



Team 435

PATHOLOGY

As a doctor you should know what can threaten your patient's life
should know what makes your patient suffers from pain

That's why you study pathology

Lecture 6

Summary:

- 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**. □

Table 12–8 Comparison of Small Cell Lung Carcinoma (SCLC) and Non–Small Cell Lung Carcinoma (NSCLC)

Feature	SCLC	NSCLC
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, neuron-specific enolase, and synaptophysin	Usually present	Usually absent
Epithelial markers Epithelial membrane antigen, carcinoembryonic antigen, and cytokeratin intermediate filaments	Present	Present
Mucin	Absent	Present in adenocarcinomas
Peptide hormone production	Adrenocorticotrophic hormone, antidiuretic 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%
<i>p16/CDKN2A</i> mutations	~10%	>50%
<i>P53</i> mutations	>90%	>50%
Dominant oncogene abnormalities		
<i>KRAS</i> mutations	Rare	~30% (adenocarcinomas)
<i>EGFR</i> 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	Uncommonly, complete response

Type	Mass location	Etiologic agent	Characteristics
Squamous cell carcinoma	Central	Clearly linked to smoking (other; pollution, radiation)	Appears as a hilar mass and frequently results in cavitation; it may be marked by inappropriate parathyroid hormone (PTH) like activity resulting in hypercalcemia
Adenocarcinoma	Peripheral	Less clearly linked to smoking	Develops on site of prior pulmonary inflammation or injury (usually on periphery)
Carcinoid	Central/Peripheral Major bronchi	Major bronchi	Low malignancy, spreading by direct extension into adjacent tissues, may result in carcinoid syndrome.
Small/Oat cell carcinoma	Central	Incidence greatly increased in smokers	Undifferentiated tumor; most aggressive bronchogenic carcinoma usually already metastatic at diagnosis; often associated with ectopic production of corticotropin (ACTH) or antidiuretic hormone (ADH), cannot be treated by surgery
Large cell carcinoma	Peripheral	~	Undifferentiated tumor which may show features of squamous cell or adenocarcinoma on electron microscopy
Mesothelioma	Pleural plaques	Asbestos increases incidence	~

Questions:

1. Which of these symptoms is NOT a general symptom of cancer?
 - A. Weight loss
 - B. Iron deficiency anemia
 - C. Muscle wasting
 - D. Dyspnea
2. Which of these carcinomas is clearly related to asbestos exposure?
 - A. Asbestosis
 - B. Small-cell carcinoma
 - C. Large-cell carcinoma
 - D. Mesothelioma
3. The most common benign tumor is?
 - A. Hamartoma
 - B. Sarcoma
 - C. Mesothelioma
 - D. Small-cell carcinoma
4. Squamous cell carcinoma usually arises ?
 - A. Centrally
 - B. Peripherally
 - C. In the pleura
5. Bronchogenic carcinoma is directly proportional to?
 - A. Sun exposure
 - B. Number of cigarettes smoked daily
 - C. Number of hookahs smoked weekly
 - D. Number of cigarettes smoked per hour
6. Which of these symptoms is completely related to smoking?
 - A. Cor pulmonale
 - B. COPD
 - C. Clubbing
 - D. Tar-stained fingers

1. D

2. D

3. A

4. A

5. B

6. D

7. Which of these is considered a paraneoplastic endocrine syndrome?

- A. Hoarseness
- B. Horner syndrome
- C. Cushing syndrome
- D. Superior vena cava syndrome

8. A patient was presented to the clinic with cough and hemoptysis. He has a history of recurrent bronchial infections. Over the past week, he noticed difficulty in breathing with cyanosis and diarrhea.

With the symptoms presented above, what is your diagnosis?

- A. Carcinoid syndrome
- B. Carcinoid carcinoma
- C. Small-cell carcinoma
- D. Cushing syndrome

9. A 40-year-old patient smoked 2 packs of cigarettes daily for the past 20 years died because of squamous cell carcinoma, a biopsy was taken from his lungs, which of the following features will be present?

- A. Pleural plaques
- B. Keratin pearls
- C. Tar-stains
- D. Asbestos accumulations

10. A patient was presented with a pale grey centrally located mass extending to the lung parenchyma. After further investigations necrosis was identified as well, the patient smokes daily and has been smoking for the past 10 years. After 6 months the patient died. What was the type of cancer he had?

- A. Large-cell carcinoma
- B. Small-cell carcinoma
- C. Mesothelioma
- D. Sarcoma

11. A patient was presented with large-cell carcinoma in its early stages. What could be the treatment?

- A. Excision and chemotherapy
- B. Antibiotics
- C. Chemotherapy without excision of the mass
- D. Excision without chemotherapy

7. C

8. A

9. B

10. B

11. A

12. Which of the following is the most aggressive bronchogenic carcinoma?
- A. Small cell carcinoma
 - B. Adenocarcinoma
 - C. Squamous cell carcinoma
13. Which of the following is develop in the site of pulmonary inflammation ?
- A. Small cell carcinoma
 - B. Adenocarcinoma (scar carcinoma)
 - C. Bronchoalveolar adenocarcinoma
14. Which of the following is primary neoplastic lesion of pleura?
- A. Adenocarcinoma
 - B. Squamous cell carcinoma
 - C. Mesothelioma
15. Which of the following is more common in women and nonsmokers?
- A. Squamous cell carcinoma
 - B. Carcinoid
 - C. Adenocarcinoma
16. Which of the following is clearly linked to smoking?
- A. Adenocarcinoma
 - B. Squamous cell carcinoma
 - C. Large cell carcinoma
17. A patient has adenocarcinoma. Which of the following is the best to do for the patient?
- A. Surgery
 - B. Chemotherapy
 - C. Medication
 - D. Consultation
18. Which of the following is less clearly linked to smoking?
- A. Large cell carcinoma
 - B. Scar carcinoma
 - C. Oat cell carcinoma

19. Which tumor is characterized by the presence of keratin pearls?

- A. Bronchoalveolar carcinoma.
- B. Squamous cell carcinoma
- C. Large cell carcinoma.

12. A	13. B	14. C	15. C	16. B	17. A	18. B	19. B
-------	-------	-------	-------	-------	-------	-------	-------

20. A 64-year-old man, who is a chain-smoker, has had a cough and a 5-kg weight loss over the past 3 months. Physical examination shows clubbing of the fingers. He is afebrile. A chest radiograph shows no hilar adenopathy, but there is cavitation within 3-cm lesion near the right hilum. Laboratory studies show a serum calcium of 12.3 mg/dL, phosphorus of 2.4 mg/dL, and albumin of 3.9g/dL. Bronchoscopy shows a lesion almost occluding the right main bronchus. A surgical procedure with curative intent is attempted. Which of the following neoplasms is most likely to be present in this patient?

- A. Large cell anaplastic carcinoma
- B. Metastatic renal cell carcinoma
- C. Non-hodgkin lymphoma
- D. Small cell anaplastic carcinoma
- E. Squamous cell carcinoma

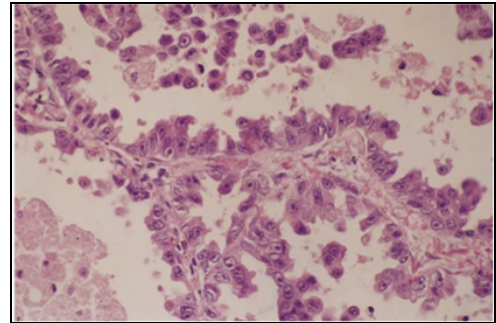
21. A 50-year-old man has developed truncal obesity, back pain, and skin that bruises easily over the past 5 months. On physical examination, he is afebrile, and his blood pressure is 160/95mm Hg. A chest radiograph shows an ill-defined, 4-cm mass involving the left hilum of the lung. Cytologic examination of bronchial washings from bronchoscopy shows round epithelial cells that have the appearance of lymphocytes but are larger. The patient is told that, although his disease is apparently localized to one side of the chest cavity, surgical treatment is unlikely to be curative. He also advised to stop smoking. Which of the following neoplasms is most likely to be present in this patient?

- A. Bronchial carcinoid
- B. Bronchioloalveolar carcinoma
- C. Large cell carcinoma
- D. Non-Hodgkin lymphoma
- E. Small cell anaplastic carcinoma

22. A 57-year-old woman 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 shown in the figure. Which of the following neoplasms is most likely to be present in this patient?

- A. Adenocarcinoma in situ
- B. Large cell anaplastic carcinoma
- C. Malignant mesothelioma
- D. Metastatic breast carcinoma
- E. Squamous cell carcinoma



23. Which of these carcinomas forms a mass centrally?

- A. Small cell carcinoma
- B. Adenocarcinoma
- C. Mesothelioma
- D. Large cell carcinoma

24. A 65 year old women with a significant smoking history presents with cough and shortness of breath. Computed tomography of the chest reveals a central mass near the left mainstem bronchus. Biopsy of the mass is performed. Histologic examination reveals small round blue cells, and a diagnosis of small cell carcinoma is made. Which of the following is a frequent characteristics of this form of lung cancer.

- A. Generally amenable to surgical cure at time of diagnosis.
- B. More common in women and less clear relation to smoking than other forms of lung cancer.
- C. Secretes a parathyroid-like hormone.
- D. Secretes either corticotropin or antidiuretic hormone.
- E. Usually found in a peripheral rather than in a central location.

Answers:

20. (E). Of all lung cancers, squamous cell carcinoma is most likely to produce paraneoplastic hypercalcemia, and there is a strong association with smoking. These tumors also can undergo central necrosis—hence a cavity may form. Localized squamous cell carcinomas, in contrast to small cell carcinomas, may be cured by surgery. Adenocarcinomas and large cell carcinomas tend to produce peripheral masses and generally are less likely to be associated with paraneoplastic syndromes. Kaposi sarcoma involving visceral organs is most often seen in association with AIDS, and it is often multifocal. Renal cell carcinomas may be associated with hypercalcemia, but metastases usually appear as multiple masses (although of all metastatic tumors, renal cell carcinoma is most likely to produce solitary metastases). Non-Hodgkin lymphomas generally do not have paraneoplastic effects; they are uncommon in the lung and are not associated with smoking. Small cell carcinomas are never localized enough for curative surgery (they are usually detected at an advanced stage), although they often produce various paraneoplastic syndromes, but less likely hypercalcemia.

21. Ans: E. Cushing syndrome is a paraneoplastic syndrome resulting from ectopic corticotropin production (most often from a pulmonary small cell carcinoma), which drives the adrenal cortices to produce excess cortisol. Small cell carcinomas are aggressive neuroendocrine tumors that tend to metastasize early. Even when they appear to be small and localized, they are not or will not remain so. Surgery is not an option for these patients. They are treated as if they have systemic disease; some chemotherapy protocols afford benefit for 1 year or more, but cure is uncommon. Adenocarcinomas and large cell carcinomas tend to be peripheral neoplasms in the lung, and they are less likely to produce a paraneoplastic syndrome. Bronchial carcinoids at the more benign end of the neuroendocrine tumor spectrum tend to be small and are not likely to produce paraneoplastic effects; rarely, they produce carcinoid syndrome. Non-Hodgkin lymphomas rarely occur within the lung, are not associated with smoking, and do not produce Cushing syndrome. Squamous cell carcinomas can be central and occur in smokers, but they are more likely to produce hypercalcemia as a paraneoplastic syndrome.

22. Ans: A. Adenocarcinoma in situ (AIS), formerly termed *bronchioloalveolar carcinoma*, can present as a peripheral tumor that can mimic pneumonia. Most of these tumors are well differentiated. Adenocarcinomas and large cell carcinomas tend to be peripheral, but the former tend to produce a localized mass, whereas cells of the latter are large and pleomorphic and form sheets; sometimes it is difficult to distinguish among them. Mesotheliomas almost always occur in the setting of prior asbestos exposure; they are large pleural masses. Metastases tend to appear as multiple nodules. Squamous cell carcinomas occasionally can be peripheral (although most are central) and are composed of pink, polygonal cells that have intercellular bridges. If well differentiated, squamous cell carcinomas show keratin pearls.

23. A

24. D

Contact us: pathology435@gmail.com

Team members

Nouf Altwaijri	Wael Al Oud
Aljohara Almazroua	Abdulaziz AlHammad
Ghaida Aljamili	Abdullah AlGhizzi
Kowthar Almousa	Abdulrahman Thekry
Nojood Alhaidri	Ahmad Alkhiary
Nouf Alabdukarim	Ammar Almansour
Raghad Alnafisah	Anas Ali
Rawan Aldhuwayhi	Faris Alwarhi
Reem AlAgeel	Khalid Ali Alghsoon
Samar AlOtaibi	Mana AlMuhaideb
	Naif Alhadi
	Saleh Alkhalifa
	Rayan Almuneef
	Salem Al Ammari

قال صلى الله عليه وسلم: من سلك طريقاً يلتمس به علماً سهل الله له به طريقاً إلى الجنة.

دعواتنا لكم بالتوفيق.

