Thyroid nodules and neoplasms

Objectives

- Know the definition of a solitary nodule in the thyroid.
- Recognize the differential diagnosis of a solitary thyroid nodule.
- Understand the classification, pathology and behavior of thyroid carcinoma.

Black: original content
Red: Important
Blue: only found in males slides

Orange: Doctor notes
Grey: Extra/Robbins
Purple: Only found in females slides

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Editing File

Thyroid nodules

Introduction

- **Hot nodules:** Nodules that take up radioactive iodine in imaging studies, produces excess thyroid hormones. more likely to be **benign**.
- **Cold nodules:** take up iodine less avidly than normal thyroid parenchyma.
- Several clinical criteria provide a clue to the nature of a given thyroid nodule:

Neoplastic "Tumor"	Non neoplastic "Hyperplasia"
- Adenoma and carcinoma. - Solitary nodules. - Nodules in males. - Nodules in younger patients.	- A dominant nodule in multinodular goiter. - Simple cysts or foci of thyroiditis.

- Radiation treatment to the head and neck → ↑incidence of thyroid **malignancy**.
- Morphologic evaluation by fine needle aspiration and histologic study of surgically resected thyroid parenchyma determine the nature of the nodule.

Adenoma

- **Benign** neoplasms derived from **follicular epithelium**. usually are solitary.
- Difficult to distinguish from a dominant nodule in multinodular goiter, or from follicular carcinomas.
- Although the vast majority of adenomas are nonfunctional, a small proportion produce thyroid hormones (toxic adenomas).
- Follicular adenomas are not forerunners to carcinomas.

Diagnosis

- Radionuclide scanning: adenomas appear as **cold nodules** relative to the adjacent normal thyroid gland. While toxic adenomas appear as *Hot* or *Warm* nodules.
- Ultrasonography and fine needle aspiration[1] biopsy: preoperative evaluation of suspected adenomas.

Prognosis

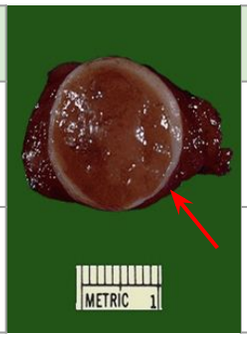
- Excellent prognosis and do not recur or metastasize.
- Removed surgically to exclude malignancy.

1. Can't distinguish between adenoma and carcinoma by fine needle aspiration.

Thyroid nodules

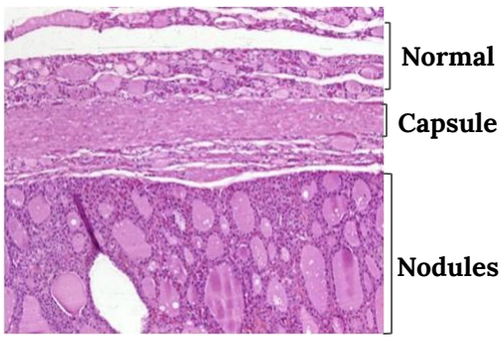
Morphology

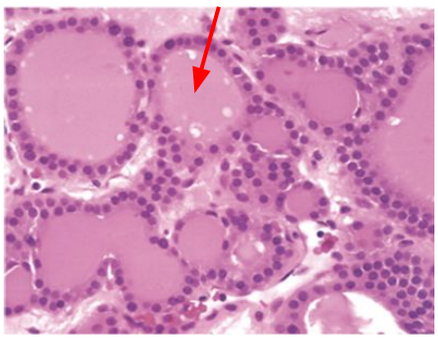
Macroscopic:

Multinodular goiters		Adenoma
- Multiple nodules. -Do not compress adjacent thyroid.		- Solitary, spherical lesion. - Compresses the adjacent non-neoplastic thyroid.
- Lack a well-formed capsule.		Neoplastic cells are demarcated from the adjacent parenchyma by: **well-defined, intact capsule**.

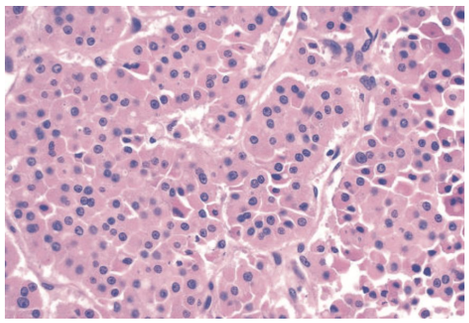
Microscopic:

- Cells are arranged in uniform follicles that contain **colloid (arrow)**.
- **Oxyphil or Hürthle cell** change: brightly eosinophilic granular cytoplasm. Clinically no different from conventional adenoma.
- Follicular carcinomas is different from follicular adenoma in which it demonstrate capsular and/or vascular invasion.





Hürthle cell adenoma

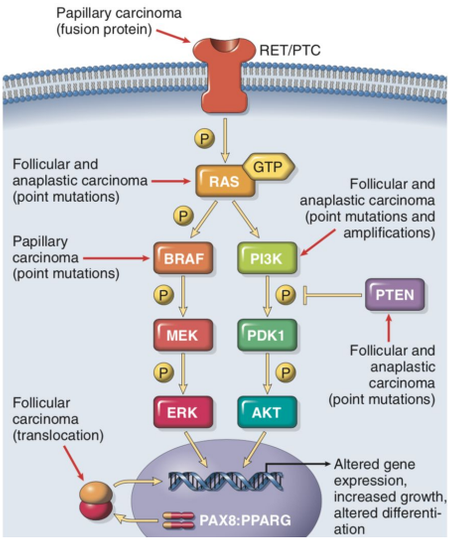


Carcinomas

Types

- **Papillary carcinoma (> 85% of cases)**
- **Follicular carcinoma (5% to 15% of cases)**
- **Medullary carcinoma (5% of cases)**
- **Anaplastic carcinoma (<5% of cases)**

Well differentiated

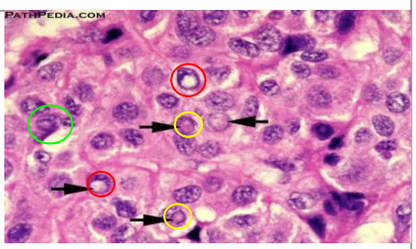
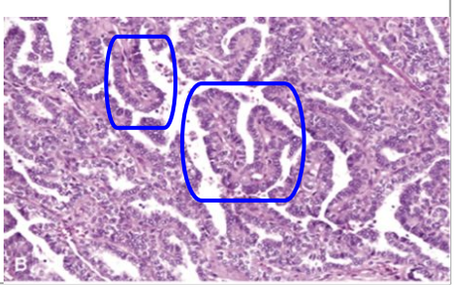


Incidence

- Exposure to **ionizing radiation.**
- The ages of 25 and 50.
- Solitary or multifocal lesions.

1- Papillary carcinoma (PTC)

- The most common form of thyroid cancer.
- Occur at any age.
- Associated with previous exposure to ionizing radiation.

Pathogenesis	Rearrangements of the tyrosine kinase receptors RET or Neurotrophic Tyrosine Kinase Receptor (NTRK1) or activating point mutations in BRAF.
Clinical manifestation	**Nonfunctional**[1] tumors, Painless mass in the neck, either within the thyroid or as metastasis in a cervical lymph node.
Prognosis	- Indolent lesions, with 10-year survival rates in excess of 95% - Less favorable among patients >40 years and the presence of extrathyroidal extension, and presence of distant metastases.
Diagnosis	- Established by fine-needle. - Based on **nuclear features** even in the absence of a papillary architecture.
Morphology 	- **The nuclei of papillary carcinoma cells:** - **Optically clear appearance, ground glass or "Orphan Annie eye"** nuclei: very finely dispersed chromatin. - Grooves. - Intranuclear inclusions (pseudoinclusions). - Papillary architecture. - Psammoma bodies: Concentrically calcified structures. **Most common variant of PTC:** follicular variant which composed predominantly or exclusively of follicles.  

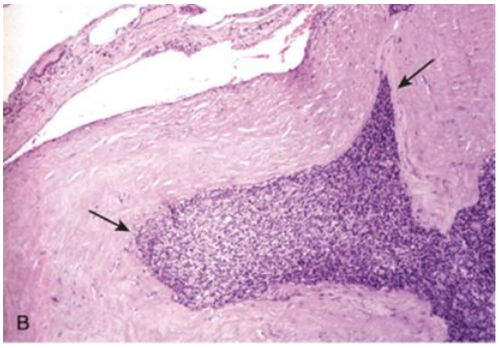
1. Not associated with hypo or hyperthyroidism.

Carcinomas

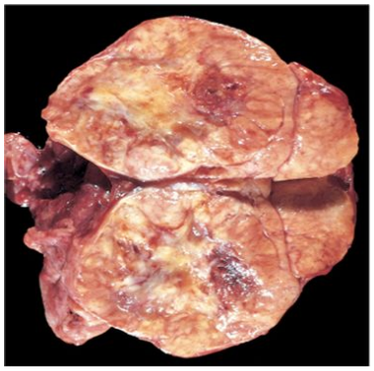
2- Follicular carcinoma

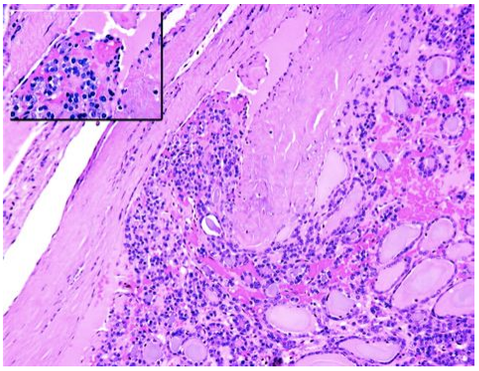
- More common in women (3:1).
- Between 40 and 60 years.
- More frequent in areas with dietary iodine deficiency.

Pathogenesis	Mutations in the RAS family of oncogenes.
Manifestation	- Solitary **cold thyroid nodules**. - Metastasize through the bloodstream to the lungs, bone, and liver.
Prognosis	- Minimally invasive (well encapsulated) → 10 year survival rate 90%. - Widely invasive carcinoma → 10 year survival rate less than 50%.
Morphology	- Fairly uniform cells forming small follicles. - Reminiscent of normal thyroid.
	Widely invasive: infiltrating the thyroid parenchyma and extrathyroidal soft tissue.
	Minimally invasive: sharply demarcated lesions. - Impossible to distinguish from follicular adenomas on gross examination. - Extensive histologic sampling of the tumor capsule–thyroid interface is needed, to exclude capsular and/or vascular invasion.



Follicular carcinomas demonstrate capsular invasion (arrows)





Minimal invasion

Carcinomas

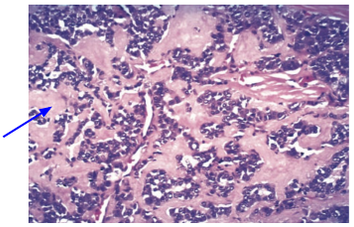
3- Medullary carcinoma

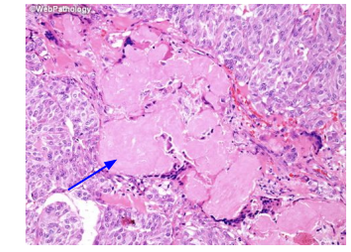
- **Neuroendocrine** neoplasms derived from the parafollicular cells, or C cells of the thyroid.
- Secrete calcitonin, which its measurement used in diagnosis and postoperative follow-up.

Pathogenesis

- 70% of tumors arise sporadically.
- 30% are Familial, occurring in the setting of multiple endocrine neoplasia (**MEN-2**) syndrome[1] 2A or 2B.
- Or Familial medullary thyroid carcinoma, or **FMTC[2]: Familial tumors without an associated MEN syndrome.**
- Both familial and sporadic forms are associated with RET proto-oncogene mutation.

Morphology



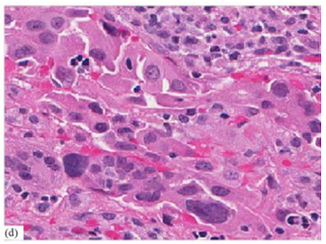


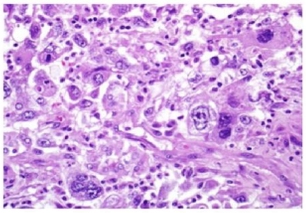
- Polygonal to spindle cells.
- **Amyloid deposition (arrows),** stain with congo red stain.
- Bilaterality.
- Multicentricity.
- Necrosis.
- Hemorrhage.

4- Anaplastic Carcinomas

- **Undifferentiated** tumors of the thyroid follicular epithelium.
- Can be arising from a more differentiated carcinoma (e.g papillary)
- Inactivating point mutations in the **p53 tumor suppressor gene**.
- 100% lethal.
- Occur in older age group > 65 year.

Morphology





- **Highly anaplastic cells:**
  - Large, pleomorphic giant cells, including occasional osteoclast-like multinucleated giant cells.
  - Spindle cells with a sarcomatous appearance.
  - Mixed spindle and giant cells.
  - Small cells.

1. In younger patients.
2. Adults. 50-60.

Summary

	Definition	Pathogenesis	Morphology	Prognosis
Adenoma	**Benign** neoplasms derived from follicular epithelium. **Cold nodules**	––	**- Macro:** Solitary lesion compressing the adjacent tissue, demarcated with intact capsule. **- Micro:** - Follicles contain colloid. - Hürthle cell.	Excellent prognosis and do not recur or metastasize.
Papillary carcinoma >85%	The **most common** form of thyroid cancer.	- Rearrangements of RET or NTRK1. - Activating point mutations in BRAF.	Nuclei: Orphan Annie eye, Grooves, pseudoinclusions, Papillary architecture and Psammoma bodies.	10-year survival rates: 95% Less favorable among patients >40
Follicular carcinoma 5% - 15%	- **Solitary** cold thyroid nodules. - **Metastasize** through the bloodstream to the lungs, bone, and liver.	Mutations in the RAS family of oncogenes.	- Small follicles. - **Widely invasive:** infiltrating the thyroid and extrathyroidal tissue **- Minimally invasive:** sharply demarcated.	- **Minimally invasive** → 10 year survival 90%. - **Widely invasive** carcinoma → 10 year survival <50%.
Medullary carcinoma 5%	**Neuroendocrine** neoplasms derived from the parafollicular cells, or C cells of the thyroid.	- Familial, with (MEN-2) 2A or 2B. - Familial medullary thyroid carcinoma. - RET proto oncogene mutation.	Polygonal to spindle cells. Amyloid deposition Bilaterality. Multicentricity. Necrosis. Hemorrhage.	––
Anaplastic carcinoma <5%	- **Undifferentiated** tumors of the thyroid follicular epithelium. - Can be arising from a more differentiated carcinoma (e.g papillary).	Inactivating point mutations in the p53 tumor suppressor gene.	Large, pleomorphic giant cells. Spindle cells with a sarcomatous appearance. Small cells.	100% lethal.

Quiz

1- Which of the following increases the incidence of thyroid malignancy?

- **A.** Hot nodules.
- **B.** Follicular adenomas.
- **C.** Radiation treatment.
- **D.** Dominant nodule in multinodular goiter.

2- A 32-year-old woman presents with a solitary, nontender, firm nodule on the left side of her neck. Thyroid function tests are within normal limits. A fine-needle biopsy reveals malignant cells. light microscopy shows ground glass nuclei, grooves and pseudoinclusions. What is the appropriate pathologic diagnosis?

- **A.** Anaplastic carcinoma.
- **B.** Follicular carcinoma.
- **C.** Lymphoma.
- **D.** Papillary carcinoma.

3-Which ONE of the following mutations is commonly seen in cases of follicular carcinoma?

- **A.** BRAF
- **B.** MEN-2
- **C.** p53
- **D.** RAS

4- Which ONE of the following carcinomas is characterized by the presence of Congo red material in its stroma?

- **A.** Medullary carcinoma.
- **B.** Anaplastic carcinoma.
- **C.** Papillary carcinoma.
- **D.** Follicular carcinoma.

5- Which of the following is the difference between follicular adenoma and follicular carcinoma?

- **A.** Presence of oxyphil cell changes.
- **B.** Vascular invasion.
- **C.** Well-defined, intact capsule.
- **D.** Presence of amyloid deposition.

6- A 50 year old man presents with a thyroid neoplasm. Detailed history elicits that his aunt had died from a "thyroid illness". His family and first order blood relatives are examined. His sister and a nephew also are found to have small thyroid tumors. His son is found to have a pheochromocytoma. Which of the following gene mutations are most likely to be associated with this condition?

- **A.** NTRK1
- **B.** RAS
- **C.** MEN-1
- **D.** RET

7- Which one of the following is most likely to have papillary carcinoma?

- **A.** 32 years old female with previous history of ionizing radiation.
- **B.** 21 years old male with painful mass in the neck.
- **C.** 69 years old male who has dyspnea.
- **D.** 47 years old female with dietary iodine deficiency.

8- Which of the following thyroid neoplasm has the worst prognosis?

- **A.** Follicular carcinoma.
- **B.** Papillary carcinoma.
- **C.** Anaplastic carcinoma.
- **D.** Medullary carcinoma.

1. C
2. D
3. D
4. A
5. B
6. D
7. A
8. C

Thanks

Khalid Alkhani
Team leader

Lama Alzamil
Team Leader

Done by the amazing:

NO DRAMA LLAMA