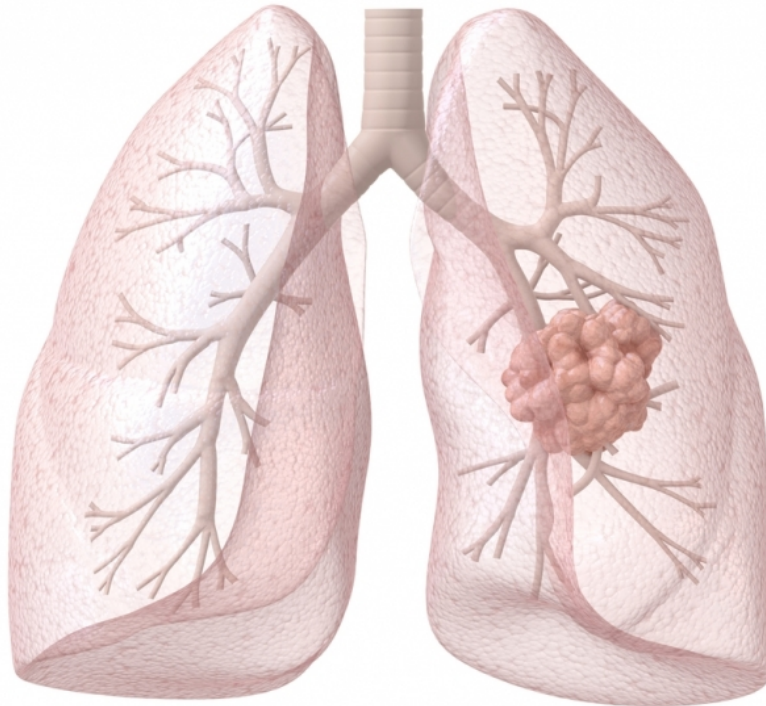


Lung Tumors



Objectives:

- Understand the incidence, age group of affected patients and predisposing factors of bronchogenic carcinoma.
- Is aware of the classification of bronchogenic carcinoma which include: squamous carcinoma, adenocarcinoma, small cell and large cell (anaplastic) carcinomas.
- Understands the clinical features and gross pathology of bronchogenic carcinoma.
- Have a basic knowledge about neuroendocrine tumours with special emphasis on small cell carcinoma and bronchial carcinoid.
- Is aware that the lung is a frequent site for metastatic neoplasms.

Important note: During the previous blocks, we noticed some mistakes just before the exam and we didn't have the time to edit the files. To make sure that all students are aware of any changes, please check out this link before viewing the file to know if there are any additions or changes. The same link will be used for all of our work:

[Pathology Edit](#)

Introduction.

At least 1,000,000 people die every year because of tumors of the lungs. It is important because smoking the very major factor for cancer of the lung. Of course whenever we talk about tumors we keep in mind that not all tumors are malignant as there are benign tumors.

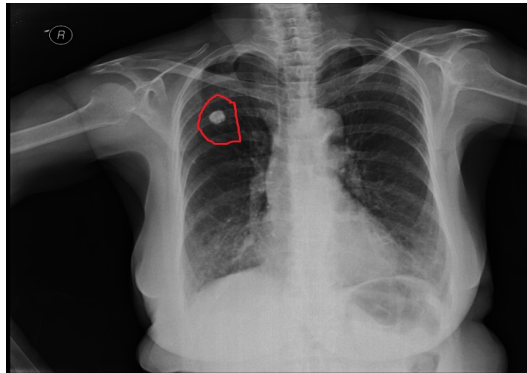
Tumor: is an abnormal mass of tissue the growth (proliferation) of which exceeds and is uncoordinated with that of normal cells within that tissue from where it risen. **we are going to start with the benign tumors:**

benign tumors.

Benign tumors of the lungs are very *rare*. The most common benign tumor of the lung is spherical , small , discrete “**Hamartoma**” that often shows up as so called **coin lesion** in chest radiographs sometimes they call it *leave me alone lesion* because it is not doing anything just setting there.

Hamartoma: is an abnormal mass tissues in the organ, theses tissues are indigenous¹ to that site. (Unlike *Choristoma* which means a mass composed from normal cells in different location, like finding pancreatic cell in liver or stomach) In lung it consists mainly of *mature cartilage*, but this sometimes admixed fat, fibrous tissue and blood vessels in various proportions.

This tumor usually discovered at the routine medical examinations by coincidence² and it is not related to any symptoms .



X-Ray shows Hamartoma “Coin lesion”

¹ Same type of tissue.

coincidence = بالصدفة ²

Malignant tumours.

Malignant tumours of the lungs represent about 90% of the tumours of the lung.

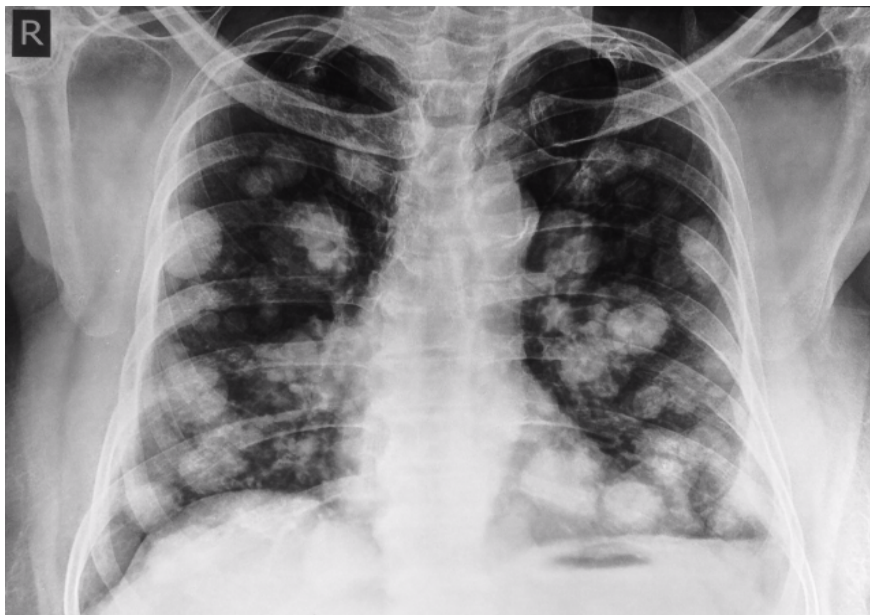
The larger part of them are **metastatic** to lung from other organ such as *gastrointestinal tract*, where the tumours that are metastatic usually will cause multiple masses and multiple nodules.

If the patient has chest X-ray and it shows a single mass in the hilum³ or sub plural in the upper lobe or lower lobe. This mostly will be *primary tumour* and it was raised from the lung.

If you ask the patient if he **smokes** or not & he says yes then you already know that he has a malignant tumour.

Clinical case: A 26 years old female who doesn't smoke. She presents with weight loss and Weaken. She said that she had mastectomy 3 years ago. When you do the chest **X-Ray** or **CT-Scan** you find that she has **multiple** nodules which are called **cannon balls**, and don't have a single lesion. Because she doesn't smoke, young, doesn't have only single nodule, you should think that she has metastatic tumours, & you have to look for the **primary tumour**.

- Almost any cancer has the ability to spread to the lungs, but the tumors that most commonly do so include bladder cancer, colon cancer, breast cancer, prostate cancer, sarcoma, Wilms tumor, and neuroblastoma.



X-Ray Picture shows Cannon balls Metastasis.

³ Hila, or **lung** roots, are relatively complicated structures that consist mainly of the major bronchi and the pulmonary arteries and veins.

Primary tumours of the lung the most important cause for them is *smoking*.

The hand of smoker you characterized by :

- 1- pigmentation in his nails and skin
- 2- clubbing fingers.
- 3- the tips of the fingers enlarged and resemble drum stick.

Note: not all clubbing indicate lung disease it could be a cardiovascular disease or congenital .



fingers enlarged and resemble drum stick.

Symptoms related to any cancer:

- 1) weight loss
- 3) iron deficiency anaemia
- 4) muscle wasting
- 5) fatigue

This apply to any cancer, in the skin, gastrointestinal, lung or another organ.



Cancer Patient

Specific symptoms for lung cancer :

- 1-cough with blood
- 2-chest pain and dyspnea
- 3-pleural effusion
- 4-wasting wight
- 6-Hoarseness⁴

⁴ Hoarseness = بحة في الصوت

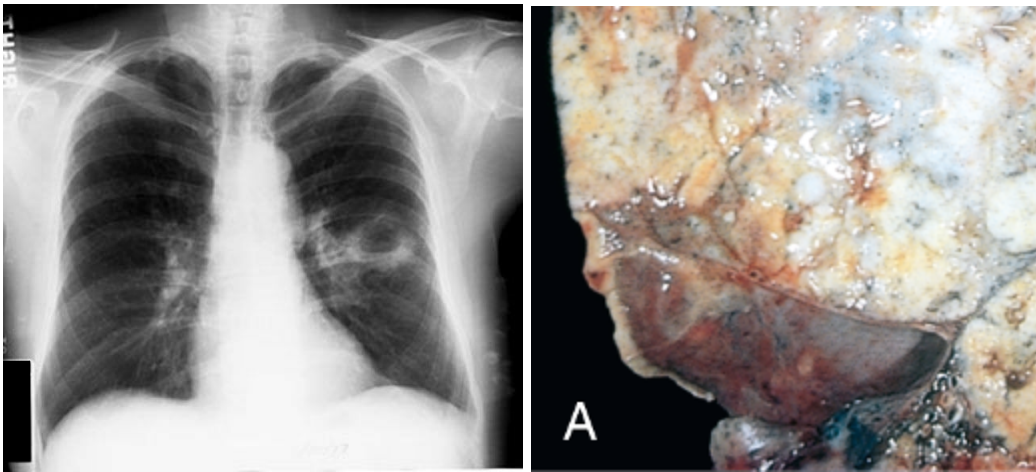
Malignant tumors divided into two types:

- **Non-Small Cell Lung Carcinoma (NSCLC):**
 1. Squamous cell carcinoma.
 2. Large cell carcinoma.
 3. Adenocarcinoma.
- **Small Cell Lung Carcinoma (SCLC).**

A. Non-Small Cell Lung carcinoma (NSCLC):

1) squamous cell carcinoma

squamous cell carcinoma is a very common tumour of the lung closely correlated with a *smoking* history, it usually present as central hilar mass but it is large and might reach the periphery.



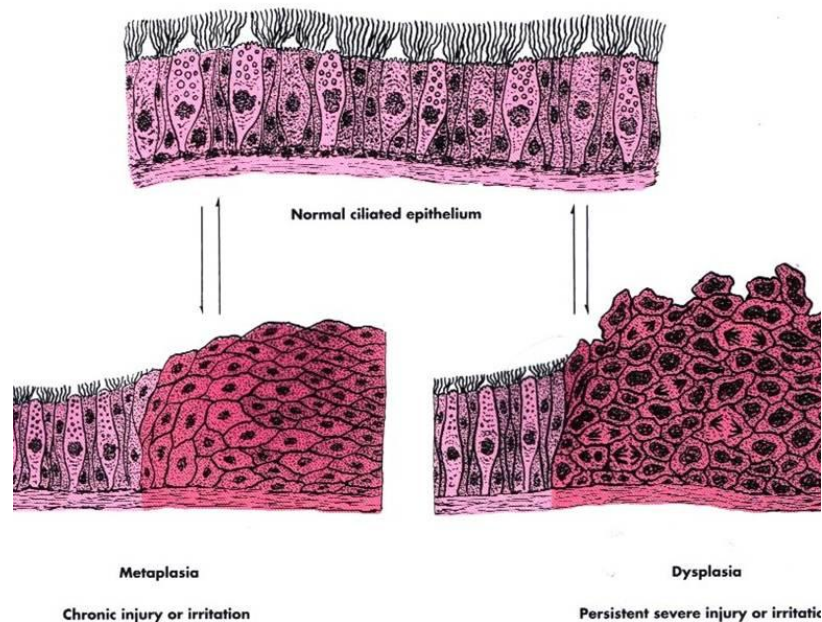
Left: X-Ray picture show patient with squamous cell carcinoma, you can see here hilum tumors.

Right: Squamous cell carcinoma usually begins as a central (hilar) mass and grows continuously into the peripheral parenchyma as seen here.

How does cancer develop cancer in smokers?

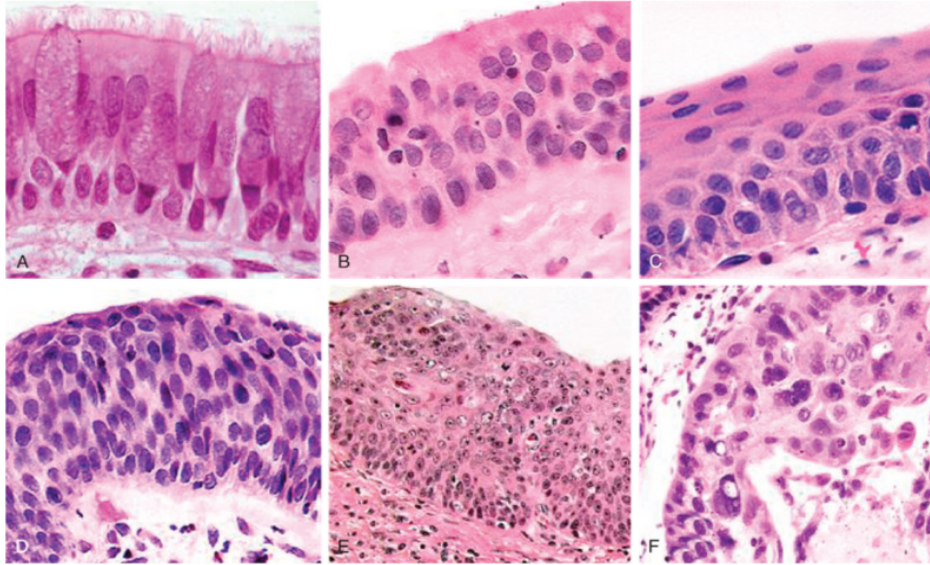
Irritation of the respiratory epithelium → Ciliated respiratory epithelium undergoes *squamous metaplasia* (might lead to having a chronic obstructive airway disease or not) → After that if he doesn't quit smoking metaplasia will turn into **dysplasia** (which is a premalignant cellular change where the cells becomes atypical) → Carcinoma in situ (when dysplastic changes involve the entire thickness of the epithelium) → Squamous cell carcinoma.

Test we do: Sputum specimen (Cytology test).



The changes in the cells of neoplasia are (We can find them by examining the pleural fluid):

- 1) nuclear hyperchromasia.
- 2) nuclear irregularity.
- 3) nuclear pleomorphism (variation in size and shape between cells).
- 4) mitosis



We know that squamous cell carcinoma is *well-differentiated* when we obtain a biopsy & find **keratin pearls** and **intercellular bridges** (it is the junction between squamous cells that links these cells together). Squamous cell carcinoma can be present with **hypercalcemia**⁵ and it is one of the **paraneoplastic syndrome**.

Complication: in squamous carcinoma the mass could involve the hilar lymph node making an obstruction in the main bronchi.

Remember: When you find a single mass it means that the tumor is primary and usually caused because of smoking, but if you find multiple nodules it means that the masses have metastasized from another region which means it's secondary.

Well-differentiated cancer cells look and behave like the normal cells in the tissue they started to grow in. They tend to be slow growing and less aggressive.

Undifferentiated or **poorly differentiated** cancer cells look and behave differently from normal cells in the tissue they started to grow in. They resemble the tissue of origin at all. They are more aggressive & tend to grow quicker, spread more often and have a worse prognosis than tumours with well-differentiated cancer cells.

⁵ is a condition in which the calcium level in your blood is above normal.

2) Adenocarcinoma of lung

TYPE OF TUMOR	LOCATION	COMMENTS	clinical manifestation
Adenocarcinoma (glandular cell) or scar carcinoma	Peripheral	1: Most common cancer in nonsmoker 2: More common in women 3: High frequency of EGFR mutations 4: Contain malignant glands secreting mucin 5: Develop in a scar	1: Compression of sympathetic chain because it is in the peripheral = Pancoast tumor (ptosis, miosis and anhidrosis) 2: Pleural involvement 3: Finger clubbing
Bronchioloalveolar carcinoma or the new name is Adenocarcinoma in situ		1: It is one type of the adenocarcinoma 2: Here the tumour cells are running with the basement membrane 3: Drive from mucin secreting cells or Clara cells 4: High frequency of EGFR mutations	

3) large cell carcinoma

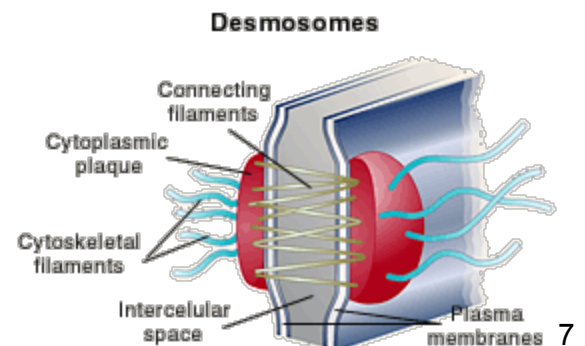
Also is called **anaplastic large cell carcinoma**. In anaplastic large cell carcinoma the cells are very undifferentiated, they are lost between being squamous or glandular cells. This type of tumor is related to **smoking** as well and it is very aggressive. However, If seeing it under electron microscope you may find some of them differentiated to glandular or squamous cells.

What do stages of tumor means? (TMN system)

- 1) Size of the **T**umor.
- 2) Presence or absence of distant **M**etastasis (انتشاره).
- 3) Presence or absence of **N**umber of regional lymph nodes.

Important note: when treating a cancer you should consider the **TNM system**. For example if the cancer is in stage 1 (small size) it shows that it has a good prognosis, but if it had metastasized to other organs the prognosis isn't good at all.

This type of tumor is always **grade 3**. Because it is **poorly differentiated**, it's unable to make new cells, like glands or even desmosomes (a structure by which two adjacent cells are attached, formed from protein plaques), and because it is primitive that's why it is **aggressive**. The tumors of the lung can **metastasize** to any organ and since it is **carcinomas** they spread by **lymphatic**. Sarcomas **metastasize** through blood vessels.



Now we will shed some light on the role of the genes and genetic therapy in lung cancer. most of the lung tumors are associated with a mutation on **TB53** or **B53** that is a tumor suppressor gene. when this gene is mutated the tumor will develop, this is the case in 90% of the lung tumors could develop. the other mutation are in **chromosome 3** there is deletion in the short arm. and also other mutation in gene **P16** and **RBG**. Now the gene can encode for protein, and when this mutated protein causes the formation of a tumor we call it **oncogene**.

what is the most important two oncogenes in lung cancer?

1) EGF1 (epithelial growth factor gene) which is found in 20% of cases of **adenocarcinoma**. in the advancement of pharmacology we have drugs called **anti-EGFR**, this drug as soon as you give it to the patient will reduce and stop the growth of the tumor thats why when we diagnose **adenocarcinoma** we do a molecular testing for this gene.

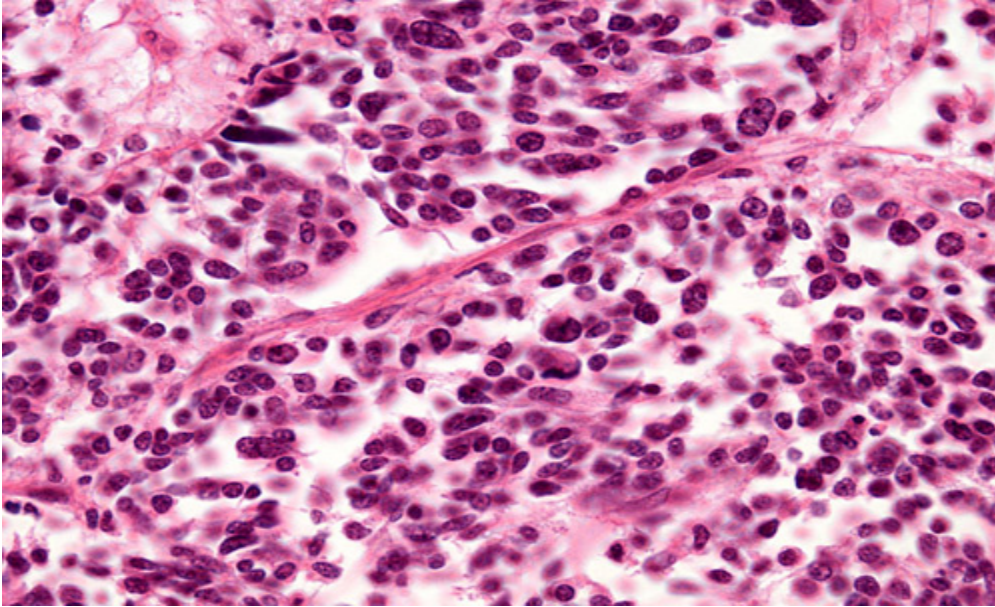
2)ALK1 (Anaplastic lymphoma kinase) this oncogene is found in small amount.

- Small cell carcinomas are treated by **chemotherapy**, while **large cell carcinomas** are treated by targeting specific mutated genes because they respond poorly to chemotherapies.

B. Small cell carcinoma or oat (الشعير) cell carcinoma

It is called **oat** because the nuclei looks like oat (حبة الشعير)

Characteristics of tumor:



Considered a neuroendocrine tumour of the lung. (Because it arises neuroendocrine cells)

- Aggressive, highly malignant, poor prognosis
- Related to smoking (unlike adenocarcinoma)
- Common in men
- Associated with cigarette smoking 95% of patients
- Present as hilar or perihilar mass
- Responds to chemotherapy.
- Least likely to be cured by surgery; it usually metastatic at diagnosis, mostly found at late stage
- Ability to secrete a host of polypeptide hormone as ACTH (adrenocorticotrophic hormone) , ADH (antidiuretic hormone).
- It may associated with Paraneoplastic Syndrome⁶, Cushing syndrome⁷, Eaton- Lambert syndrome⁸.

⁶ consequence of cancer in the body but that unlike mass effect is not due to the local presence of cancer cells.^[1] These phenomena are mediated by humoral factors (by hormones or cytokines) secreted by tumor cells or by an immune response against the tumor

⁷ describes the signs and symptoms associated with prolonged exposure to inappropriately high levels of the hormone cortisol. This can be caused by taking glucocorticoid drugs, or diseases that result in excess cortisol, adrenocorticotrophic hormone (ACTH).

⁸ Autoimmune disease which immune system attacks owns body tissues.



SUMMARY

Carcinomas of the Lung

- The four major histologic subtypes are adenocarcinomas (most common), squamous cell carcinoma, large cell carcinoma, and small cell carcinoma.
- Each of these is clinically and genetically distinct. SCLCs are best treated by chemotherapy, because almost all are metastatic at presentation. The other carcinomas may be curable by surgery if limited to the lung. Combination chemotherapy also is available along with anti-EGFR therapy for those adenocarcinomas with EGFR mutations, and ALK inhibitors for those with ALK mutations.
- Smoking is the most important risk factor for lung cancer; in women and nonsmokers, adenocarcinomas are the most common cancers.
- Precursor lesions include squamous dysplasia (for squamous cancer) and atypical adenomatous hyperplasia and adenocarcinoma in situ (formerly bronchioloalveolar carcinoma) (for some adenocarcinomas).
- Tumors 3 cm or less in diameter characterized by pure growth along preexisting structures (lepidic pattern) without stromal invasion are now called adenocarcinoma in situ.
- Lung cancers, particularly SCLCs, can cause *paraneoplastic syndromes*.

Carcinoid Tumors:

Carcinoid tumors are malignant tumors composed of cells that contain dense-core neurosecretory granules in their cytoplasm and, rarely, may secrete hormonally active polypeptides.

It is **well differentiated** and curable. Usually it will present as a nodule **peripherally** or **centrally** and by the secretion of its hormones it can rarely cause *carcinoid syndrome*, which is characterized by intermittent attacks of diarrhea, flushing (**vasodilation**), thrashing and cyanosis which are caused by **vasoactive amines**.

Neuroendocrine tumors: They are **neoplasms** that arise from cells of the **endocrine (hormonal)** and **nervous systems**.

Dr.Rekabi: They are Specialized cells in the mucosa between the epithelial cells and when examining them under the microscope you will find that they have granules in the cytoplasm which are neurosecretory granules that have vasoactive amines, hormones and many things. That's the reason we call it neuroendocrine / carcinoma or tumor.

- We have to diagnose it and differentiate it from adenocarcinoma and squamous cell carcinoma because the treatment, management and prognosis differ.

Cases:

Case 1: patient cut his leg because he had a bone tumour and now he has this cough, Doctor gave him a medication but it didn't work after examination we will find has **metastatic tumor**.

Case 2: patient had stage 1 squamous cell carcinoma, the patient need to **surgery** and remove the tumor

Case 3: Patient had adenocarcinoma stage 1 or 2, Surgeon can excise⁹ it for him.

Case 4: A patient came to have a check up, after examination everything showed normal except the elevation of the calcium, we say we will do a chest X-ray, the patient says that he has a cough and took a pink medication. after taking the x-ray you will find كرة قدم جالسة بصدرة so it could be the representing sign of **squamous cell neoplasm**. Now why do these people have hypercalcemia? it is caused by secretion of a parathyroid hormone-related peptide and this is usually common in this type of carcinoma not all people have it.

Case 5: When I have oat cell carcinoma there is only one way of treating it and it is **chemotherapy** and the prognosis is usually **bad** because by the time you start the treatment there is already metastasis happened these cells are very aggressive and they go everywhere, the other thing that this tumor can cause is another Paraneoplastic syndrome it can secrete **ACTH** (Adrenocorticotropic Hormone) and another hormone called **ADH** (antidiuretic hormone), when secreting this hormone it imitates¹⁰ the hormone or protein that is secreted from pituitary gland that stimulates the adrenal gland to secrete corticosteroid (patient that has nothing wrong with pituitary gland but he has oat cell carcinoma secreting as a Paraneoplastic syndrome this ectopic¹¹ hormone secretion . She has moon face and then she has hirsutism¹² and that all of the corticosteroid from elevated level of ACTH ectopic because she has lung cancer, after doing chest x-ray we find a small orange in her bronchi then we do sputum cytology, then we find small cell carcinoma. It is associated with **secondary Cushing syndrome** because of ectopic ACTH secretion by neuroendocrine tumor.



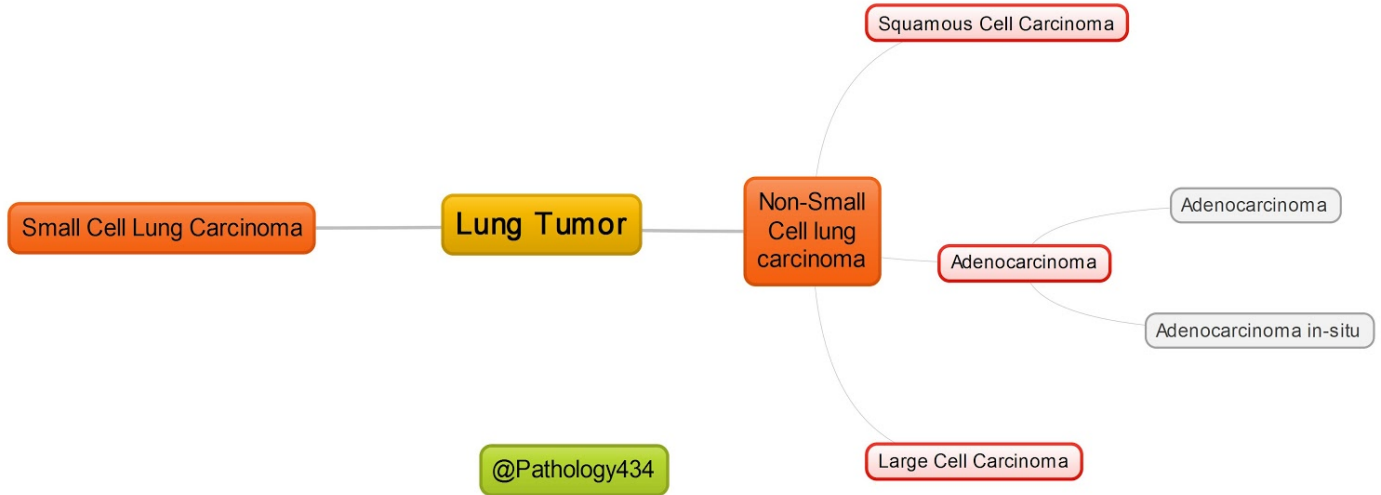
⁹ excise = استئصال

¹⁰ imitates = يقلد او يحاكي

¹¹ ectopic = (هاجم، غير طبيعي)

¹² hirsutism = شوارب

Summary



Matching Question.

A) IRON deficiency anemia	1) Squamous cell carcinoma
B) Not related to smoking	2) Small cell carcinoma
C) Eaton-Lambert syndrome	3) Large cell carcinoma
D) Peripherally located	4) Adenocarcinoma
E) Mucin production	5) Bronchoalveolar carcinoma
F) Associated with smoking	
G) Undifferentiated	
H) Well differentiated	
I) Centrally located	
J) Adenocarcinoma in situ	
K) PTH	
L) Paranur Endocrine secretions	

MCQs.

1- Which of the following is the most common type of lung cancer :

- a) Large cell carcinoma
- b) Small cell carcinoma
- c) Squamous cell carcinoma
- d) Bronchoalveolar carcinoma .

2- Which of the following tends to spread faster :

- a) Small cell carcinoma
- b) Adenocarcinoma
- c) Squamous cell carcinoma
- d) Large cell carcinoma

3- Which of the following is NOT true regarding squamous cell carcinoma :

- a) It can cause hypercalcemia
- b) It starts centrally and moves to the peripheries of the lung
- c) Cells are linked with desmosomes
- d) It is one of the few lung cancers found more frequently in non smokers

4- A 67 year old non smoker female presents with worsening dyspnea for the past 6 weeks. She has noticed 13 kg weight loss and occasional excessive sweating. On examination, she is in mild respiratory distress. Her RR is 22 and her BP is 134\76. The physician has also noticed ptosis on her left eye and miosis . chest X-ray shows peripheral mass in her right upper lobe of the right lung . what the most probable diagnosis :

- a) Large cell carcinoma
- b) Small cell carcinoma
- c) Adenocarcinoma
- d) Squamous cell carcinoma

5- A 53-year-old male smoker presents to the emergency department with exertional dyspnea that has progressed to dyspnea at rest and a cough for 1 month. Two weeks ago, he started having headaches and noticed swelling of his face. He noticed some urination disorders. Laboratory tests has shows excessive concentration of ADH (antidiuretic hormone).A chest radiograph demonstrates a suspicious nodule in the right hilar region. Which of the following types of lung cancer is most commonly associated with the signs and symptoms this patient is experiencing?

- a) Adenocarcinoma of the lung
- b) Small cell lung cancer (SCLC)
- c) Large cell carcinoma
- d) Squamous cell lung cancer .

6- 49-year-old man has sudden onset of severe lower abdominal pain with hematuria. He passes a ureteral calculus. Laboratory studies show that the calculus is composed of calcium oxalate. He is found to have a serum calcium concentration of 10.2 mg/dL, serum phosphorus level of 2.9 mg/dL, and serum albumin level of 4.6 g/dL. A chest radiograph shows a 7-cm hilar mass in the right lung. Chest CT scan shows prominent central necrosis in this mass. Which of the following neoplasms is most likely to be associated with these findings?

- a) Metastatic colonic adenocarcinoma
- b) Small cell anaplastic carcinoma
- c) Bronchioloalveolar carcinoma
- d) Squamous cell carcinoma

7- A 57-year-old woman comes to her physician because she has had a cough and pleuritic chest pain for the past 3 weeks. On physical examination, she is afebrile. Some crackles are audible over the left lower lung on auscultation. A chest radiograph shows an ill-defined area of opacification in the left lower lobe. After 1 month of antibiotic therapy, her condition has not improved, and the lesion is still visible radiographically. CT-guided needle biopsy of the left lower lobe of the lung is performed, and the specimen has the histologic appearance of neoplastic growth along pre existing alveolar septa without invasion . Which of the following neoplasms is most likely to be present in this patient?

- a) Adenocarcinoma
- b) Bronchioloalveolar carcinoma
- c) Hamartoma
- d) Squamous cell carcinoma

8- A 40-year-old woman has never smoked and works as a file clerk at a university that designates all work areas as “nonsmoking.” She goes to the physician for a routine health maintenance examination. On physical examination, there are no remarkable findings. A routine chest radiograph shows a 3-cm, sharply demarcated mass in the left upper lobe of the lung. Fine-needle aspiration of the mass is attempted, but the pathologist performing the procedure remarks, “This is like trying to biopsy a ping-pong ball.” No tissue is obtained. Thoracotomy with wedge resection is performed. On sectioning, the mass has a firm, glistening, bluish white cut surface. A culture of the mass yields no growth. Which of the following terms best describes this mass?

- a) Hamartoma
- b) Adenocarcinoma
- c) Large-cell carcinoma
- d) Squamous cell carcinoma

9- A 64-year-old nonsmoking woman presents to her primary care physician with a 2-month history of cough, progressive shortness of breath, and recent development of hemoptysis. She has been depressed recently with the death of her 69-year-old husband, who had a 60 pack-year smoking history and passed away due to end-stage COPD. A chest radiograph reveals a suspicious lesion in the left hilar region. CT of the thorax confirms a 3-cm left central hilar lesion and a 1-cm ipsilateral peribronchial lymph node. Bronchoscopy yields bronchial washings indicative of lymphocyte-like small round cells growing in sheets of scant cytoplasm. What is the best treatment for this patient's condition?

- a) Surgical removal of the lesion
- b) Anti- EGF
- c) Chemotherapy
- d) Anti-ALK

10 - which of the following is a general symptom of cancers :

- a) Horner's syndrome
- b) Cachexia
- c) Eaton-Lambert syndrome
- d) Cushing's syndrome

Answers (matching):

- 1) A , F , H , I , K
- 2) A ,C , F , I , L
- 3) A , G
- 4) A , B , H , E
- 5) A , D , J

Answers (MCQs):

- 1) C
- 2) A
- 3) D
- 4) C
- 5) B
- 6) D
- 7) B
- 8) A
- 9) C
- 10) B

More Questions.

1- Which of the following is the most aggressive bronchogenic carcinoma ?

- a) Small cell carcinoma
- b) Adenocarcinoma
- c) Squamous cell carcinoma

2- Which of the following is develop in the site of pulmonary inflammation ?

- a) Small cell carcinoma
- b) Adenocarcinoma (scar carcinoma)
- c) Bronchoalveolar adenocarcinoma

3- Which of the following is primary neoplastic lesion of pleura?

- a) Adenocarcinoma
- b) Squamous cell carcinoma
- c) Mesothelioma

4- Which of the following is more common in women and nonsmokers?

- a) Squamous cell carcinoma
- b) Carcinoid
- c) Adenocarcinoma

5- Which of the following is clearly linked to smoking?

- a) Adenocarcinoma
- b) Squamous cell carcinoma
- c) Large cell carcinoma

6- A patient has adenocarcinoma. Which of the following is the best to do for the patient?

- a) Surgery
- b) Chemotherapy
- c) Medication
- d) Consultation

7- Which of the following is less clearly linked to smoking?

- a) Large cell carcinoma
- b) Scar carcinoma
- c) Oat cell carcinoma

8- Which tumor is characterized by the presence of keratin pearls?

- a) Bronchoalveolar carcinoma.
- b) Squamous cell carcinoma
- c) Large cell carcinoma.

9- What kind of tumors causes Horner's syndrome?

- a) Pancoast tumor
- b) Mesothelioma
- c) Oat cell carcinoma

10- What region of the lung the squamous cell carcinoma is present?

- a) Apex.
- b) Base.
- c) Hilum

Direct questions :

Q1: What is the histological changes in the cancer of the lungs?

1- Squamous metaplasia of the respiratory epithelium in the broncogenic carcinoma.

Q2: Change the range from dysplasia to carcinoma in situ. Q2: What is horner syndrome ?

It is pancoast tumor (superior sulcus tumor) With (ptosis, miosis, anhidrosis).

Q3: What are the characteristic of small cell carcinoma ?

- 1- Undifferentiated tumor
- 2- Most aggressive bronchogenic carcinoma
- 3- Cause metastases at the time of diagnosis
- 4- Associated with production of (ACTH) or (ADH)
- 5- Increased in smokers
- 6- Can not treated by surgery

Q4: What is the diagnosis of pleural disease?

- 1- Radiological investigation .
- 2- Cytological examination .
- 3- Bacteriological assessment and culture

Q5: An adult-26-years did an X-Ray Screening (Pre-employment).he had no complains .there was a coin lesion in the middle of the right lung (sharp edges). In the histology there were a cartilage "bronchi", adipose tissue and epithelial cells (hamartoma) this is an adenochondroma Note: screening: looking for a disease in a healthy person.

Answers:

- 1- A
- 2- B
- 3- C
- 4- C
- 5- B
- 6- A
- 7- B
- 8- B
- 9- A
- 10- C

Contact us on: Pathology434@gmail.com

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Good Luck!

مها الربيعة
مشاعل حسين
سارة محمد الجاسر
ريم لبني
منى المتعب

عمر الرهيبي
عبدالرحمن المزعل
مشهور الزارعي
حسين الكاف
أحمد الصالح