Neutropenic Fever: Review Questions

Michelle J. Iandiorio, MD

QUESTIONS

Choose the single best answer for each question.

1. **A 20-year-old man with a 2-year history of acute lymphocytic leukemia that has been in remission for 1 year presents with fever and rash 1 week after administration of maintenance chemotherapy (ie, methotrexate, vincristine, cytarabine, dexamethasone). Physical examination is notable only for a temperature of 103°F (39.4°C), tachycardia, and skin lesions on his right flank and left shoulder. The lesions are erythematous macules, some with central vesicles and some with central black eschars (Figure). The catheter site shows no signs of infection. The patient is pancytopenic with an absolute neutrophil count of 0 cells/μL. Serum electrolyte levels are normal but moderate transaminitis is noted. The patient is started on vancomycin, piperacillin-tazobactam, and acyclovir. Direct fluorescent antibody testing of the skin lesions is negative for varicella-zoster virus and herpes simplex virus. Blood cultures reveal growth of a gram-negative rod. The patient remains febrile but no new lesions develop, and he maintains low-normal blood pressures. Which of the following changes should be made to this patient's antimicrobial therapy?**
   (A) Add an aminoglycoside
   (B) Add antifungal therapy
   (C) Change piperacillin-tazobactam to cefepime
   (D) No change is required

2. **A 24-year-old woman with newly diagnosed acute myelogenous leukemia becomes neutropenic after induction therapy with daunorubicin and cytarabine. She is placed on prophylactic oral levofloxacin and remains in the hospital for observation. Six days later, she becomes febrile to 103°F (39.6°C). Her white blood cell count is 700 cells/μL with an absolute neutrophil count of 0 cells/μL. Physical examination is unremarkable except for some erythema and mild discomfort around the catheter site. How should this patient be managed?**
   (A) Change levofloxacin to cefepime
   (B) Change oral levofloxacin to intravenous (IV) administration
   (C) Continue oral levofloxacin
   (D) Discontinue levofloxacin and administer IV cefepime and vancomycin

Figure. Skin lesions on the left shoulder of the patient described in question 1.

Dr. Iandiorio is an assistant professor, Division of Infectious Diseases, Department of Internal Medicine, University of New Mexico, Albuquerque, NM.

Questions 3 and 4 refer to the following case.

A 23-year-old man with newly diagnosed acute myelogenous leukemia has been on IV cefepime and vancomycin for the past 4 days for neutropenic fever. Blood cultures drawn from his peripherally inserted central catheter (PICC) on the first day of fever reveal growth of *Pseudomonas aeruginosa*. He continues to be febrile but his blood pressure remains normal. There is no erythema or exudate at the PICC site. He has mild mucositis and nonbloody diarrhea and continues to have an absolute neutrophil count less than 100 cells/μL.

3. **Which of the following is the most appropriate next step in the management of this patient?**
   (A) Add amikacin to current regimen and keep the PICC in place
   (B) Add IV amikacin to current regimen and remove the PICC
   (C) Add an antifungal agent to current regimen and keep the PICC in place
   (D) Discontinue cefepime and vancomycin and initiate ciprofloxacin alone and remove the PICC

4. **The patient's fever resolves 2 days later and repeat blood cultures are negative. However, his diarrhea continues, and stool cultures return positive for *Clostridium difficile* toxin. Which of the following is the next best step in this patient's management?**
   (A) Add metronidazole to the current regimen
   (B) Administer IV vancomycin for coverage of methicillin-susceptible *Staphylococcus aureus* and *C. difficile*
   (C) Isolate the patient and discontinue all parenteral antibiotics
   (D) Place the patient on bowel rest and initiate total parenteral nutrition

ANSWERS AND EXPLANATIONS

1. **(A) Add an aminoglycoside.** The patient's skin lesions are characteristic of ecthyma gangrenosum, which is classically seen with disseminated pseudomonal infection. Because *Pseudomonas* can be drug-resistant, it is recommended that 2 agents with antipseudomonal activity be used until results of sensitivity studies are available.[1] Empiric antifungal therapy is recommended after 1 week of persistent fever in patients on broad-spectrum antibiotics;[2] the case patient has had febrile neutropenia for only 3 days. Both cefepime and piperacillin-tazobactam are active against gram-negative bacilli and are appropriate agents for neutropenic fever; therefore, changing piperacillin-tazobactam to cefepime would not be beneficial.[3]

2. **(D) Discontinue levofloxacin and administer IV cefepime and vancomycin.** Because this patient has become febrile, cefepime and vancomycin should be initiated for broader coverage for a potential infection with methicillin-resistant *S. aureus*. Cefepime is an appropriate broad-spectrum agent for neutropenic fever. Vancomycin should be added when a hospitalized patient has evidence of a line infection (ie, discomfort and erythema around catheter site). Continuing levofloxacin is not indicated in this case because the patient is considered high-risk for complications (ie, absolute neutrophil count < 100 cells/μL, peak temperature > 39°C, and evidence of a catheter-site infection). Levofloxacin has excellent bioavailability, and thus there is no added benefit with changing oral administration to IV administration if oral medication is well-tolerated.[2]

3. **(B) Add IV amikacin to current regimen and remove the PICC.** Patients with pseudomonal bacteremia should be treated initially with 2 agents with activity against *Pseudomonas* until sensitivity data are available. Broad-spectrum coverage should be continued in patients with febrile neutropenia, especially those with mucositis. Vascular access devices can be left in place if there is no sign of tunnel infection. However, if bacteremia is still present or there is evidence of catheter-site infection, the device should be removed.

4. **(A) Add metronidazole to the current regimen.** Metronidazole and vancomycin are both appropriate treatments for *C. difficile* colitis, but only metronidazole is effective both orally and parenterally. IV

vancomycin is not effective against *C. difficile* colitis. Discontinuing antibiotics would not treat this patient's colitis and definitely would not be appropriate in this patient with bacteremia and neutropenia with gastrointestinal mucosal breakdown.[2]

REFERENCES

1. Safdar N, Handelsman J, Maki DG. Does combination antimicrobial therapy reduce mortality in gram-negative bacteraemia? A meta-analysis. Lancet Infect Dis 2004;4:519–27.
2. Hughes WT, Armstrong D, Bodey GP, et al. 2002 guidelines for the use of antimicrobial agents in neutropenic patients with cancer. Clin Infect Dis 2002; 34:730–51.
3. Bow EJ, Rotstein C, Noskin GA, et al. A randomized, open-label, multicenter comparative study of the efficacy and safety of piperacillin-tazobactam and cefepime for the empirical treatment of febrile neutropenic episodes in patients with hematologic malignancies. Clin Infect Dis 2006;43:227–459.

SELF-ASSESSMENT QUESTIONS ON THE WEB

Now you can access the entire self-assessment series on the Web. Go to www.turner-white.com, click on the "Hospital Physician" link, and then click on the "Self-Assessment Questions" option.

INFECTIOUS DISEASES

A current list of certification and recertification exam dates and registration information is maintained on the American Board of Internal Medicine Web site, at www.abim.org.

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