To the Editor—Patients with hematologic malignancies and neutropenia are at increased risk for several infectious complications. They are predisposed to higher rates of bloodstream infections (BSIs) than the general population. Although BSI is caused by bacteremia in ~3% of cases within the general population,1 malignancy (odds ratio [OR], 1.94) and receiving immunosuppression within 14 days of bacteriuria (OR, 8.13) are risk factors for urinary-tract–related BSIs.2 However, few studies have evaluated the occurrence of secondary BSIs from bacteriuria in neutropenic patients. This study was performed to define the incidence of secondary BSIs in patients with acute myeloid leukemia (AML) with neutropenia and bacteriuria and to determine whether neutropenic patients with asymptomatic bacteriuria have a higher rate of BSI than the general population.

Our study took place in a 900-bed Midwestern tertiary-care hospital with ~2,000 annual hematology and oncology admissions. We performed a cohort study of all adult patients with AML who were admitted to the hematology service between February 2010 and November 2013. A case was defined as any patient with neutropenia and bacteriuria during the study period.

Bacteriuria was defined by urine culture growth of >100,000 colony-forming units per milliliter (CFU/mL) of a pathogenic organism. Neutropenia was defined by an absolute neutrophil count of <500 cells per cubic millimeter (cells/mm³) of blood. Secondary BSI was defined by a positive blood culture of the same species as the urine culture within 48 hours of collection of the positive urine culture. Data were collected from the University of Michigan microbiology laboratory and electronic medical records of patients with AML. Patients with bacteriuria were evaluated for the presence of neutropenia and bacteremia. Data collected included demographics, date of first fever if present, date antibiotics were started, antibiotic(s) administered, urinalysis, urine culture results (date of collection and organism), and presence of urinary symptoms. The primary outcome was the rate of bacteremia with the same organism (ie, species) as the urine culture within 48 hours of initial collection. Information on microorganisms, antibiotic use prior to culture, the presence of urinary symptoms, and the urinalyses were obtained through electronic records using the honest broker. This study was approved by the University of Michigan Institutional Review Board.

In total, 1,807 patients with AML were admitted during the study period. Within the initial cohort, 139 patients (0.8%) had bacteriuria. Of the 139 patients with bacteriuria, 102 were neutropenic at the time of culture. Of these patients, 10 of 102 (9.8%) developed bacteremia with the same pathogen as the urine culture. Of 10 isolates, 5 were Enterococcus faecium; it was the most common pathogen that grew in urine and blood cultures within our cohort. Among the E. faecium isolates, 4 of 5 were vancomycin resistant. Other microorganisms isolated included Escherichia coli, Klebsiella pneumonae, and Enterobacter cloacae. Of 10 patients with BSI, 7 had no documented urinary symptoms. Additionally, 7 of 10 of the patients with BSIs did not receive antibiotics prior to obtaining urine and blood cultures or received antibiotics that did not cover the isolated pathogen. Finally, 7 of 10 urinalyses obtained from patients with bacteriuria and BSIs were negative for leukocyte esterase and pyuria (Table 1).

Approximately 10% of the patients in our study who were neutropenic with bacteriuria developed bacteremia. A prior study by Krieger et al2 demonstrated that 2.7% of hospitalized patients within the general population with nosocomial bacteriuria developed BSIs. Most patients in our study who developed bacteremia did not have urinary symptoms documented in their medical record or an abnormal urinalysis; most of the patients who developed bacteremia had no pyuria (Table 1). Patients with neutropenia have a decreased inflammatory response, and pyuria may not occur given a lack of white blood cells; therefore, it is not surprising that most of our patients had no pyuria or leukocyte esterase positivity on their urinalysis.

Current guidelines recommend the use of antibiotics in specific patient populations with asymptomatic bacteriuria including pregnant women, patients undergoing transurethral resection of the prostate, and patients undergoing urologic procedures for which mucosal bleeding is anticipated.4 Treatment of asymptomatic bacteriuria in neutropenic patients is not currently recommended. However, as demonstrated in our study, neutropenic patients may not display classic urinary symptoms indicative of a urinary tract infection (UTI) such as dysuria, urinary frequency, or urgency. Additionally, urinalyses in these patients are unlikely to be predictive of a UTI. Of those patients who developed secondary BSIs, 70% did not receive antibiotics that covered the specific pathogen isolated from urine and blood cultures (prior to the bacteremia). Because the crude mortality rate in patients with BSI and...
underlying malignancy is between 18% and 42%, it may be worthwhile to consider treatment in neutropenic patients with asymptomatic bacteriuria to potentially lower the incidence of BSI.5

Our study has several limitations, including the small number of patients in our final analysis despite a much larger initial cohort. Additionally, the lack of symptoms documented indicative of a UTI may be due to incomplete documentation in the medical record. Despite these limitations, our study suggests that neutropenic patients with bacteriuria, even without symptoms, may benefit from preemptive treatment. Larger studies are necessary to confirm the findings from our study, which demonstrate that common predictors of UTI were not accurate in our neutropenic patients.

Table 1. Prevalence of Findings in Neutropenic Patients with Bloodstream Infection (BSI) Secondary to Urinary Tract Infection

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Urinary Symptoms</th>
<th>Normal Urinalyses (Negative for Leukocyte Esterase)</th>
<th>Antibiotics That Covered Pathogenic Organism Prior to Cultures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with BSI, No. (%)</td>
<td>3/10 (30)</td>
<td>7/10 (70)</td>
<td>3/10 (30)</td>
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