

Lung Cancer: Review Questions

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QUESTIONS

Choose the single best answer for each question.

1. Which of the following statements regarding the epidemiology of lung cancer is correct?

- (A) Chronic obstructive pulmonary disease (COPD) is not associated with an increased risk of lung cancer
- (B) Cigar smoking is associated with an equal risk of lung cancer as compared with cigarette smoking
- (C) Occupational exposure to radon is associated with an increased risk of lung cancer
- (D) The risk of developing lung cancer for cigarette smokers exposed to asbestos is equal to that of those not exposed to asbestos

2. 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. Physical examination reveals prominent neck veins and edema of the upper limbs. 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) Carcinoid tumor of the lung
- (C) Large cell lung cancer
- (D) Small cell lung cancer (SCLC)
- (E) Squamous cell lung cancer

3. Paraneoplastic syndromes are clinical disorders associated with malignant diseases but not directly related to the physical effects of primary or metastatic tumors.^{1,2} Several paraneoplastic syndromes are more closely associated with a particular subtype of bronchogenic carcinoma.² Which of the following paraneoplastic syndrome is appropriately matched with its most commonly associated histologic type of lung cancer?

- (A) Ectopic Cushing's syndrome/bronchial carcinoid tumor
- (B) Hypercalcemia/adenocarcinoma

- (C) Hypertrophic pulmonary osteoarthopathy and digital clubbing/SCLC
- (D) Lambert-Eaton myasthenic syndrome (LEMS)/squamous cell carcinoma
- (E) Syndrome of inappropriate antidiuretic hormone (SIADH)/SCLC

4. A 60-year-old man with known squamous cell cancer of the lung presents to the clinic for a follow-up appointment with complaints of dyspnea on exertion. The patient has completed 3 cycles of cisplatin and gemcitabine. Surveillance computed tomography (CT) scan of the thorax performed 2 days prior indicates a stable 2-cm right lower lung lesion, a stable 1-cm right mediastinal lymph node, and a new moderate-sized right pleural effusion. The patient subsequently undergoes a right thoracentesis, which yields an exudative effusion with cytology positive for squamous cells. Which of the following is the patient's current stage of disease?

- (A) Stage IIA
- (B) Stage IIB
- (C) Stage IIIB
- (D) Stage IV

5. 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?

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- (A) Combination chemotherapy alone with etoposide and cisplatin
- (B) Combination chemotherapy with a platinum-based regimen and concurrent thoracic radiotherapy
- (C) Single-agent chemotherapy and sequential thoracic radiotherapy with prophylactic cranial irradiation
- (D) Surgical resection of the 3-cm left hilar lesion, combination chemotherapy with a platinum-based regimen, and sequential thoracic radiotherapy

ANSWERS AND EXPLANATIONS

1. (C) **Occupational exposure to radon is associated with an increased risk of lung cancer.** Lung cancer is the most common malignancy associated with occupational exposures. After cigarette smoking, radon exposure is the second leading cause of lung cancer in the United States. Other occupational causes of lung cancer include arsenic, chromates, chloromethyl ethers, nickel, and aromatic hydrocarbons, among others.³ Asbestos exposure alone is associated with an increased risk of lung cancer, and the effect is magnified in the presence of cigarette smoking.³ A substantial amount of evidence supports an association between COPD and lung cancer. Although exposure to cigarette smoke (either by smoking cigarettes or secondhand exposure) can be a confounding variable in determining whether COPD has a direct association with lung cancer, evidence suggests that COPD is associated with a two- to fourfold increased frequency in primary lung cancer.^{3–5} Cigar smoking is another known cause of lung cancer, but the risk it poses for the development of lung cancer is lower in comparison with the effect of cigarette smoking.^{3,6} This is most likely due to variations in smoking frequency and depth of inhalation from smoking cigarettes as opposed to cigars and pipes.^{3,7}
2. (D) **SCLC.** This patient has signs and symptoms of superior vena cava syndrome (SVCS), a clinical diagnosis defined as a partial or total obstruction of the superior vena cava by tumor invasion, external compression, or thrombus formation. SVCS is most commonly associated with swelling of the face and upper limbs, cough, chest pain, and venous distension of the neck.^{8,9} Although there are benign etiologies of SVCS, malignancy remains the most common cause. Approximately 80% of cases are due to bronchogenic carcinoma, with the majority of such cases caused by SCLC. SCLC commonly occurs in the hilar regions, and smoking is the primary risk factor in 90% of cases.¹⁰
3. (E) **SIADH/SCLC.** SIADH is most commonly associated with SCLC. While only 1% to 5% of lung cancer patients have symptomatic SIADH, combination chemotherapy can lead to resolution of SIADH in more than 80% of patients with SCLC.¹ Hypercalcemia typically occurs as a result of bony metastases and is most commonly associated with squamous cell carcinoma.² Ectopic Cushing's syndrome results from uncontrolled secretion of adrenocorticotropic hormone (ACTH) and its precursors from nonpituitary tissue. Lung tumors account for approximately half of all cases of ectopic Cushing's syndrome, and a majority are attributed to ACTH production by SCLC cells.¹¹ Unfortunately, most patients with Cushing's syndrome from SCLC present with extensive disease and have a poor response to chemotherapy.¹ LEMS develops through autoimmune mechanisms almost exclusively associated with SCLC. Effective chemotherapy in SCLC patients with neurologic paraneoplastic syndromes such as LEMS may result in improvements in neurologic symptoms.¹ Hypertrophic pulmonary osteoarthropathy and digital clubbing are most frequently associated with non-small cell lung cancer (NSCLC), primarily the adenocarcinoma subtype.¹² The exact mechanism for this syndrome is unknown, although contributory mechanisms may include neurogenic, hormonal, and vascular pathophysiologies.¹
4. (C) **Stage IIB.** Lung cancers are classified as either non-small cell or small cell carcinomas. The majority (80%) of tumors in the lung are non-small cell carcinomas.¹³ This patient has squamous cell carcinoma classified as a NSCLC. NSCLC and SCLC are staged and treated differently, largely because SCLCs are aggressive tumors that have metastasized at the time of diagnosis, and they also tend to respond well to chemotherapy. While surgical intervention (ie, resection) in combination with chemo- and radiotherapy is more common in early stages of NSCLC, chemo- and radiotherapy are the treatments of choice for SCLC. For a patient with NSCLC, lymph node involvement other than ipsilateral bronchopulmonary or hilar nodes (N1 lesions) excludes stages IIA and IIB.¹³ Involvement of the contralateral hilar or mediastinal lymph nodes, ipsilateral or contralateral scalene, or supraclavicular lymph nodes excludes classification in stage IIIA.¹³ Additionally, this patient presented with newly diagnosed malignant

pleural effusions, which characterizes this patient's disease as stage IIIB. Stage IV represents metastasis to other organs of the body, which is not present in this case. This patient's advanced NSCLC stage IIIB was unresponsive to initial chemotherapy. If this patient's functional status is good and he has minimal comorbidities, he may be a candidate for other agents. However, his prognosis is extremely poor.¹⁴

5. (B) Combination chemotherapy with a platinum-based regimen and concurrent thoracic radiotherapy. Lung cancer is the major cause of cancer-related death in men and women in the United States. Although this woman was not an active smoker, she had significant tobacco exposure from her husband. Passive smoking is associated with an increased rate of lung cancer, with a statistically significant increase in the squamous and small cell histologic subtypes.¹⁵ SCLC can present with central hilar lesions contributing to the most common symptoms of cough, shortness of breath, and hemoptysis.¹⁴ The central location of the mass makes bronchoscopy a good option to further elucidate the histology of the lesion. The description of the lymphocyte-like small round cells found on this patient's bronchial washings is consistent with SCLC or oat cell carcinoma.¹⁴ SCLC can be practically classified as either limited or extensive disease; limited disease is characterized by a tumor that can be encompassed within a single, tolerable radiation port.¹⁴ Combination chemotherapy with a platinum-based regimen and concurrent thoracic radiotherapy is the mainstay treatment for local SCLC tumor growth.¹⁴ Combination chemotherapy is superior to single-agent chemotherapy, and concurrent chemoradiation offers better 5-year survival rates than sequential therapy.¹⁴ Surgical resection is not typically part of the treatment algorithm for SCLC largely due to its early spread and good response to chemotherapy. Finally, prophylac-

tic cranial irradiation has been shown to reduce the incidence of brain metastasis in patients with limited SCLC, and guidelines for the treatment of SCLC recommend that all patients who have complete remission after chemotherapy undergo prophylactic cranial irradiation.¹⁶

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