

Tumors of Lung

COLOR INDEX:

MAIN TEXT (BLACK)

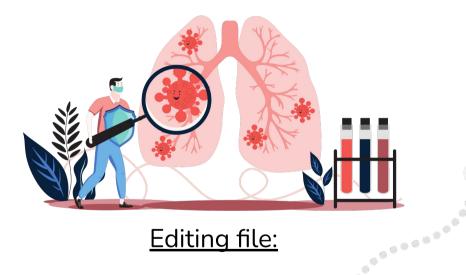
FEMALE SLIDES (PINK)

MALE SLIDES (BLUE)

IMPORTANT (RED)

DR'S NOTE (GREEN)

EXTRA INFO (GREY)



Editing file:



Objectives



Know the epidemiology of lung cancer



Aware of the new classification of bronchogenic carcinoma which include squamous carcinoma, adenocarcinoma, small cell and large cell (anaplastic) carcinomas



Understand the predisposing factors of bronchogenic carcinoma



Understands the clinical features and gross pathology of bronchogenic carcinoma. Know the precursors of squamous carcinoma (squamous dysplasia) and adenocarcinoma (adenocarcinoma in situ and atypical adenomatous hyperplasia)



Have a basic knowledge about neuroendocrine tumors with special emphasis on small cell carcinoma and bronchial carcinoid



Aware that the lung is a frequent site for metastatic neoplasms



Highly recommended!!!!!



Introduction

Primary lung cancer is a common disease BUT metastatic tumors are more common than the primary tumors.

95% of primary lung tumors are carcinomas.

Remaining 5% span a miscellaneous group that include

Carcinoids

mesenchymal malignancies (e.g., fibrosarcoma, leiomyomas)

lymphoma

benign lesions

Epidemiology

Carcinoma

Peak incidence is at 55 to 65 years of age.

Incidence of lung cancer is declining in men but increasing in women

Carcinoma of the lung is the most important cause of cancer-related deaths in industrialized countries

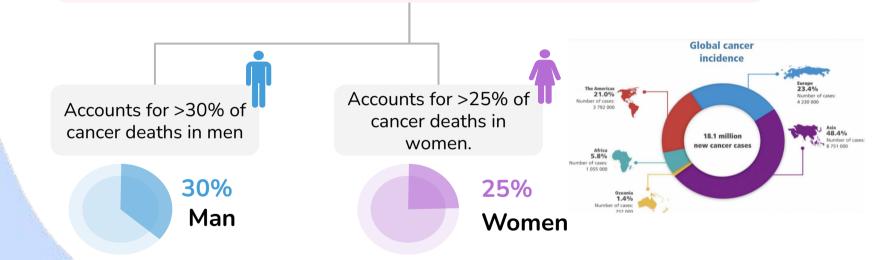




Table 13.6 Histologic Classification of Malignant Epithelial Lung Tumors (2015 WHO Classification, Simplified Version)

Adenocarcinoma

Acinar, papillary, micropapillary, solid, lepidic predominant, mucinous subtypes

Squamous cell carcinoma

Large cell carcinoma

Neuroendocrine carcinoma

Small cell carcinoma

Large cell neuroendocrine carcinoma

Carcinoid tumor

Mixed carcinomas

Adenosquamous carcinoma

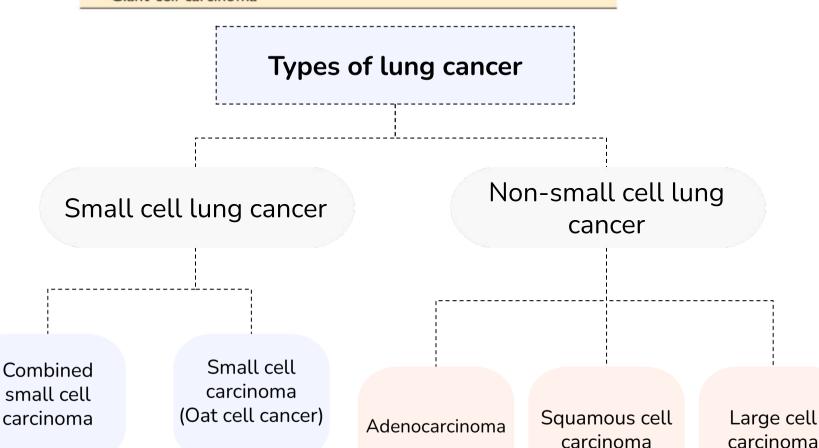
Combined small cell carcinoma

Other unusual morphologic variants

Sarcomatoid carcinoma

Spindle cell carcinoma

Giant cell carcinoma





Etiology and Pathogenesis

85% of lung cancers occur in cigarette smokers.

Most types are linked to cigarette smoking, but the strongest association is with squamous cell carcinoma and small cell carcinoma.

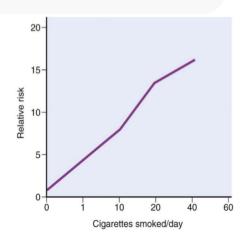
Is directly proportional to the number of cigarettes smoked daily and the number of years of smoking.

Cessation of cigarette smoking for at least 15 years brings the risk down.

Passive smoking increases the risk to approximately twice than non-smokers.

Cigarette smokers show various histologic changes, including squamous metaplasia of the respiratory epithelium which may progress to dysplasia, carcinoma in situ and ultimately invasive carcinoma.

- The risk of lung cancer is determined by the number of cigarettes smoked.
- The risk is 20 to 40 times greater among habitual heavy smokers.



Etiology and Pathogenesis

Study: " if women smoke like men , they will die like men"

- For unclear reasons, women are more susceptible to carcinogens in tobacco smoke than men.
- Female smokers have a much greater risk of death from lung cancer and COPD in recent years than female smokers 20 or 40 years ago.
- Female smokers today smoke more like men than women in previous generations, beginning earlier in adolescence and, until recently.

Radiation

All types of radiation may be carcinogenic and increase the risk of developing lung cancer. radium and uranium workers are at risk.

Asbestos

increased incidence of cancer with asbestos exposure, especially in combination with cigarette smoking.

Industrial exposure

to nickel and chromates, coal, mustard gas, arsenic, iron etc.

Predisposing factors

Air pollution

May play some role in increased incidence. Indoor air pollution especially by radon.

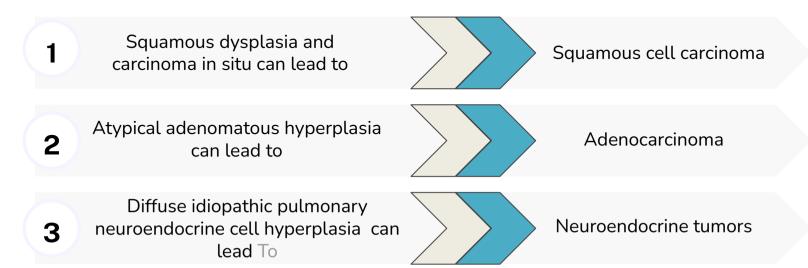
Scarring

sometimes old infarcts, wounds, scar, granulomatous infections are associated with adenocarcinoma.

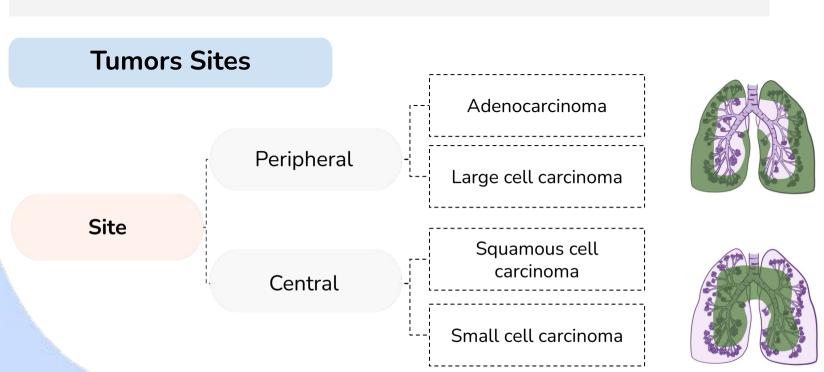
Gender

Women more susceptible Than men

Precursor lesions



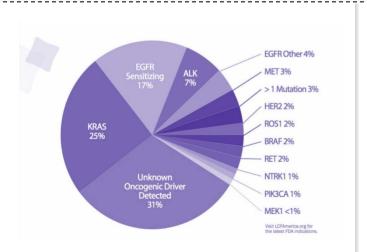
It should be noted that the term "precursor" does not imply that progression to invasion will occur in all cases



- Adenocarcinomas is now the most frequent histologic carcinoma.
- Usually, peripheral located tumors and arising from the peripheral airways and alveoli.

More common in young women

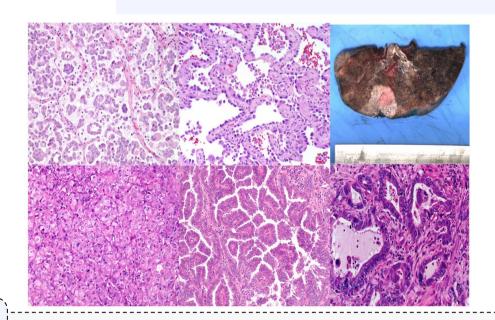
- About 10% in whites.
- 30% in Asians, particularly those arising in non-smoking women, harbor mutations that activate the epidermal growth factor receptor (EGFR).
- EGFR and KRAS mutations can occur and in 30% of adenocarcinomas.
 - *tumors with this mutation are often sensitive to drugs that inhibit EGFR signaling
 - **if you remember from foundation block, this is the gene that control the "checkpoints" of the cell proliferation



Adenocarcinoma

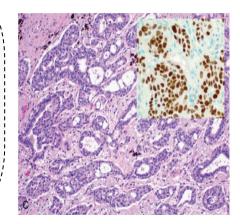
	Туре	Description	Picture
The spectrum	Atypical adenomatous hyperplasia	 Small lesion (≤5 mm) characterized by dysplastic pneumocytes lining alveolar walls that are mildly fibrotic looks like normal lung, normal interstitium, but only thickened, no invasion 	A
	Adenocarcinoma in situ (AIS)	 Lesion that is less than 3 cm is composed entirely of dysplastic cells growing along preexisting alveolar septae no growth patterns other than lepidic* no feature of invasion component, LVI no necrosis looks like ADH but bigger *lipidic means that it looks like a normal lung but has thickened interstitium and atypical cells 	-B
	Minimally invasive adenocarcinoma (MIA)	 ≤3 cm describes small solitary adenocarcinomas with either pure lepidic growth or predominant lepidic growth with ≤5 mm of stromal invasion. They have different growth pattern acinar pattern (gland-forming) papillary: finger like projection solid 	

Adenocarcinoma



- A. a lung with adenocarcinoma
- B. Malignant glands lined by cells showing irregular nuclei and prominent nucleoli.

- IHC*: TTF-1 positive (brown nuclear stain)**.
 - *immunohistochemistry
 - **TTF-1 has also been a useful marker for differentiating primary lung adenocarcinoma from pleural
 - mesothelioma



- Targeted therapies, such as EGFR inhibitor therapy for adenocarcinomas with EGFR mutations, can be effective
- in addition to surgery, that is why it is important to screen for the mutation of the tumor
 - *mostly all of the NSCLC don't respond very well to chemotherapy, however targeting a special oncoproteins is more approved .

SQUAMOUS CELL CARCINOMA

Overview

Large lesions may undergo central necrosis, giving rise to cavitation.

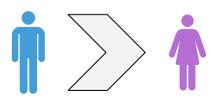
Squamous cell carcinomas often are preceded by the development, over years, of squamous metaplasia (because of the irritation) or dysplasia in the bronchial epithelium, which then transforms to carcinoma in situ.

Eventually, the small neoplasm reaches a symptomatic stage, when a well-defined tumor mass begins to obstruct the lumen of a major bronchus, often producing distal atelectasis and infection.

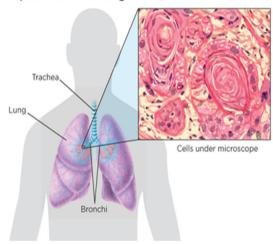
on the opposite of adenocarcinoma the tumor is central not on the periphery

Epidemiology

- more common in men than women
- closely correlated with a smoking history



Squamous Cell Lung Cancer



SQUAMOUS CELL CARCINOMA

#Explanation from Robbins

Description	Picture
# Some of the earliest and mild changes in smoking damaged respiratory epithelium induce globlet cell hyperplasia	A
#Basal or reserve cell hyperplasia	В
#Squamous cell metaplasia	C
 severe dysplasia, because it reached to the whole thickness, but still it is somewhat organized #More ominous changes include the appearance of squamous dysplasia characterised by the presence of disordered squamous epithelium with loss of nuclear polarity, nuclear hyperchromasia pleomorphism and mitotic figures 	D
 disorganization or loss of polarity → carcinoma in situ 	E
 invasive squamous cell carcinoma # E& F squamous dysplasia may in turn progress through the stages of mild to moderate to severe dysplasia . 	F

SQUAMOUS CELL CARCINOMA

Overview

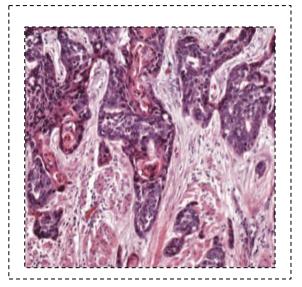
These tumors range from well- differentiated squamous cell neoplasms showing keratin pearls and intercellular bridges (space between cells), and polygonal large cells, to poorly differentiated neoplasms exhibiting only minimal squamous cell features

Squamous cell
carcinoma appearing as
a central (hilar) mass
that is invading
contiguous
parenchyma



Well- differentiated squamous cell carcinoma, showing keratinization and pearls.

- if we have keratin pearls
- → well differentiated
- the less the keratin pearls
- → poorly differentiated



Large Cell Carcinoma

Definition

- These group of carcinomas are undifferentiated.
- Undifferentiated malignant epithelial tumors that lack the cytologic features of neuroendocrine carcinoma and show no evidence of glandular or squamous differentiation.
- Poor prognosis.

Epidemiology

Frequency: 10 %.

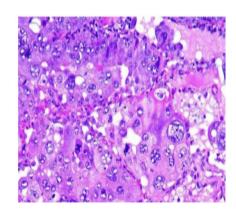
Strongly associated with smoking.

Cells

The cells typically have large nuclei, prominent nucleoli, and moderate amounts of cytoplasm.

Site

Large-cell carcinoma are usually located peripherally.





Carcinoid Tumor

Definition

Malignant tumors composed of cells that contain dense-core

neurosecretory granules in their cytoplasm.

Epidemiology

- Account for 2% of all primary lung cancers.
- No sex predilection and are not related to cigarette smoking or other environmental factor.
- Usually seen in adults.

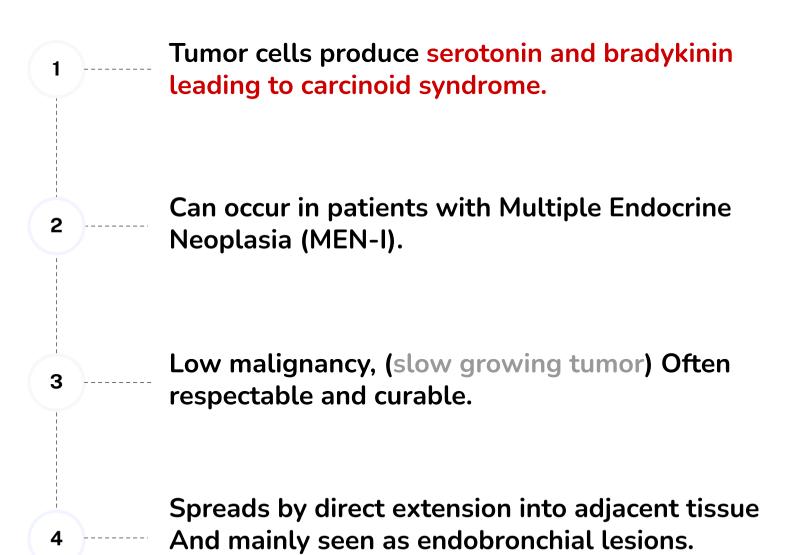
Site

Can be central or peripheral in location.

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Carcinoid Tumor

Complications and Prognosis



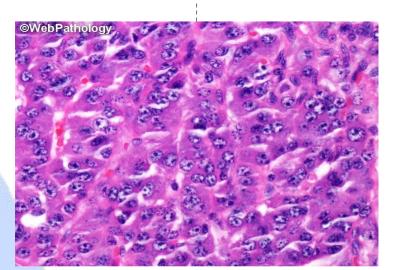
Carcinoid Tumor

Types of Carcinoid Tumor

typical carcinoids

الخلايا من جوا كانها ملح وفلفل شوفوا نقط بيضاء وسوداء

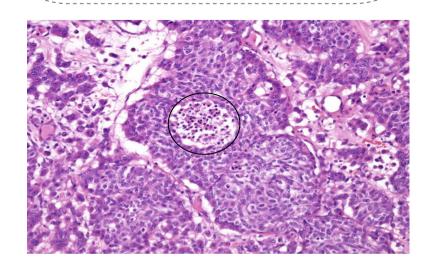
are composed of nests of uniform cells that have regular round nuclei with "salt-and-pepper" chromatin, absent or rare mitoses and little pleomorphism



Atypical carcinoid

الدائرة السوداء تعبر عن الفيتشر الابرز ومكتوبة بالإحمر. □

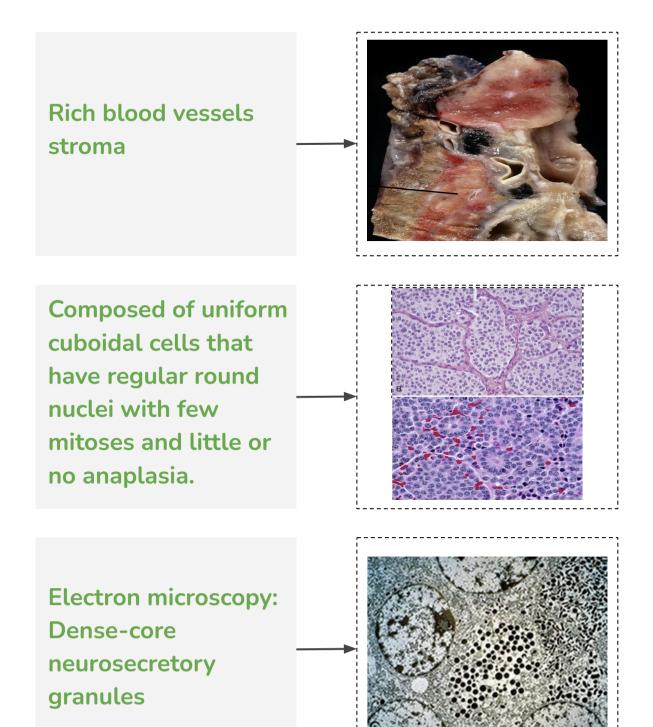
and small foci of necrosis. These tumors have a higher incidence of lymph node and distant metastasis than typical carcinoids



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Histologic appearance demonstrating small, rounded, uniform nuclei and moderate cytoplasm+ الصور من برا الكتاب والسلايد

Carcinoid Tumor



,....

Definition

a type neuroendocrine tumors arising from neuroendocrine cells.

Epidemiology

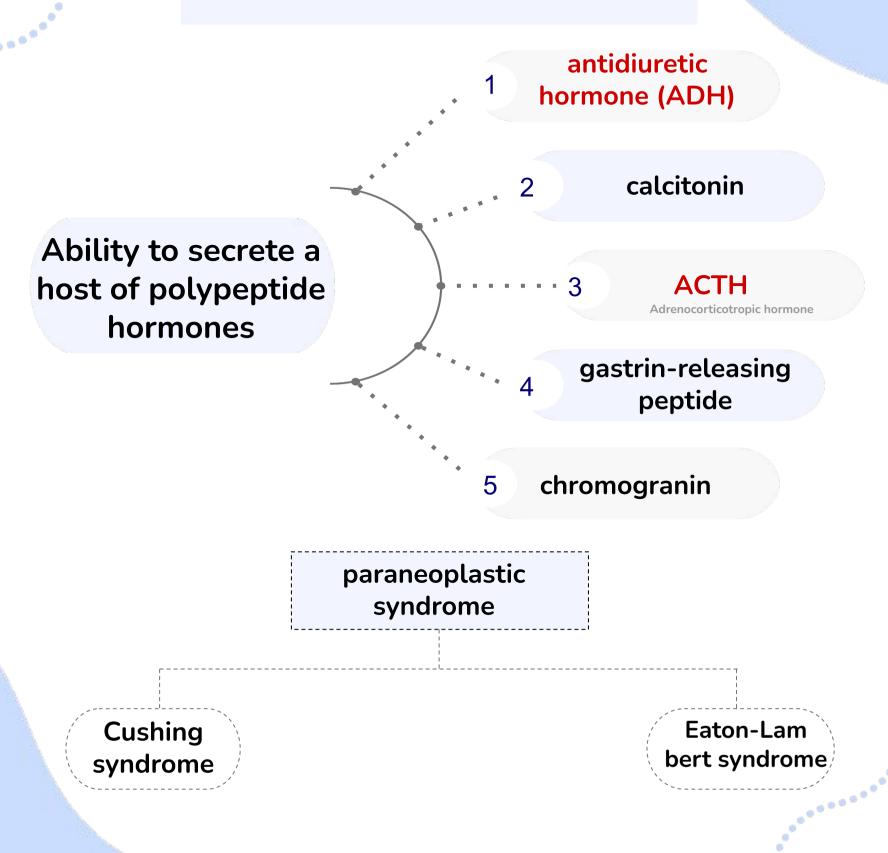
- More common in men.
- Strongly associated with cigarette smoking. 95% of patients are smokers.

Prognosis & Treatment

Highly malignant and aggressive tumor, poor prognosis, rarely respectable.

least likely form to be cured by surgery; usually already metastatic at diagnosis

Chemotherapy responsive.



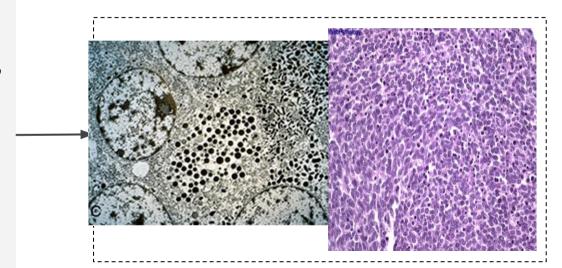
Gross: Centrally located perihilar mass with early metastases (Early involvement of the hilar and mediastinal nodes)





Microscopic:

- Microscopically composed of small, dark, round to oval, lymphocyte-like cells with little cytoplasm.
- Necrosis, apoptosis, crushing artifact
- Electron microscopy: dense-core neurosecretory granules.



Clinical picture:

- -Can be silent or insidious lesions.
- -chronic cough and expectoration, hemoptysis, and bronchial obstruction, often with atelectasis.
- -Hoarseness, chest pain, superior vena cava syndrome, pericardial or pleural effusion.
- -Symptoms due to metastatic spread.

Clinical Picture	Description			
Superior vena cava syndrome	invasion leads to obstruction of venous drainage which leads to dilation of veins in the upper part of the chest and neck resulting in swelling and cyanosis of the face, neck, and upper extremities.			
Pancoast tumor (superior sulcus tumor)	 Apical neoplasms may invade the brachial sympathetic plexus to cause severe pain, numbness and weakness in the distribution of the ulnar nerve. Pancoast tumor is often accompanied by destruction of the first and second ribs and thoracic vertebrae. It often coexists with Horner syndrome. 			
Horner syndrome	invasion of the cervical thoracic sympathetic nerves and it leads to ipsilateral enophthalmos, miosis, ptosis, and facial anhidrosis.			
Hoarseness	from recurrent laryngeal nerve paralysis.			
Pleural effusion	often bloody.			

Paraneoplastic syndrome

Definition

very important all symptoms !!!!!!!!!!

Paraneoplastic syndrome of lung cancer, are extrapulmonary, remote effects of tumors.

 3% to 10% of lung cancers develop paraneoplastic syndromes

Small cell carcinomas

- ACTH (leading to Cushing's syndrome)
- ADH (water retention and hyponatremia)

Carcinoid tumors

-Produce serotonin and bradykinin leading to carcinoid syndrome (flushing, wheezing, diarrhea, and cardiac valvular lesions

Squamous cell carcinomas

-may secrete parathyroid hormone-like peptide and prostaglandin E that lead to hypercalcemia

Adenocarcinomas

-can lead to hematologic manifestations

.....

Complications and spread of Paraneoplastic syndrome.

3

5

Pericardial or pleural spaces Infiltrate the superior vena cava.

Phrenic nerve invasion
usually causes
diaphragmatic paralysis:
- May invade the brachial or
cervical sympathetic plexus
(Horner's Syndrome).

Lymph nodes

Primary tumour

Liver

Adrenal glands

Blood vessel

Circulating

Lymphatic spread:

- Successive chains of nodes (scalene nodes).
- Involvement of the supraclavicular node (Virchow's node).

A tumor may extend directly into the esophagus, producing obstruction sometimes complicated by a fistula.

to liver (30-50%), adrenals (>50%), brain (20%) and bone (20%).

Complications and spread of Paraneoplastic syndrome.

Bronchiectasis

Obstructive pneumonia

Complications

Pleural effusion

Superior vena cava syndrome

Prognosis

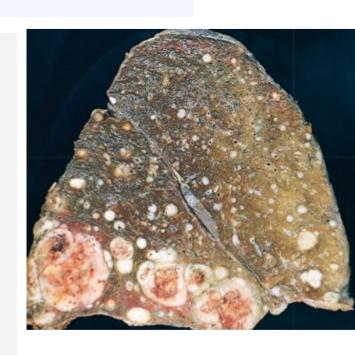
NSCLC have a better prognosis than SCLC

Outlook is poor for most patients

	Small Cell Lung	
Feature	Carcinoma	Non-Small Cell Lung Carcinoma
Histology		
	Scant cytoplasm; small, hyperchromatic nuclei with fine chromatin pattern; nucleoli indistinct; diffuse sheets of cells	Abundant cytoplasm; pleomorphic nuclei with coarse chromatin pattern; nucleoli often prominent; glandular or squamous architecture
Neuroendocrine Markers		
For example, dense core granules on electron microscopy; expression of chromogranin, synaptophysin, and CD56	Present	Absent
Epithelial Markers		
Epithelial membrane antigen, carcinoembryonic antigen, and cytokeratin intermediate filaments	Present	Present
Mucin	Absent	Present in adenocarcinomas
Peptide hormone production	Adrenocorticotropic hormone, anti-diuretic hormone, gastrin-releasing peptide, calcitonin	Parathyroid hormone—related peptide (PTH-rp) in squamous cell carcinoma
Tumor Suppressor Gene Abnormalities		
3p deletions	>90%	>80%
RB mutations	~90%	~20%
p16/CDKN2A mutations	~10%	>50%
TP53 mutations	>90%	>50%
Dominant Oncogene Abnormalities		
KRAS mutations	Rare	~30% (adenocarcinomas)
EGFR mutations	Absent	~20% (adenocarcinomas, nonsmokers, women)
ALK rearrangements	Absent	4%-6% adenocarcinomas, nonsmokers, often have signet ring morphology
Response to chemotherapy and radiotherapy	Often complete response but recur invariably	Incomplete

Metastatic Carcinoma of the lung

- Pulmonary Metastases are More Common than Primary Lung Tumors.
- Metastatic tumors in the lung are typically multiple and circumscribed.
 When large nodules are seen in the lungs radiologically, they are called cannonball metastases.
- The common primary sites are the breast, stomach, pancreas, and colon.



Mesothelioma

Definition

- Malignant tumor of mesothelial cells lining the pleura
- Highly malignant neoplasm.

Epidemiology

Most patients (70%) have a history of exposure to asbestos.

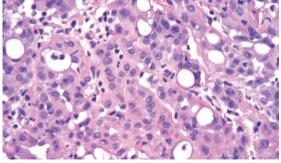
Smoking is not related to mesothelioma.

The average age of patients with mesothelioma is 60 years.

Findings

- Three main histological variants: epithelioid, spindle cell, biphasic.
- Pleural mesotheliomas tend to spread locally(started unilateral then spread to be bilateral) within the chest cavity, invading and compressing major structures.
- Metastases can occur to the lung parenchyma
- and mediastinal lymph nodes, as well as to extrathoracic sites e.g., liver, bones, peritoneum
- Treatment for mesothelioma is largely ineffective and prognosis is poor: few patients survive more than 18 months after diagnosis





Summary

positive

الجدول من مصدر خارجی بس ممکن یسهل علیکم کثیر

CANCER	CHARACTERISTIC HISTOLOGY	ASSOCIATION	LOCATION	COMMENT
Small cell carcinoma	Poorly differentiated small cells with neuroendocrine differentiation, chromogranin positive	Male smokers	Central	Rapid growth and early metastasis; may produce endocrine (e.g., ADH or ACTH) or nervous system(e.g., Lambert-Eaton myasthenic syndrome) paraneoplastic syndromes
Adenocarcinoma	Glands, mucin (or TTF-l expression by immunohistochemistry (IHC)	Most common tumor in nonsmokers and female smokers	Peripheral	Adenocarcinoma in-situ exhibits columnar cells that grow along preexisting bronchioles and alveoli may present as pneumonia-like consolidation on imaging
Squamous cell carcinoma	Keratin pearls, intercellular bridges or p40 expression by IHC	Most common tumor in male smokers	Central	May produce PTHrP (Parathyroid hormone-related protein)
Large cell carcinoma	Poorly differentiated large cells (no glands, mucin, TTF-1, keratin pearls, intercellular bridges, or p40)	Smoking	Central or peripheral	Diagnosis of exclusion
Carcinoid tumor	Well differentiated neuroendocrine cells (nests); chromogranin 	Not significantly related to smoking	Central or peripheral; when central, classically forms a polyp-like mass in the bronchus	Low-grade malignancy; rarely, can cause carcinoid syndrome

Summary

- 1. The three major histologic subtypes are adenocarcinoma (most common), squamous cell carcinoma, and small cell carcinoma, each of which is clinically and genetically distinct.
- 2. Adenocarcinomas are the most common cancers overall and are especially common in women and in non-smokers.
- 3. Precursor lesions include atypical adenomatous hyperplasia and adenocarcinoma in situ for adenocarcinomas and squamous dysplasia for squamous cancer.
- 4. Tumors 3 cm or less in diameter characterized by pure growth along pre-existing structures without stromal invasion are called adenocarcinoma in situ.
- 5. SCLCs are best treated with chemotherapy, because almost all are metastatic at presentation. The other carcinomas may be curable by surgery if limited to the lung.
- 6. Targeted therapies, such as EGFR inhibitor therapy for adenocarcinomas with EGFR mutations, can be effective, an excellent example of personalized cancer therapy. Immunotherapies are under development and show promise.
- 7. Lung cancers commonly cause a variety of paraneoplastic syndromes.



Most likely case scenario will be related to smoking +women are more susceptible than men

	Nonsmokers + Location is peripheral		
Adenocarcinoma	EGFR and KRAS mutations can be present		
	Diagnosed by : IHC and TTF-1 positive as a marker		
	more in men + Location is central + may undergo central necrosis		
	differentiated:keratin pearls + intercellular bridges + polygonal large cells		
Squamous cell carcinoma	undifferentiated: little squamous features		
	release parathyroid hormone-like peptide and PGE lead to hypercalcemia		
	Undifferentiated with no cytologic features of neuroendocrine carcinoma and		
Large cell carcinoma	no evidence of glands or squamous features +		
	Location : can be central or peripheral but usually peripheral		
	neurosecretory granules + can have carcinoid syndrome +		
	can occur with MEN-1(gene)+		
Carcinoid tumor	Location is central or peripheral		
	Typical :normal nuclei with (salt and pepper) chromatin		
	atypical:small foci of necrosis		
	Neuroendocrine cells + with smokers +		
Small call carcinoma	secrete hormones mentioned in click here		
Small cell carcinoma	associated with cushing +lambert-eaton syndrome and others		
	Location is central		
	exposure to asbestos and affect the pleura		
Mesothelioma	Histology : epithelioid spindle cells, Biphasic		
	Location: mesothelial cells lines the pleura		



1- Which of the following has a feature of small foci of necrosis					
A) squamous cell carcinoma	B)Typical Carcinoid tumor	C)Atypical Carcinoid tumor	D) Large cell carcinoma		
2- Which of following is related to exposure of asbestos					
A)Mesothelioma	B)Squamous cell carcinoma	C) All of lung tumors	D) Small cell carcinoma		
3- Which of the following tumors is related to EGFR and KRAS					
A)Adenocarcinoma	B)Small cell carcinoma	C)Large cell carcinoma	D)Carcinoid Tumor		
4- Which of the following can be located only peripherally					
A)Large cell carcinoma B)Carcinoid tumor C)Adenocarcinoma D)Small cell carcinoma					
5- Which of the following is only located centrally					
A)Adenocarcinoma B)Squamous cell carcinoma C)Large cell carcinoma D) Carcinoid Tumor					



1- a 25 year old women came to emergency experiencing persistent cough with blood and has					
dyspnea,after taking his	tory there was repeated r	espiratory infections and	fatigue and weight loss		
without following a diet	plan and noticeable whe	ezing sound when breath	ning then Doctor		
suspected a mass to ma	ke sure a IHC was done a	ınd TTF-1 is positive.Whi	ch of the following is		
the right diagnosis?					
A)Mesothelioma	B)Small cell carcinoma	C)Adenocarcinoma	D)Squamous cell carcinoma		
2- a 55 year old Arthur N	Morgan has a history of sr	moking for 37 years he vis	sited the doctor years		
ago and was advised to	stop smoking but he didr	n't care so in his recent vis	it he complained of		
chronic cough and hoars	seness and trouble in swa	llowing then a biopsy wa	s taken from the center		
of the lung and the path	nologist saw keratin pearl	s with intercellular bridge	s and cells were well		
differentiated what do u	think is the diagnosis?				
A)Small cell carcinoma	B) Large cell carcinoma	C) Carcinoid Tumor	D) Squamous cell carcinoma		
·	B) Large cell carcinoma ved a biopsy of a mass loc	·	carcinoma		
3- the pathologist receiv		ated peripherally on lung	carcinoma from a heavy smoker		
3- the pathologist receive patient called Arthur Mo	ved a biopsy of a mass loc	rated peripherally on lung	from a heavy smoker undifferentiated cells		
3- the pathologist received patient called Arthur Mowenith large nuclei and mo	red a biopsy of a mass loc organ and what he saw u	rated peripherally on lung nder the microscope was: asm and no signs of gland	from a heavy smoker undifferentiated cells ds or mucin and		
3- the pathologist received patient called Arthur Mowenith large nuclei and mo	ved a biopsy of a mass loc organ and what he saw u oderate amount of cytopla	rated peripherally on lung nder the microscope was: asm and no signs of gland	from a heavy smoker undifferentiated cells ds or mucin and		
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1- A 75 year old man is diagnosed with carcinoid tumor and was experiencing in his last 2 months symptoms like diarrhea, flushing and wheezing and blood test was done and was found that certain molecules were elevated like serotonin and?					
A)ADH	A)ADH B)Angiotensin C)ACTH D)Bradykinin				
2- A 67 year old man heavy smoker came to the ER was scared cuz he was experiencing swelling and cyanosis in his face and neck with hoarseness what do u think these symptoms apply to which of the following tumors?					
A)Squamous cell carcinoma	B)Large Cell carcinoma	C)Small cell carcinoma	D)Adenocarcinoma		
3- A mass was found on the apices of the lung involved with destruction to 1st and 2nd ribs to one of the patients that has numbness, swelling and pain radiating all over his upper arm and has weakness in areas supplied by ulnar nerve, Which of the following is correct?					
A)Cushing syndrome	B)Superior vena cava syndrome	C)Pancoast tumor	D)Horner syndrome		
4- a 55 year old man called Foulan has been exposed to danger due to his work nature for over 30 years of his career, during his work he often uses materials that contains asbestos without protective measures, recently he started experiencing dyspnea, persistent cough, fatigue and loss of weight. A biopsy was done what do u think is the diagnosis?					
A)Adenocarcinoma	B)Mesothelioma	C)Small cell carcinoma	D)Squamous cell carcinoma		
5)A 55 year old patient was a heavy smoker was diagnosed with a mass that caused water retention and hyponatremia which of following is suspected to be the cause					
A)Adenocarcinoma	B)Squamous cell carcinoma	C)Small cell carcinoma	D)Large cell carcinoma		

Pathology team

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Leader

Abdulaziz Nasser

Leader

Ghaida saad

Shahad Alzenaidy

Aram Alzahrani

Haya alkhlaiwi

Elaaf Albadi

Norah Albahily

Joud Alahmri



Waleed Alanazi

Khalid Alkanhal

Khalid Aldukheyl

Moath Alabdussalam

Nasser Alabdussalam

Abdulaziz Alanazi



Abdulaziz Alobathani

