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Febrile Neutropenia

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CLINICAL SCENARIO

A 68-year-old woman with diffuse large B-cell lymphoma treated with cytotoxic chemotherapy is admitted from the hematology clinic to the intensive care unit with a fever (102.4°F) and hypotension (80/50 mm Hg; mean arterial pressure, 60 mm Hg). Laboratory examination is significant for an absolute neutrophil count of 280/μl.

INTRODUCTION

Febrile neutropenia (FN) is a medical emergency that requires prompt initiation of antimicrobial therapy. Neutropenia can limit the inflammatory response; thus, fever is often one of the few early infectious manifestations in patients with neutropenia. Disruptions to anatomical barriers in the skin, lungs, and gastrointestinal (GI) tract from cytotoxic therapies is the most common source of infection in patients with neutropenia (1). High-risk features include a longer duration of neutropenia (>7 days), advanced malignancies, hemodynamic instability, and end-organ dysfunction (2). This discussion will focus on the management of fever in severe neutropenia (absolute neutrophil count <500/μl).

MICROBIOLOGY

Bacteria are the most commonly identified cause of FN. Gram-negative and gram-positive organisms, particularly those found in the oropharynx and GI tract, are prevalent causative pathogens (1). Although abundant in the alimentary track, anaerobic bacteria are infrequently identified on cultures.

Fungal pathogens are also important to consider in neutropenic fever, especially in patients with prolonged neutropenia. Invasive fungal infections, such as with *Candida* or *Aspergillus* species, are particularly common in patients at high risk with persistent fevers (3).

Viral causes should also be considered, including reactivation of latent infections in seropositive patients and community-acquired respiratory viruses.

TREATMENT

Given the risk of morbidity and mortality associated with FN, empiric antibiotic therapy should be administered within 60 minutes of presentation. Monotherapy with an antipseudomonal agent such as penicillin, cephalosporin, or carbapenem is the first-line regimen, with oral antibiotic therapy being an acceptable approach in patients with low-risk FN (4). Other antibiotic agents may be added in patients with evidence of sepsis or focal findings or in the case of concern for antibiotic resistance. Gram-positive coverage should be added in patients with skin or soft-tissue infection, catheter-associated infection, pneumonia, or hemodynamic instability.

The choice of antibiotic agent may be narrowed based on culture data if available. The duration of antibiotic therapy when cultures are negative remains controversial; some guidelines recommend continuing antibiotic therapy for the duration of neutropenia, whereas other studies have shown it is safe to discontinue antibiotic therapy in patients in clinically stable condition without fevers for 72 hours (4).

In patients with high-risk neutropenia with persistent fever for >96 hours, empiric antifungal coverage should be added, with *Candida* species being the most likely pathogen (5). Treatment with an azole may be an alternative in patients not already receiving antifungal prophylaxis or in patients in hemodynamically stable condition.

(Received in original form August 17, 2023; accepted in final form April 4, 2024)

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ATS Scholar Vol 5, Iss 3, pp 460–461, 2024

DOI: 10.34197/ats-scholar.2023-0080OT

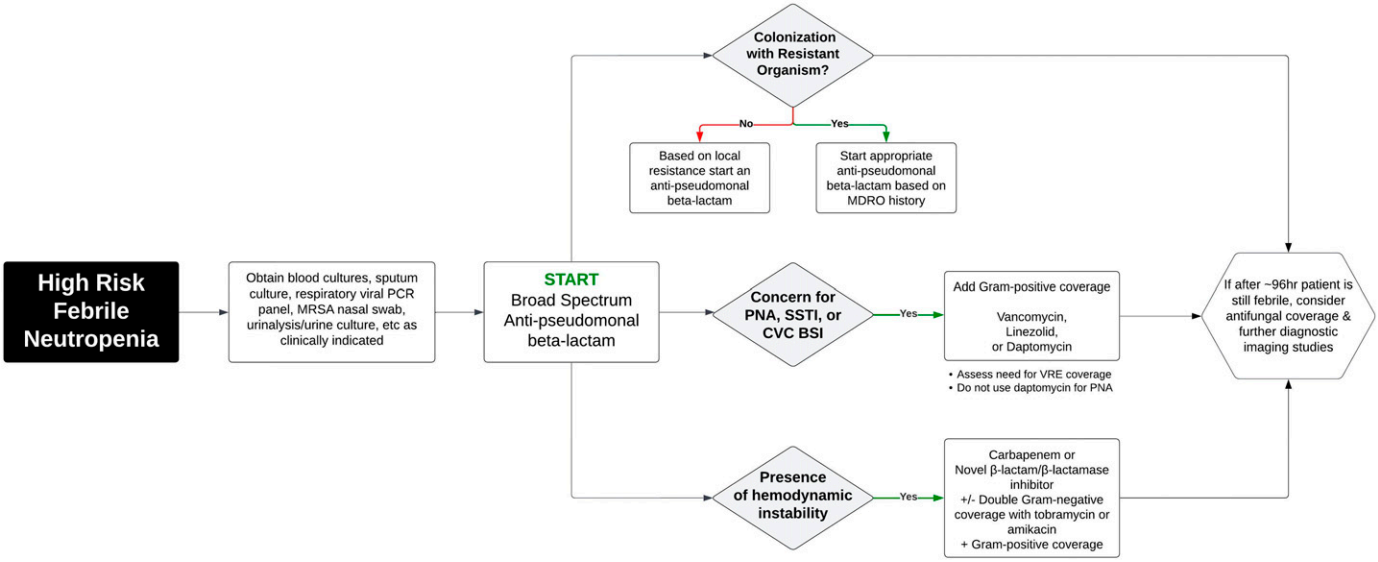

Figure 1. An algorithm for empiric management of high-risk febrile neutropenia. CVC BSI = central venous catheter–related bloodstream infection; MDRO = multidrug-resistant organism; MRSA = methicillin-resistent *Staphylococcus aureus*; PCR = polymerase chain reaction; PNA = pneumonia; SSTI = skin and soft tissue infection; VRE = vancomycin-resistant enterococcus.

CASE CONCLUSIONS

The patient promptly initiated treatment with vancomycin and cefepime and required vasopressor support in the intensive care unit. Her blood cultures returned positive for *Pseudomonas*. When the patient was in hemodynamically stable condition, the antibiotic regimen was narrowed to oral ciprofloxacin for a 14-day course.

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