

Pulmonary Complications of HIV Infection: Review Questions

May M. Lee, MD

QUESTIONS

Choose the single best answer for each question.

Questions 1 and 2 refer to the following case.

A 29-year-old woman with AIDS and a most recent CD4+ cell count of 10 cells/ μ L is admitted to the hospital with a 1-week history of nonproductive cough, shortness of breath, and dyspnea on exertion. She is only able to walk a room's length before she needs to rest. She also reports fever, chills, and sweats prior to admission. Highly active antiretroviral therapy (HAART) has been discontinued due to an unknown intolerance and she has not been taking other medications. The patient is emaciated and is in mild respiratory distress. Vital signs are temperature, 103°F; blood pressure, 121/62 mm Hg; heart rate, 127 bpm; respiratory rate, 25 breaths/min; and oxygen saturation, 88% on room air. Head and neck examination reveals a white exudate throughout the posterior oropharynx as well as on her tongue. Cardiovascular examination reveals tachycardia with regular rate and rhythm and no murmurs. Lung examination reveals diffuse crackles with poor air movement throughout. Laboratory examination reveals a normal white blood cell count and basic metabolic panel and a lactate dehydrogenase (LDH) level of 376 U/L (normal, 116–245 U/L). A chest radiograph is performed (Figure 1) followed by bronchoscopy with bronchoalveolar lavage to confirm the diagnosis.

1. What is the most appropriate treatment for this patient?

- (A) Amphotericin B
- (B) Isoniazid, ethambutol, rifampin, and pyrazinamide
- (C) Trimethoprim/sulfamethoxazole (TMP/SMX)
- (D) TMP/SMX and prednisone
- (E) Vancomycin



Figure 1. Chest radiograph of the patient described in questions 1 and 2.

2. Assuming that this patient has never had a prior acute opportunistic infection, which of the following medications should she have been prescribed as prophylaxis?

- (A) Azithromycin and fluconazole
- (B) TMP/SMX and azithromycin
- (C) TMP/SMX, azithromycin, and fluconazole
- (D) TMP/SMX and fluconazole
- (E) Prophylaxis is not necessary

3. A 49-year-old African American woman with a history of HIV and type 2 diabetes mellitus presents to the emergency department (ED) with a 2-week history of general malaise, fever, headache, cough, and dyspnea. She also notes gradual onset of right lateral chest pain that is sharp, nonradiating, relieved with acetaminophen, and exacerbated by cough and deep breathing. The patient appears ill and is in mild distress. Her vital signs are temperature, 103°F; heart rate, 111 bpm; respiratory rate, 18 breaths/min; blood pressure, 129/88 mm Hg; and oxygen saturation, 97% on room air. Cardiovascular examination reveals tachycardia with a regular rhythm and no appreciable murmurs. Lungs are clear to auscultation bilaterally. She has no chest wall tenderness or neck stiffness. The

For copies of the Hospital Physician
Pulmonary Disease Board Review Manual
sponsored by AstraZeneca,
visit us on the Web
at www.turner-white.com.

Dr. Lee is a fellow, Section of Pulmonary and Critical Care, Department of Internal Medicine, University of Chicago Hospitals, Chicago, IL.

neurologic examination is grossly intact; she is alert and oriented. A chest radiograph shows a right-sided solitary pulmonary nodule with mediastinal widening in the right paratracheal region. Computed tomography shows an ill-defined subpleural nodule in the right upper lobe with soft tissue masses seen in the right paratracheal, subcarinal, hilar, and para-aortic regions. Bronchoscopy is performed with transbronchial needle biopsy of the right paratracheal and subcarinal masses. Methenamine silver stain of biopsied tissue reveals numerous narrow-based, budding extracellular yeasts of *Cryptococcus neoformans* within the alveolar spaces. What laboratory data should be collected next?

- (A) Cryptococcal subgroup typing
- (B) Lumbar puncture
- (C) Serum cryptococcal antigen titers
- (D) Sputum evaluation
- (E) Transthoracic needle biopsy of the right upper lobe nodule

Questions 4 and 5 refer to the following case.

A 34-year-old homosexual man with AIDS and a most recent CD4+ cell count of 0 cells/ μ L presents to the ED with a 2-week history of pleuritic chest pain, shortness of breath, and dry cough. He reports that shortness of breath occurs with minimal exertion. He denies fever or chills but admits to a 10-lb weight loss over the past 4 months. On admission, his temperature is 97°F, heart rate is 103 bpm, blood pressure is 124/81 mm Hg, respiratory rate is 18 breaths/min, and oxygen saturation is 98% on room air. Head and neck examination is significant for a nodular pigmented lesion on his hard palate. Cardiovascular examination reveals tachycardia with a regular rhythm and no murmurs. Lung examination discloses crackles in all fields with both end-expiratory and inspiratory wheezes. Skin examination shows multiple plaque-like hyperpigmented lesions on his legs, back, and arms. A chest radiograph is performed (**Figure 2**). Bronchoscopy reveals extrinsic compression throughout the tracheobronchial tree with fresh blood in the airways and no purulent discharge.

4. What is the most likely cause of this patient's symptoms and radiographic findings?

- (A) *Mycobacterium tuberculosis*
- (B) Human herpesvirus 8 (HHV-8)
- (C) *Pneumocystis jirovecii*
- (D) *Streptococcus pneumoniae*
- (E) Epstein-Barr virus

5. Incidence of this patient's illness in the United States has decreased as a result of which of the following?



Figure 2. Chest radiograph of the patient described in questions 4 and 5.

- (A) Azithromycin prophylaxis
- (B) Corticosteroids
- (C) HAART
- (D) TMP/SMX prophylaxis

ANSWERS AND EXPLANATIONS

1. **(D) TMP/SMX and prednisone.** Based on the clinical presentation and findings on chest radiograph, this patient has *P. jirovecii* (formerly known as *P. carinii*) pneumonia (PCP). Despite the decline in incidence of PCP in the post-HAART era, it remains the most common opportunistic pneumonia and a major cause of death in HIV-infected patients.¹ Clinically, patients with HIV and PCP have a gradual onset of symptoms characterized by fever, cough, and progressive dyspnea. Other symptoms may include fatigue, chills, chest pain, and weight loss. Patients with PCP also tend to have abnormal gas exchange resulting in lower arterial oxygen saturations. Up to 25% of patients with PCP present with a normal chest radiograph.² The most common radiographic findings are diffuse bilateral alveolar or interstitial infiltrates, while other findings include pneumothorax, lobar or segmental infiltrates, cysts, nodules, or pleural effusions. The most common laboratory abnormalities associated with *P. jirovecii* infection are a CD4+ cell count of less than 200 cells/ μ L and an elevated LDH level. TMP/SMX remains the initial drug of choice for treatment of PCP. Consensus guidelines recommend that HIV-infected patients with hypoxia (partial pressure of arterial oxygen on room air < 70 mm Hg or alveolar-arterial gradient > 35) be treated with adjunctive corticosteroids.¹
2. **(B) TMP/SMX and azithromycin.** Immunosuppression that results from HIV infection significantly increases the risk for acquiring opportunistic bacterial,

Table. Therapy Recommended as Primary Prophylaxis to Prevent Opportunistic Disease in HIV-Infected Patients

| Pathogen | Indication | First Choice | Alternative |
|------------------------------------|--|---|--|
| <i>Pneumocystis jiroveci</i> | CD4+ cell count < 200 cells/ μ L or oropharyngeal candidiasis | Trimethoprim/sulfamethoxazole (TMP/SMX; 1 double-strength tablet daily or 1 single-strength tablet daily) | Dapsone 50 mg twice daily; dapsone 50 mg daily plus pyrimethamine 50 mg weekly plus leucovorin 25 mg weekly; aerosolized pentamidine 300 mg monthly; or atovaquone 1500 mg daily |
| <i>Toxoplasma</i> | CD4+ cell count < 100 cells/ μ L and IgG antibody to <i>Toxoplasma</i> | TMP/SMX double-strength tablet daily | TMP/SMX single-strength tablet daily; dapsone 50 mg daily plus pyrimethamine 50 mg weekly plus leucovorin 25 mg weekly; or atovaquone 1500 mg daily |
| <i>Mycobacterium avium</i> complex | CD4+ cell count < 50 cells/ μ L | Azithromycin 1200 mg weekly or clarithromycin 500 mg twice daily | Rifabutin 300 mg daily or azithromycin 1200 mg daily plus rifabutin 300 mg daily |

Adapted from Kaplan JE, Masur H, Holmes KK. Guidelines for the prevention of opportunistic infections among HIV-infected persons—2002. Recommendations of the U.S. Public Health Service and the Infectious Diseases Society of America. Available at <http://aidsinfo.nih.gov/contentfiles/OpreventionGL.pdf>. Accessed 5 May 2008.

viral, fungal, and protozoan infections. These opportunistic infections are a major cause of morbidity and mortality in the HIV population. For this patient with a CD4+ cell count of 10 cells/ μ L, prophylaxis should have included TMP/SMX and azithromycin for prevention of PCP, toxoplasmosis, and *M. avium* complex (Table).³ Fluconazole is effective for preventing cryptococcal infection in patients with a CD4+ cell count less than 50 cells/ μ L, but it is not routinely recommended. Additionally, fluconazole is only recommended for the prevention of *Candida* infection if the patient has had frequent or severe recurrences.

3. (B) Lumbar puncture. The lungs are thought to be the primary portal of almost all cryptococcal infections. Infection disseminates through the blood, frequently causing meningoencephalitis. Meningitis is the most common initial manifestation of cryptococcal infection in both HIV-infected and non-HIV-infected patients.⁴ Pulmonary cryptococcal infection is the second most common presentation of cryptococcal infection and the cause of this patient's symptoms. Symptoms, which may be present from a few days to a few weeks, are nonspecific and commonly include cough, fever, dyspnea, thoracic pain, and headache. On computed tomography, solitary or multiple subpleural pulmonary nodules are the most common finding. Patients may also have air-space consolidation, interstitial micronodules or reticulo-micronodules, or lymphadenopathy. Diagnosis of cryptococcosis requires direct evidence in sputum, bronchial washings, bronchoalveolar lavage fluid, or biopsy. Indirect proof in the form of cryptococcal antigen in the blood or cerebrospinal fluid may also be useful. Because most immunocompromised hosts will present with extrapulmonary disease, all patients with a positive respiratory sample should be evalu-

ated for disseminated disease, even in the absence of symptoms. It is important to rule out central nervous system involvement to determine if intracerebral pressures should be decreased with serial lumbar punctures and to establish the need for flucytosine therapy for synergy. In this case, because there is direct evidence of pulmonary cryptococcosis (biopsy specimen), sputum analysis and transthoracic needle biopsy are not necessary. Testing for anticryptococcal antibodies is not useful for diagnosis or management of cryptococcal infection because it can be negative in many cases. Results of antigen titers would not guide management of infection caused by *Cryptococcus*. Typing of clinical isolates is typically only used for research purposes.

4. (B) HHV-8. This patient has Kaposi sarcoma (KS), an angioproliferative tumor associated with HHV-8. AIDS-related KS has a variable course ranging from an incidental finding to rapidly progressive disease, resulting in significant morbidity and mortality. Typically, tumors involve the skin and lymph nodes, although visceral organs may also be involved. Dermatologic manifestations often appear on the lower extremities, face, oral mucosa, and genitalia and may be papular, plaque-like, or exophytic and fungating. Pulmonary involvement is common in AIDS-related KS. Dyspnea and cough are the most common presenting symptoms; hemoptysis may also occur. A plain chest radiograph shows nodular thickening along the peribronchovascular bundles often radiating from the hila (Figure 2). As pulmonary lesions progress, nodules become confluent and irregular, which may lead to dense air-space consolidation. KS is a highly vascular tumor and biopsy is associated with a significant incidence of hemorrhage.⁵ Alveolar hemorrhage may also be associated with KS, although this

(continued on page 34)

(from page 30)

is a nonspecific finding. The incidence of cutaneous tuberculosis is low and is not likely the cause of this patient's symptoms. *P. jiroveci* may also be associated with skin lesions but most commonly involves the skin around the external auditory canal and nasal passages. Clinically, skin lesions related to PCP appear similar to molluscum contagiosum. Epstein-Barr virus in HIV-infected patients has been associated with non-Hodgkin's lymphoma and oral hairy leukoplakia.

5. (C) **HAART.** The incidence of KS has been declining precipitously since the mid-1990s. HAART is also associated with regression of existing KS lesions and improved survival among patients with or without

chemotherapeutic treatment. Corticosteroids, TMP/SMX, and azithromycin are not used to treat KS.

REFERENCES

1. Thomas CF Jr, Limper AH. Pneumocystis pneumonia. *N Engl J Med* 2004;350:2487–98.
2. DeLorenzo LJ, Huang CT, Maguire GP, Stone DJ. Roentgenographic patterns of *Pneumocystis carinii* pneumonia in 104 patients with AIDS. *Chest* 1987;91:323–7.
3. Kaplan JE, Masur H, Holmes KK. Guidelines for the prevention of opportunistic infections among HIV-infected persons—2002. Recommendations of the U.S. Public Health Service and the Infectious Diseases Society of America. Available at <http://aidsinfo.nih.gov/contentfiles/OIpreventionGL.pdf>. Accessed 5 May 2008.
4. Lortholary O, Nunez H, Brauner MW, Dromer F. Pulmonary cryptococcosis. *Semin Respir Crit Care Med* 2004;25:145–57.
5. Aboulafia D. The epidemiologic, pathologic, and clinical features of AIDS-associated pulmonary Kaposi's sarcoma. *Chest* 2000;117:1128–45.

Copyright 2008 by Turner White Communications Inc., Wayne, PA. All rights reserved.