

Serious Fungal Infections: Review Questions

Pallavi Bhargava, MD

Pranatharthi H. Chandrasekar, MD, FACP

QUESTIONS

Choose the single best answer for each question.

- 1. A 56-year-old man undergoes coronary artery bypass grafting after a myocardial infarction. He develops a temperature of 102.3°F a few days after surgery. On physical examination, the sternotomy wound margins are erythematous, and a purulent discharge is noted. Cultures obtained at the time of sternal wound débridement grow *Pseudomonas aeruginosa*. Intravenous (IV) therapy is begun with tobramycin and piperacillin; the fever resolves over next few days. A week later, the patient has rigors and a temperature as high as 102°F. The sternal wound is healing well, and repeat wound culture is negative for organisms. The subclavian triple lumen venous catheter site appears normal. One of 3 sets of blood cultures is positive for yeast. Which of the following is the most appropriate next step in the treatment of this patient?**

 - Remove the triple lumen catheter and observe
 - Insert a new catheter over the guidewire and withhold antifungal therapy
 - Remove the triple lumen catheter and initiate treatment with fluconazole
 - Repeat the blood cultures, since the yeast in the blood is likely to be a contaminant
- 2. A 47-year-old woman is seen in her doctor's office with a 1-day history of right eye redness and swelling and headache on the same side. Her past medical history is significant for poorly controlled diabetes mellitus. Physical examination shows a tachypneic woman with a low-grade temperature of 99.8°F, a mildly proptotic right eye, and decreased extraocular movements. The right cheek is erythematous, and nasal turbinates have a dusky appearance with a small area of black discoloration. Results of arterial blood gas analysis are pH 7.23, PCO₂ 25 mm Hg, PO₂ 70 mm Hg, bicarbonate 10 mEq/L, and oxygen saturation 98% while the patient is breathing room air. Which of the following is the most appropriate next step in the treatment of this patient?**

 - Initiate therapy with broad-spectrum antibiotics and obtain blood, sinus, and nasal cultures
 - Obtain an immediate computed tomography (CT) scan of the nose, paranasal sinuses, orbit, and brain and request urgent surgical consultation for possible débridement
 - Begin IV therapy with amphotericin B and observe
 - Begin IV therapy with a high dose of fluconazole and observe
- 3. A 45-year-old woman is seen by her physician because of a 1-week history of fever, cough, breathlessness and pleuritic chest pain. She underwent allogeneic peripheral stem cell transplantation 2 months ago for myelodysplastic syndrome and developed graft-versus-host disease 1 month later. The patient reports no history of exposure to tuberculosis and had a negative tuberculin test prior to transplant. Her medications include prednisone 30 mg daily, cyclosporin A, trimethoprim-sulfamethoxazole (1 double-strength tablet) 3 times weekly, and oral administration of penicillin 250 mg twice daily. Physical examination reveals scattered crackles over both lung fields; the rest of the examination shows no abnormalities. A chest radiograph shows bilateral nodular infiltrates with cavitation and few pleural-based lesions. The patient's peripheral leukocyte count is $4.8 \times 10^3/\text{mm}^3$ (absolute neutrophil count $3 \times 10^3/\text{mm}^3$, hemoglobin 9.8 g/dL, and platelet count $18 \times 10^3/\text{mm}^3$). Which of the following is the most appropriate next step in the treatment of this patient?**

 - Perform venous Doppler ultrasonography of the lower extremities and obtain an immediate ventilation/perfusion scan of the lungs

Dr. Bhargava is a Fellow in the Division of Infectious Diseases at Wayne State University School of Medicine, Detroit, MI. Dr. Chandrasekar is Professor of Medicine, Division of Infectious Diseases, Wayne State University School of Medicine, Detroit, MI.

- B) Send induced sputum samples for analysis for *Pneumocystis carinii* and initiate therapy with a high dose of trimethoprim-sulfamethoxazole
- C) Begin empiric antifungal IV therapy with fluconazole and attempt to decrease immunosuppression
- D) Perform a CT scan of the chest and possibly a bronchoalveolar lavage/open lung biopsy

EXPLANATION OF ANSWERS

1. **(C) Remove the triple lumen catheter and initiate treatment with fluconazole.** The patient has candidemia associated with an indwelling intravenous catheter. *Candida albicans* is the most common species associated with candidemia. The absence of signs of infection at the catheter site does not exclude a line-related infection. Neutropenia, immunosuppressive and anticancer therapy, prolonged antibiotic use, upper gastrointestinal surgery, parenteral nutrition, and presence of implanted devices including intravenous cannulae are risk factors for development of candidemia. The most appropriate next step in management would be removal of the catheter and initiation of therapy with a systemic antifungal agent for treatment of acute infection and prevention of late sequelae of candidemia—particularly endophthalmitis, endocarditis, arthritis, and osteomyelitis. Removing the catheter alone is not adequate. A new catheter should not be inserted over a guidewire in the infected site of the old catheter. It is inappropriate to assume that a positive blood culture for *Candida* species represents contamination. Fluconazole therapy is less toxic and equal in efficacy to conventional amphotericin B for vascular catheter-related candidemia in patients who are clinically stable and not neutropenic. However, the *Candida* species involved should be considered when choosing between fluconazole and amphotericin B because *Candida krusei* is resistant to fluconazole, and *Candida glabrata* frequently exhibits an intermediate level of susceptibility to fluconazole.
2. **(B) Obtain an immediate computed tomography (CT) scan of the nose, paranasal sinuses, orbit, and brain and request urgent surgical consultation for possible débridement.** Patients with diabetes mellitus, particularly in ketoacidosis, who present with such clinical features must be suspected of having an invasive fungal infection involving the rhinoorbital region. Early symptoms mimic those of bacterial sinusitis; therefore, it is critical to assess the extent of disease

involvement and then arrange for débridement, biopsy for histology, and cultures before initiating empiric antimicrobial treatment. This patient has zygomycosis, which is an uncommon fungal infection caused by species of *Rhizopus*, *Rhizomucor*, *Absidia* and *Cunninghamella*. It affects patients with serious preexisting diseases such as diabetic ketoacidosis, acute leukemia, and uremia. The case patient demonstrates the characteristic clinical presentation of zygomycosis originating in the nose and paranasal sinuses. The mainstay of therapy is surgery. Extensive débridement of craniofacial lesions is essential, and at times orbital exenteration may be required. Frequently, repeated débridement is necessary. High dose IV administration of amphotericin B (1–1.5 mg/kg of body weight) is of value; in patients intolerant of amphotericin B, one of the lipid formulations may be used. None of the currently available azoles has any role in the treatment of this infection.

3. **(D) Perform a CT scan of the chest and possibly a bronchoalveolar lavage/open lung biopsy.** Invasive pulmonary aspergillosis (IPA) is the most likely diagnosis in this patient. IPA is encountered in patients with prolonged neutropenia, those undergoing bone marrow or solid organ transplantation, and those treated with high-dose corticosteroids. Multiple diagnostic approaches should be used rapidly if invasive aspergillosis is suspected. High-resolution CT scans of the chest and sinuses can play a role in early diagnosis, particularly in patients with normal chest radiographs; bronchoalveolar lavage/open lung biopsy may also be helpful. A definitive diagnosis rests upon demonstration of septate, hyaline branching hyphae in lung tissue with a concurrent positive culture of a respiratory specimen for *Aspergillus* species. The mortality rate for IPA is extremely high. Amphotericin B (conventional and lipid formulations) and itraconazole are the antifungal agents approved for the treatment of this fatal disease. Fluconazole has no role in the treatment of aspergillosis. Decreasing the intensity of immunosuppression can be helpful. Pulmonary embolism is less likely, given the subacute onset of cough, fever, bilateral crackles on lung examination, and nodular appearing infiltrates. *Pneumocystis carinii* pneumonia (PCP) is occasionally seen in this subgroup of patients on corticosteroids; with the routine use of prophylaxis with trimethoprim-sulfamethoxazole, PCP is uncommon. Also, the chest radiographs in patients with PCP usually show interstitial infiltrates; nodules and cavitation are rare.