vessels**

*Variants mean types or patterns of papillary carcinoma

**Notice: this follicular is type of papillary and there is another one which is type of carcinoma

2. Follicular Carcinomas

Prognosis

- Minimally invasive (well encapsulated, mushroom-like), 10 year survival rate 90%.
- Widely invasive carcinoma, 10 year survival rate less than 50%.

Risk factor

- More frequent in areas with dietary iodine deficiency

this neoplasm tend to metastasize through blood stream

In Follicular carcinoma there will be capsular and/or vascular invasion. (one of the two is enough)

3. Anaplastic Carcinomas

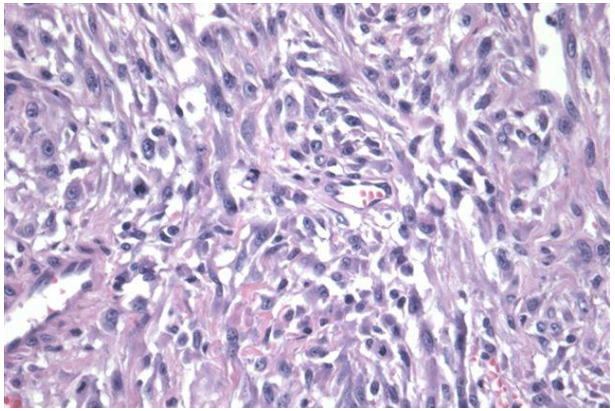
Features

- Anaplastic carcinomas of the thyroid are undifferentiated tumors of the thyroid follicular epithelium.
- Can be arising from a more differentiated carcinoma (papillary)
- Rapidly progressive and **Lethal (100%)**
- Older age group >65 year

Morphology

Highly anaplastic cells:

- large, pleomorphicgiant cells, including occasional osteoclast-like multinucleate giant cells
- spindle cells with a sarcomatous appearance
- mixed spindle and giant cells
- small malignant cells



4. Medullary Carcinomas

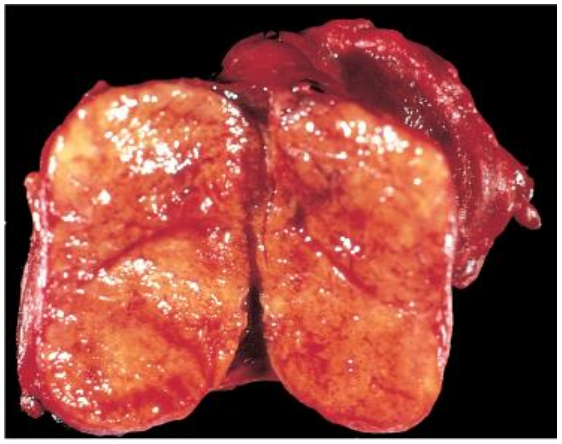
Features

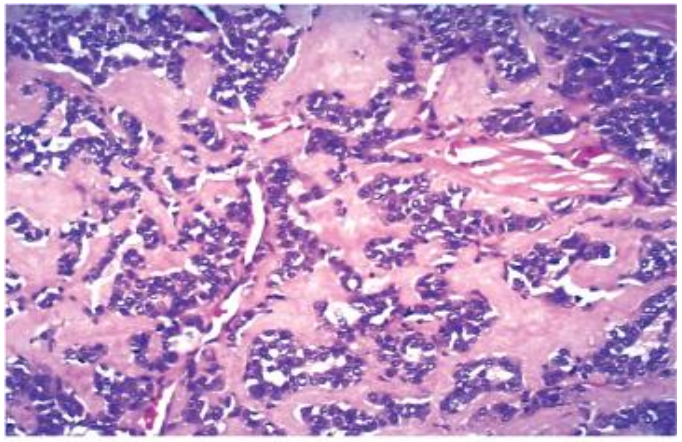
- Medullary carcinomas of the thyroid are neuroendocrine neoplasms derived from the parafollicular cells, or C cells, of the thyroid.
- Medullary carcinomas, similar to normal C cells, secrete calcitonin, the measurement of which plays an important role in the diagnosis and postoperative follow-up of patients.
- About 70% of tumors arise sporadically.
- The remainder occurs in the setting of MEN syndrome 2A or 2B or as Familial tumors without an associated MEN syndrome (familial medullary thyroid carcinoma, or FMTC)

Morphology

- Polygonal to spindle cells
- Plasmacytoid appearance
- **Amyloid deposition**
- Bilaterally
- Multicentricity (multicentric C cell hyperplasia)
- Necrosis &Hemorrhage

These tumors typically show a solid pattern of growth and do not have connective tissue capsules





Summary
(from Robbin's basic pathology)

SUMMARY

Thyroid Neoplasms

- Most thyroid neoplasms manifest as *solitary thyroid nodules*, but only 1% of all thyroid nodules are neoplastic.
- *Follicular adenomas* are the most common benign neoplasms, while papillary carcinoma is the most common malignancy.
- Multiple genetic pathways are involved in *thyroid carcinogenesis*. Some of the genetic abnormalities that are fairly unique to thyroid cancers include *PAX8/PPARG* fusion (in follicular carcinoma), chromosomal rearrangements involving the *RET* oncogene (in papillary cancers), and mutations of *RET* (in medullary carcinomas).
- *Follicular adenomas and carcinomas* both are composed of well-differentiated follicular epithelial cells; the latter are distinguished by evidence of capsular and/or vascular invasion.
- *Papillary carcinomas* are recognized based on nuclear features (ground glass nuclei, pseudoinclusions) even in the absence of papillae. These neoplasms typically metastasize by way of lymphatics, but the prognosis is excellent.
- *Anaplastic carcinomas* are thought to arise by dedifferentiation of more differentiated neoplasms. They are highly aggressive, uniformly lethal cancers.
- *Medullary cancers* are nonepithelial neoplasms arising from the parafollicular C cells and can occur in either sporadic (70%) or familial (30%) settings. Multicentricity and C cell hyperplasia are features of familial cases. Amyloid deposits are a characteristic histologic finding.

Thank You!

We hope you found this helpful and informative.

Done by :
Khalid Alsuhaibani

Reviewed by :
Ghaida Alawaji

Team Leaders :
Ghaida Alawaji & Abdullah Alatar

Contact us :


@pathology433


Pathology433@gmail.com