

Thyroid Nodules and Neoplasms

Editing File

Color index:

Main text (black)

Female Slides (Pink)

Male Slides (Blue)

Important (Red)

Dr's note (Green) Extra Info (Grey)







To define solitary nodule in the thyroid.



To Recognize the differential diagnosis of a solitary thyroid nodule, neoplastic and non-neoplastic.



To list the benign causes of thyroid nodules.



To Understand the classification, pathogenesis, gross and microscopic morphology and behavior of thyroid carcinoma (papillary, follicular, medullary and anaplastic)

THIS LECTURE WAS PRESENTED BY DR.AMANY FATHADDIN & DR.MOHAMMED ALSWAYYED



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Thyroid Nodules

Several clinical criteria provide a clue to the nature of a given thyroid nodule:

Solitary nodules, in general, are more likely to be neoplastic than are multiple nodules.

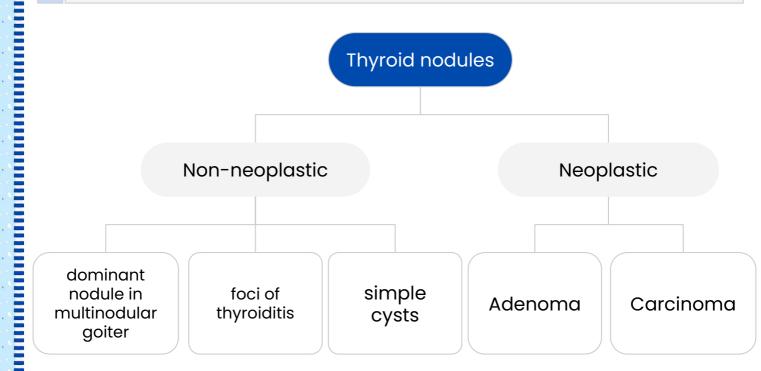
Nodules in males are more likely to be neoplastic than are those in females.

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

A history of radiation treatment to the head and neck region is associated with an increased incidence of thyroid malignancy.

Nodules that take up radioactive iodine in imaging studies (hot nodules) are more likely to be benign than malignant.

Ultimately, it is the morphologic evaluation of a given thyroid nodule by fine needle aspiration, combined with histologic study of surgically resected thyroid parenchyma, that provides the most definitive information about its nature.





Follicular Adenoma

Follicular Adenoma

	Follicular Adenoma		
	Overview	 Adenomas of the thyroid are benign neoplasms derived from follicular epithelium. In general, follicular adenomas are not forerunners to carcinomas; nevertheless, shared genetic alterations support the possibility that at least a subset of follicular carcinomas arise in preexisting Overview adenomas. *On clinical and morphologic grounds, they may be difficult to distinguish from a dominant nodule in multinodular goiter, or from follicular carcinomas. 	
		Gross	 The typical thyroid adenoma is Solitary, spherical lesion that compresses the adjacent non neoplastic thyroid. The neoplastic cells are demarcated from the adjacent parenchyma by a well-defined, intact capsule. These features are important in making the distinction from multinodular goiters, which contain multiple nodules on their cut surface, do not demonstrate compression of the adjacent thyroid parenchyma, and lack a well-formed capsule.
	Morphology	Microscopic	- Constituent cells are arranged in uniform follicles that contain colloid. - Occasionally, the neoplastic cells acquire brightly eosinophilic granular cytoplasm (Oxyphil or Hürthle cell change), the clinical presentation and behavior of a Hürthle cell adenoma are no different from those of a conventional adenoma. *The hallmark of all follicular adenomas is the presence of an intact well-formed capsule encircling the tumor. "Robbins" *Careful evaluation of the integrity of the capsule is therefore critical in distinguishing follicular adenomas from follicular carcinomas, which demonstrate capsular and/or vascular invasion.
	Diagnosis	 Radionuclide scanning: adenomas appear as cold nodules (non-functioning = not producing follicles or thyroid hormones) relative to the adjacent normal thyroid gland. Essential techniques used in the preoperative evaluation of suspected adenomas are ultrasonography and fine needle aspiration biopsy. 	
	Prognosis	exclude mo	denomas carry an excellent prognosis and do not recur or

metastasize.



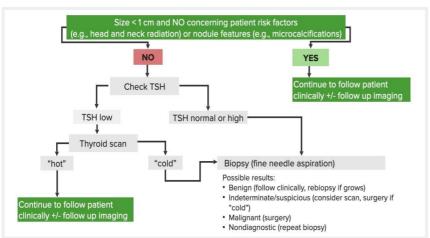


Carcinomas of the Thyroid: 1.5% of all cancers

- Papillary carcinoma (> 85% of cases) "Most common type"
- Follicular carcinoma (05% to 15% of cases)
- Medullary carcinoma (5% of cases)
- Anaplastic carcinoma (<5% of cases) "The worst, very ugly, poor differentiation"

Environmental Factors:

The major risk factor predisposing to thyroid cancer is exposure to **ionizing radiation**, particularly during the first 2 decades of life.



How to Diagnose Carcinoma (Extra Pic)



Clinical Note

Patient with Papillary carcinoma may Present as asymptomatic nodules or metastasis to cervical lymph nodes in Advanced disease: hoarseness, cough, dyspnea also maybe Associated with familial adenomatous polyposis, Cowden syndrome while patient with Follicular carcinoma present with Painless, slow-growing thyroid nodule, Cold nodules on scintigraphy, Commonly it spreads hematogenously to lungs or bones & Typically, regional lymph nodes are not involved, it is also Associated with Cowden syndrome. In Medullary carcinoma patient can manifest with:

Diarrhea, flushing (calcitonin and from tumor-secreted vasoactive intestinal peptide (VIP), prostaglandin and serotonin), Cushing's syndrome due to adrenocorticotropic hormone (ACTH).



Papillary Carcinoma

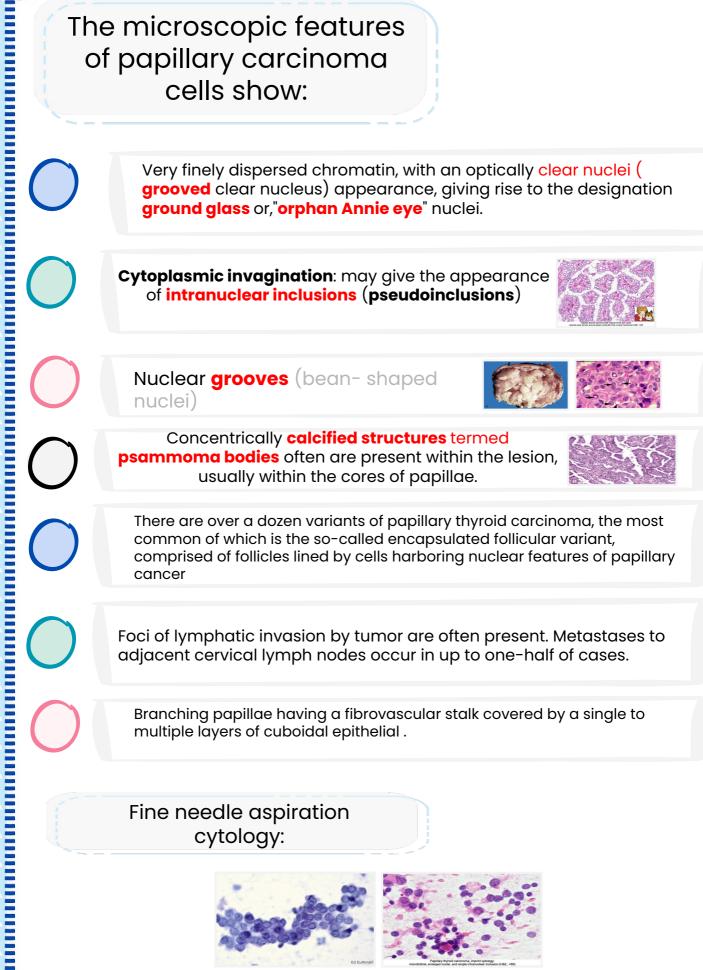
Overview

- Papillary carcinomas represent the most common form of thyroid cancer.
- These tumors may occur at any age, and they account for the vast majority of thyroid carcinomas.

Associated with previous exposure to ionizing radiation.				
	Papillary Carcinoma			
Pathogenesis	 Rearrangements in genes that encode the receptor tyrosine kinases RET and NTRK1. Activating point mutations in BRAF. 			
Clinical Manifestation	Papillary carcinomas are nonfunctional tumors, so they manifest most often as a painless mass in the neck, either within the thyroid or as metastasis in a cervical lymph node.			
Diagnosis	 A preoperative diagnosis usually can be established be fine-needle aspiration. The diagnosis of papillary carcinoma is based on nuclear features even in the absence of a papillary architecture. 	У		
Prognosis	 Papillary carcinomas are indolent lesions, with 10-year survival rates in excess of 95%. Prognosis of PTC is dependent on several factors including age (in general, the prognosis is less favorable among patients older than 55 years), the presence of extra-thyroidal extension, and presence of distant metastases (stage). 			
Morphology	Papillary carcinomas are solitary or multifocal lesions. Some tumors may be well circumscribed and encapsulated; others infiltrate the adjacent parenchyma and have ill-defined margins. The cut surface sometimes reveals papillary foci that point to the diagnosis			



The microscopic features of papillary carcinoma cells show:





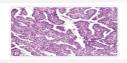


Nuclear grooves (bean-shaped nuclei)





Concentrically calcified structures termed **psammoma bodies** often are present within the lesion, usually within the cores of papillae.

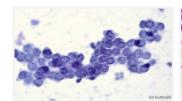


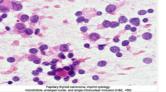
There are over a dozen variants of papillary thyroid carcinoma, the most common of which is the so-called encapsulated follicular variant, comprised of follicles lined by cells harboring nuclear features of papillary cancer

Foci of lymphatic invasion by tumor are often present. Metastases to adjacent cervical lymph nodes occur in up to one-half of cases.

Branching papillae having a fibrovascular stalk covered by a single to multiple layers of cuboidal epithelial.

Fine needle aspiration cytology:







Follicular Carcinoma

	Follicular Carcinoma
Epidemiology	 5% to 15% of primary thyroid cancers More common in women (3:1) Peak incidence between 40 and 60 years More frequent in areas with dietary iodine deficiency
Pathogenesis	 Mutations in RAS or in components of the PI3K/AKT signaling pathway One third to one half of follicular carcinomas also have a unique (2;3) translocation that disrupts PAX8 gene
Morphology	 On microscopic examination, most follicular carcinomas are composed of fairly uniform cells forming small follicles, reminiscent of normal thyroid Follicular carcinomas may be: widely invasive, infiltrating the thyroid parenchyma and extrathyroidal soft tissues minimally invasive. are sharply demarcated lesions that may be impossible to distinguish from follicular adenomas on gross examination. This distinction requires extensive histologic sampling of the tumor capsule—thyroid interface, to exclude capsular and/or vascular invasion
Clinical manifestation	- Manifest most frequently as solitary cold thyroid nodules
Prognosis	 These neoplasms tend to metastasize through the bloodstream to the lungs, bone, and liver. Minimally invasive (well encapsulated): 10 year survival rate of 90%, similar to adenoma Widely invasive carcinoma: 10 year survival rate less than 50%



Medullary carcinoma

Medullary Carcinoma		
Overview	 Medullary carcinomas of the thyroid are neuroe derived from the parafollicular cells, or C cells, Medullary carcinomas, similar to normal C cells, the measurement of which plays an important rand postoperative follow-up of patients. 	of the thyroid. , secrete calcitonin ,
Epidemiology	 About 70% of tumors arise sporadically. The remaining 30% are familial, occurring in the endocrine neoplasia (MEN) syndrome 2A or 2B, of thyroid carcinoma without an associated MEN statement of discussed later. 	or familial medullary
Pathogenesis	 Familial medullary thyroid carcinomas occur in multiple endocrine neoplasia type 2 (MEN-2) and are associated with germ line RET proto-oncogene mutations. RET mutations are also seen in approximately one-half of nonfamilial (sporadic) medullary thyroid cancer. 	
	 Medullary carcinomas may arise as a solitary not manifest as multiple lesions involving both lobes Multicentricity is particularly common in familio Larger lesions often contain areas of necrosis. 	s of the thyroid.
	 On microscopic examination, composed of polygonal to spindle-shaped cells, which may form nests, trabeculae, and even follicles. 	
Morphology	 Amyloid deposits, are present in the adjacent stroma in many cases and are a distinctive feature. 	
	 One of the characteristic features of familial medullary carcinomas is the presence of multicentric C cell hyperplasia in the surrounding thyroid parenchyma, a feature usually absent in sporadic lesions. 	



Anaplastic Carcinoma

	Anaplastic Carcinoma			
	Overview	 Least common carcinoma Anaplastic carcinomas of the thyroid are undifferentiated tumors of the thyroid follicular epithelium. Approximately one-fourth of patients with anaplastic thyroid carcinomas have a history of a well-differentiated thyroid carcinoma Prevalence: Older age group > 65 year. 		
	Pathogenesis	These highly aggressive tumors can arise de novo or, more commonly, by progression of a well-differentiated papillary or follicular carcinoma. Molecular alterations present in anaplastic carcinomas include those also seen in well-differentiated carcinomas, as well as additional mutations that are specific to anaplastic carcinoma. The most common of these unique mutations are loss-of-function mutations in TP53		
	Microscopicall Y	These neoplasms are composed of highly anaplastic cells, which may be: 1) Large pleomorphic giant cell. 2) Spindle shaped cell. 3) In some cases mixture of spindle and giant cells.		
	Clinical manifestation	Anaplastic carcinomas manifest as bulky masses that typically grow rapidly beyond the thyroid capsule into adjacent neck structures.		
	Prognosis	Lethal 100%		





- From the slides +Robbins
- Follicular adenomas are the most common benign neoplasms, while papillary carcinoma is the most common malignancy.
- Multiple genetic pathways are involved in thyroid carcinogenesis.
- Follicular adenomas and carcinomas 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 the lymphatics, but the prognosis is excellent.
- Anaplastic carcinomas are highly aggressive.
- Medullary cancers are non epithelial 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.

Deep Focus Question

Which patient's presentation is most concerning for thyroid cancer?

- A 36-year-old woman with a history of hypothyroidism on levothyroxine treatment for the past 8 years with a slightly enlarged thyroid gland without any distinct nodules.
- A 27-year-old asymptomatic male with a firm, fixed 2 cm thyroid nodule. В.
- A 45-year-old woman with symptoms of weight gain, fatigue, cold intolerance, and dry skin. C.
- A 30-year-old man with symptoms of excessive sweating, weight loss, hyperactivity, exophthalmos, and a slightly enlarged thyroid gland without any palpable nodules.
- A 33-year-old woman with a history of hypothyroidism with a 1 cm mobile thyroid nodule.

Answer: B

Deep Focus Question



Which type of thyroid cancer has a hereditary component and is associated with MEN-2 syndrome?

- Papillary thyroid cancer
- Anaplastic thyroid cancer
- C. Follicular thyroid cancer
- Medullary thyroid cancer
- Cortical thyroid cancer

Answer: D

Deep Focus Question



Which of the following types of thyroid cancer has the worst prognosis?

- Papillary
- Follicular
- Anaplastic
- Medullary

Answer: C



Keywords

Follicular Adenoma	 benign neoplasms derived from follicular epithelium. Solitary, spherical lesion well-defined, intact capsule. Oxyphil or Hürthle cell change
Papillary Carcinoma	 exposure to ionizing radiation. Rearrangements in genes that encode the receptor tyrosine kinases RET and NTRK1 Activating Point mutations in BRAF painless mass in the neck metastasis in a cervical lymph node clear nuclei (grooved clear nucleus) appearance ground glass or, "orphan Annie eye" nuclei. intranuclear inclusions (pseudoinclusions) Papillary architecture psammoma bodies: calcified structures
Follicular Carcinoma	 Mutations in RAS or in components of the PI3K/AKT signaling pathway translocation that disrupts PAX8 gene lodine deficiency solitary cold thyroid nodules Widely invasive: infiltrating the thyroid parenchyma & extrathyroidal soft tissues. Minimally invasive: are sharply demarcated lesions
Medullary Carcinoma	 neuroendocrine neoplasms derived from the parafollicular cells, or C cells, of the thyroid occurs in the setting of MEN-2 syndrome · 2A · or 2B MEN syndrome RET proto-oncogene mutations polygonal to spindle-shaped cells, may form nests, trabeculae, follicles Congo-Red staining: amyloid deposits from calcitonin multicentric/multiple C cell hyperplasia in the surrounding thyroid parenchyma C-cells containing neurosecretory granules
Anaplastic Carcinoma	 loss-of-function mutations in TP53. bulky masses that grow rapidly beyond the thyroid capsule Large pleomorphic giant Spindle shaped cell.



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MCQs



Question 1

Which hormone is secreted in medullary carcinoma?

A

TSH

B

T3, T4

G

Calcitonin

D

PTH

Question 2

What is the major predisposing factor to thyroid cancer?

A

Obesity

B

Exposure to ionizing radiation

C

Smoking

D

Family history of thyroid cancer

Question 3

Which gene mutation is commonly found in papillary carcinoma?

A

RET

B

BRAF

G

NTRK1

D

TP53

Question 4

What is the most likely diagnosis for a patient with a small lump in the neck and palpable cervical lymph node



Follicular carcinoma



Papillary carcinoma



Anaplastic carcinoma



Medullary carcinoma



1-C \ 2-B \ 3-B \ 4-B





Question 5

What is the characteristic feature of medullary carcinoma

Amyloid deposit

psammoma bodies

Papillary structure

Tall columnar cells

genetic testing

Question 6

How to diagnose Papillary carcinoma?

Nuclear features

Bone marrow aspiration

Ultrasound imaging

Question 7

How do adenomas appear in radionuclide scanning?

Hot nodules Cold nodules

Producing thyroid Functioning nodules hormones

Question 8

A patient came to the clinic with iodine deficiency what is most likely tumor will he develop?

Medullary carcinoma Follicular carcinoma

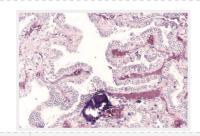
Anaplastic carcinoma Papillary carcinoma





Cases

1.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. The tumor is excised and examined by light microscopy (shown in the image). What is the appropriate pathologic diagnosis?



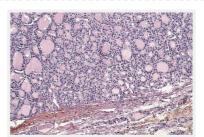
A.Anaplastic carcinoma

B.Follicular carcinoma

C.Medullary carcinoma

D.Papillary carcinoma

2.A 33-year-old woman presents with a swelling in her neck, which she first noticed 2 months ago. Physical examination reveals a solitary, nontender nodule of the thyroid gland measuring 2 cm in diameter. Thyroid function tests are within normal limits. The nodule does not accumulate 125 lodine on thyroid scintiscan. A biopsy of the nodule is shown in the image. Which of the following is the most likely diagnosis?



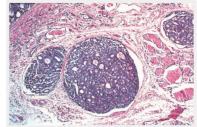
A.Follicular adenoma

B.Medullary thyroid carcinoma

C.Multinodular goiter

D.Papillary thyroid carcinoma

3. A 45-year-old man presents with swelling in the anterior portion of his neck. Physical examination reveals an enlarged nodular thyroid. Thyroid function tests are within normal limits. A thyroid scintiscan shows a dominant "hot" nodule. A biopsy of this nodule reveals neoplastic cells with evidence of vascular and capsular invasion (shown in the image). X-rays demonstrate distant bony metastases. What is the most likely diagnosis?



A.Anaplastic carcinoma

B.Follicular carcinoma

C.Medullary carcinoma

D.Metastatic carcinoma

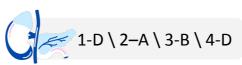
4. A 55-year-old woman comes to the office due to a neck lump she noticed while showering. The patient generally feels fine, and medical history is unremarkable. She has not had weight loss, dysphagia, or palpitations. Temperature is 37.0°C (98.6°F), pulse is 80/min, and blood pressure is 125/80 mmHg. On physical examination, a nontender nodule occupying the right thyroid lobe is noted. The rest of the physical examination shows no abnormalities. Laboratory results show normal TSH levels. Ultrasound of the neck reveals a 2 cm homogenous, anechoic nodule with an absence of internal flow. Fine need aspiration reveals cells with nuclear atypia. The lesion is surgically excised and sent to histology, which shows a spherical lesion with an intact capsule. The cells are arranged in uniform follicles with colloid. Which of the following is the most likely diagnosis?

A.Subacute granulomatous thyroiditis

B.Anaplastic carcinoma

C.Papillary carcinoma

D.Thyroid adenoma









EXTRA CASES MAY REQUIRE EXTRA INFO

1.A 40-year-old woman is referred to the clinic for the evaluation of a thyroid nodule. Medical history is significant for Hodgkin lymphoma as a teenager, for which she received radiation treatment. Temperature is 36°C (97.4°F), pulse is 82/min, respirations are 14/min, and blood pressure is 120/70 mmHg. Physical examination shows a 2cm x 2cm hard nodule on the right lobe of the thyroid gland. The remainder of the physical examination shows no abnormalities. Ultrasound imaging suggests a malignancy, and fine needle aspiration is performed. Fine needle aspiration is most likely to show which of the following pathological findings?

A.Normal cells with fibrosis that extend to local structures

B.Malignant proliferation of follicles that invade the capsule

C.Malignant cells in an amyloid stroma

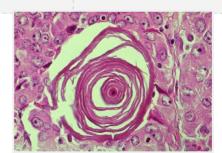
D.Malignant cells with nuclear clearing and indentations

2.A 45-year-old man comes to the office due to a neck mass. The patient first noticed it a few months ago while shaving, but he did not seek medical care at that time. He also describes worsening weakness, abdominal pain, and constipation. Medical history is insignificant other than appendectomy at age 16. On physical examination, a painless lump is noted on the left lobe of the thyroid. Multiple painless cervical lymph nodes are also noted. The rest of the physical examination is normal. TSH levels are within normal limits. PTH and calcium levels are elevated. Ultrasound is performed and reveals a solid and hypoechoic mass with microcalcifications. Which of the following features is most likely to be seen on fine-needle biopsy?

A.Pleomorphic and spindle-shaped anaplastic cells invading local structures B.Varying sizes of follicles filled with colloid

C.Crowded tall, columnar cells forming papillae without fibrovascular cores D.Sheets of polygonal cells in an amyloid stroma

3. A 63-year-old woman comes to the office due to a neck lump. She is otherwise healthy, and medical history is unremarkable. She does not use tobacco, excessive alcohol, or illicit substances. The patient has not noticed any weight loss, but she does endorse some changes in her voice lately. Temperature is 37.0°C (98.6°F), pulse is 75/min, and blood pressure is 135/85 mmHg. Physical examination reveals a fixed, non-tender nodule occupying the right thyroid lobe. Laboratory testing shows normal TSH levels. Ultrasound is obtained and reveals a 2.5 cm, hypoechoic nodule with increased central flow. Fine-needle biopsy is performed and shows the following: This finding can also be seen in which of the following conditions?



A.Squamous cell carcinoma of the lung

B.Schwannoma

C.Sarcoidosis

D.meningiomas



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