Hematologic Malignancies/Stem Cell Transplantation Program
Clinical Section

UCLA Health System
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CS 6.1 DIAGNOSIS AND MANAGEMENT OF FEVER AND NEUTROPENIA

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Purpose and Background

Patients with neutropenia are at high risk for life-threatening bacterial and/or fungal infections. Because these patients have severely impaired host defense systems, it is critical to deliver appropriate antibiotic therapy quickly to prevent complications from these infections.

Objective

To establish uniform guidelines for the treatment of patients with neutopenia and fever in order to prevent life-threatening infectious complications.

Procedure

1. For patients receiving high dose chemotherapy and/or radiation who report an allergy to penicillin consider skin tests placed at the time of admission to document the status of the allergy (i.e, anaphlaxis). If penicillin skin tests are negative, patient can safely be given imipenem, penicillins, or cephalosporins.

2. Neutropenia is defined as absolute neutrophil count (ANC) $\leq$ 500. Fever is defined as temperature > 38.0 ^{o}C.

3. When a patient with neutropenia develops fever (not specifically attributable to non-infectious causes), 2 sets of blood cultures will be obtained 15 minutes apart. Bacterial and fungal cultures will be sent. When venous access is good, one set of cultures will be obtained from a peripheral vein and a second set will be obtained from a central catheter (otherwise, catheter draw will be adequate). The following additional tests will be obtained as part of the fever work-up: urine culture, sputum culture when appropriate, culture of any site of infection, and chest x-ray. Assessment and physical examination, with particular attention to the mouth and perineum will be obtained. For patients with persistent fever, additional fever work-ups, including blood cultures will be obtained at least every 48 hours.

4. Antibiotic therapy will be administered within 30 minutes of the first fever. Patients eligible for an active antibiotic protocol will be started on the protocol drug. Patients not eligible for a protocol will receive broad spectrum antibiotic coverage (usually Imipenem for adults, Ceftazidime for children). This will be continued until

resolution of fever and neutropenia. Additional antibiotics may be added if the patient has a clear source for the fever that requires broader or alternative antibacterial coverage. Vancomycin should be given only if patient has evidence of a central line infection or a blood culture positive for an organism (MRSA, coagulase-negative staphylococcus) resistant to imipenem, the penicillins, or cephalosporins. Empiric vancomycin for persistent unexplained fever has been shown in placebo-controlled trials to be ineffective in neutropenic patients and should not be used if the patient is stable.

5. Patients with allergies and/or a positive skin test to penicillin will be treated with a quinolone or aztreonam plus vancomycin. An aminoglcoside (usually amikacin) can also be used. Third generation Cephalosporins can be considered in patients with a history of a mild allergy (rash) to penicillin.

6. If a patient develops a positive culture for an organism that is resistant to the antibiotic which is being given, the antibiotic treatment will be tailored to treat that organism.

7. The average time for a febrile neutropenic patient to become afebrile on appropriate antibiotic therapy is 3-4 days. Thus, modification of initial empiric antibiotic therapy is not always necessary if the patient has persistent fever but is stable. If a patient has persistent fever and neutropenia after 4 or more days of therapy with broad spectrum antibiotic therapy, empiric anti-fungal therapy (IV voriconazole, amphotericin, or caspofungin) may be started and continued until the fever and neutropenia have resolved. Use of oral posaconazole for empiric antifungal therapy is unproven. Similarly, empiric vancomycin for persistent unexplained fever has been shown in placebo-controlled trials to be ineffective in neutropenic patients and should not be used if the patient is stable. Excessive use of vancomycin increases the risk for VRE infection.

8. If a patient has a documented or highly suspicious fungal infection and is intolerant of amphotericin (i.e. renal toxicity), IVvoriconazole or caspofungin should be considered.

9. Vancomycin will be used only in patients with clinical suspicion of central line infection or a positive culture for a gram-positive organism resistant to imipenem, or in patients who are penicillin allergic. Empiric vancomycin for persistent unexplained fever should not be used.

10. Antibiotics will be discontinued when fever and neutropenia resolve except in patients with a documented infection that may require an additional defined interval of treatment.

11. When patients are enrolled on antibiotic study protocols, the study protocol takes precedence over these SOP guidelines.

References

1. Hughes WT, et al. 2002 IDSA guidelines for use of antimicrobial agents in neutropenic patients with cancer. Clinical Inf Dis 2002; 34:730-751.

2. Winston DJ, et al. Beta-lactam antibiotic therapy in febrile granulocytopenic patients. Ann Intern Med 1991; 115:849-859.

3. Cometta A, et al. Vancomycin versus placebo for treating persistent fever in patients with neutropenic cancer receiving piperacillin-tazobactam monotherapy. Clin Infect Dis 2003;37:382-389.

ATTACHMENTS:

Attachment A: Procedure History
Attachment B: New/Revised Procedure Checklist

APPROVAL:

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PROCEDURE HISTORY

Date	Initials	Page	Item and Summary of Changes
7/28/09			SOP Title Change
7/28/09			Format Changed
7/28/09			References updated
7/28/09			SOP Revised

Attachment A