Teachable Moment | LESS IS MORE

Management of Patients With Febrile Neutropenia
A Teachable Moment

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Story From the Front Lines

A woman in her 30s with stage 2A breast cancer came to the emergency department after recording a temperature of 38.6°C at home. She had completed cycle 4 of adjuvant doxorubicin and cyclophosphamide chemotherapy 7 days prior. Her oncologist had instructed her to check her temperature if she had any symptoms. She had felt fatigued for the prior 2 hours but reported no other symptoms. She had no other medical conditions, and her only medication was as-needed ondansetron for chemotherapy-induced nausea. In the emergency department, her temperature was 38.4°C; blood pressure, 126/78 mm Hg; heart rate, 86 bpm; and respiratory rate, 14/min. She seemed comfortable and did not have an indwelling catheter. Physical examination had normal results. Absolute neutrophil count was 420 cells/μL (reference, 1500-8000 cells/μL; to convert to billions per liter, multiply by 0.001), and a complete metabolic panel had normal results. A chest x-ray and urinalysis showed no signs of infection; blood culture samples were obtained.

She was hospitalized for treatment of febrile neutropenia, and empirical intravenous antimicrobial therapy with vancomycin and piperacillin-tazobactam was initiated. She had no further fevers in the hospital. Her absolute neutrophil count improved to 1200/μL on day 2 without additional growth factor support. Blood cultures recorded no growth, and discharge was planned for day 3 after completion of 48 hours of empirical antibiotic therapy. On the morning of day 3, however, her serum creatinine level increased to 1.9 mg/dL (baseline, 0.7 mg/dL; to convert to micromoles per liter, multiply by 88.4) without changes in urine output or electrolyte/acid-base status. A workup for acute kidney injury did not reveal obvious causes, and this was presumed to be secondary to antibiotic use. Further antibiotics were withheld and her creatinine level improved over the next 3 days to 1.5 mg/dL, when she was discharged.

Teachable Moment

Febrile neutropenia (absolute neutrophil count <1000 cells/μL, and temperature ≥38.3°C by oral or tympanic thermometry) is one of the most common oncological complications.[1,2] It occurs in 10% to 50% of patients with solid cancers, and more than 80% with hematologic cancers.[2] In 2012 alone, there were an estimated 91 650 adult hospitalizations for cancer-related neutropenia in the United States, with a mean length of stay of 9.6 days and a mean cost per hospitalization of $24 770.[3]

The initial laboratory evaluation of all patients with febrile neutropenia includes a complete blood cell count with differential leukocyte count, renal and hepatic function tests, and drawing at least 2 sets of blood samples for culture. The Infectious Diseases Society of America and the American Society of Clinical Oncology promote the use of the Multinational Association for Supportive Care in Cancer (MASCC) score to identify low-risk patients with febrile neutropenia for whom outpatient treatment with oral antibiotics may be appropriate (**Table**).[1,2] While inherently subjective, severe symptoms have included tachypnea (respiratory rate, >24/min), tachycardia (heart rate, >120 bpm), and hypoxemia (oxygen saturation, <90% breathing room air).[4] The MASCC score ranges from 0 to 26 and dichotomizes patients into low risk (≥21) or high risk (<21). After a period of observation of 4 hours in the emergency department or clinic, low-risk patients can be treated as outpatients with oral fluoroquinolones plus amoxicillin-clavulanate (or clindamycin if penicillin allergic) with close monitoring.[1] In the initial validation study, only 3 of 79 (4%) low-risk patients who were treated on an outpatient basis with oral antibiotics after a period of observation required eventual hospitalization, and there were no long-term complications.[5] There are 2 caveats: first, febrile neutropenia remains a "medical emergency"—all patients must present to a clinic or an emergency department, and prompt administration of antibiotics within an hour of triage is crucial. Second, no risk score can replace clinical judgment, and the clinician must consider factors such as ability to tolerate oral intake, as well as patient access to a caregiver, telephone, and transportation, while making the decision for outpatient therapy.[1] In high-risk patients with febrile neutropenia, hospitalization and intravenous monotherapy with an antipseudomonal β-lactam agent is recommended.[2] Guidelines recommend against the routine initial use of vancomycin, even in high-risk patients, with consideration if patients have suspected catheter-related infection, skin or soft-tissue infection, pneumonia, or hemodynamic instability.[2]

Despite these guidelines, hospitalization and inappropriate intravenous antibiotic use in low-risk patients are common. A 5-year study from an academic US medical center found that 98% of low-risk patients with febrile neutropenia received guideline-discordant care.[4] This low-risk patient with a MASCC

Table. The Multinational Association for Supportive Care in Cancer Score

Characteristic	Points
Burden of febrile neutropenia symptoms[a]	
No or mild symptoms	5
Moderate symptoms	3
Severe or morbid symptoms	0
No hypotension (systolic blood pressure >90 mm Hg)	5
No chronic obstructive pulmonary disease	4
Solid or hematologic cancer with no previous fungal infection	4
No dehydration necessitating parenteral fluids	3
Outpatient status at onset of fever	3
Age <60 y	2

[a] The points attributed to this variable are not cumulative. The maximum theoretical score is 26. A score of 21 or greater is considered low risk, and a score of less than 21 high risk.

score of 26 should have been evaluated for outpatient therapy with oral antibiotics but was instead hospitalized for 6 days, received unnecessary intravenous antibiotics, developed an acute kidney injury, and spent anxious time away from her family. Unnecessary hospitalization and antibiotic use are also associated with the emergence of multidrug-resistant organisms in these patients who are susceptible to infection. Outpatient management and close follow-up is a validated treatment strategy in low-risk patients with febrile neutropenia (MASCC score ≥21).

ARTICLE INFORMATION

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