lated from sputum samples obtained from 7 patients were not considered to represent systemic infection. Five (16%) of the patients with VRE bacteremia had polymicrobial infections with Stenotrophomonas maltophilia (2 patients), Escherichia coli (1), Pseudomonas aeruginosa (1), and Staphylococcus aureus (1). Most patients (71%) were neutropenic (absolute neutrophil count, <500 cells/µL) when they developed VRE bloodstream infection or VRE infection of another site.

Our data indicate that the prevalence of VRE colonization among patients with hematologic malignancies and HSCT recipients is lower than rates reported among patients awaiting liver transplantation [1, 4]. Nevertheless, a substantial portion of patients with VRE colonization developed systemic infection, especially during neutropenia [5]. Although we did not investigate infection-related mortality and length of hospitalization in this epidemiologic study, it might be prudent to consider preemptive antimicrobial therapy with agents that have activity against VRE in these high-risk febrile patients with VRE colonization during cytotoxic therapy–induced neutropenia, particularly in those with severe orointestinal mucosal erosion.

Acknowledgments

Potential conflicts of interest. A.S. is a member of the speakers’ bureaus of Merck, Cubist, and Bristol-Myers Squibb. K.V.I.R. is a member of the speakers’ bureaus of Elan, Cubist, Pfizer, and Bristol-Myers Squibb. M.J.M.: no conflicts.

Table 1. Patients with hematological malignancies and intestinal vancomycin-resistant enterococci (VRE) colonization who developed subsequent bacteremia.

<table>
<thead>
<tr>
<th>Patient group</th>
<th>No. of patients</th>
<th>No. (%) of patients with intestinal colonization</th>
<th>No. (%) of patients with subsequent bacteremia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with leukemia</td>
<td>955</td>
<td>56 (5.9)</td>
<td>17 (30)</td>
</tr>
<tr>
<td>HSCT recipients</td>
<td>653</td>
<td>32 (4.7)</td>
<td>9 (28)</td>
</tr>
<tr>
<td>Patients with lymphoma</td>
<td>507</td>
<td>11 (2.2)</td>
<td>3 (27)</td>
</tr>
<tr>
<td>Total</td>
<td>2115</td>
<td>99</td>
<td>29 (29)</td>
</tr>
</tbody>
</table>

NOTE. HSCT, hematopoietic stem cell transplant.

References


Preemptive Antifungal Therapy among Neutropenic Patients

To the Editor—We read the recently published article by Maertens et al. [1] in which they suggest a very interesting approach to the management of invasive fungal infections. However, some questions and considerations can be raised.

First, Maertens et al. [1] excluded patients with severe aplastic anemia and patients who had undergone autologous or nonmyeloablative allogeneic stem cell transplantation. In a large study from Fred Hutchinson Cancer Research Center (Seattle, WA) reported by Marr et al. [2], an increased incidence of invasive aspergillosis was documented both among recipients of allogeneic stem cell transplants and among recipients of autologous stem cell transplants. A strict correlation was also found not only between duration and severity of neutropenia, but also between lymphopenia and viral infection, especially later after stem cell transplantation.

Furthermore, patients who undergo nonmyeloablative allogeneic stem cell transplantation are at risk of developing invasive fungal infection associated with immunosuppression that results from previous heavy treatment, which often includes autologous stem cell transplantation. Most nonmyeloablative conditioning regimens contain fludarabine or other purine analogues, which increase the risk of invasive fungal infection. To exclude these patients from the study reduces its clinical impact.

Second, in many institutions, the antifungal prophylaxis regimen includes azoles and amphotericin B, which have activity against molds; use of these agents can interfere with the results of galactomannan EIA [3]. Is such a preemptive strategy necessarily a good alternative to prophylaxis involving agents with activity against Aspergillus?

Third, the role played by daily blood cultures for patients receiving steroids is not clear. How many of these cultures doc-
Acknowledgments

Potential conflicts of interest. All authors: no conflicts.

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References


Reply to Stefani et al.

To the Editor—We thank Stefani et al. [1] for their interest in our article [2]. The objective of our study was to assess the feasibility of an EIA/CT scan–based preemptive antifungal approach in a population that often receives empirical therapy on the basis of persistent neutropenic fever. The performance and reproducibility of the Platelia EIA (Bio-Rad) at a cutoff of 0.5 and the reliability of the “halo sign” on CT scan prove to be excellent, although this is true within the boundaries of a well-defined population [3–5]. Basically, this population consists of adult patients with prolonged chemotherapy-induced neutropenia, including patients treated for acute leukemia or high-risk myelodysplastic syndrome and those undergoing myeloablative allogeneic hematopoietic stem cell transplantation (HSCT). Fortunately, this group overlaps with the group of patients who also frequently receive empirical antifungal therapy. We agree with Stefani and colleagues that patients with aplastic anemia and those undergoing allogeneic HSCT with reduced-intensity conditioning are also at risk for invasive aspergillosis. However, most of these transplant recipients experience a short course of neutropenia and develop fungal infections late after transplantation, when they receive corticosteroids or other immunosuppressants for graft-versus-host disease. Unfortunately, in this nonneutropenic scenario, the halo sign (one of the cardinal elements of our approach) has a low specificity [6]. In addition, only limited data are available about the performance of the EIA in cases of aplastic anemia and after nonmyeloablative transplantation. Therefore, we decided to target exclusively the high-risk neutropenic group and to exclude all other subjects from the protocol. We feel that an additional evaluation of noninvasive diagnostic techniques is needed before such techniques can be implemented in preemptive approaches in nonneutropenic patients. Contrary to the Seattle data [7], we have observed a low incidence (<1%) of invasive aspergillosis among persons who have undergone autologous HSCT over the past decade. As such, we do not consider these patients to be at considerable risk for invasive aspergillosis.

The use of agents with anti-Aspergillus activity is indeed a confounding factor, because this treatment reduces the serum concentration of galactomannan, resulting in a delayed detection. As discussed in our article, the feasibility of an EIA-based strategy in health care centers that administer prophylaxis with these agents should be further tested. We used fluconazole as the prophylactic agent because the drug does not interfere with the diagnostic assay and has an excellent prophylactic efficacy against Candida infection.

One set of blood samples was obtained daily for culture from patients receiving high-dose corticosteroid treatment. The purpose of these cultures was not to detect fungemia, but rather to detect bacteremia in patients who may not develop fever as a result of the antipyretic action of the steroids. We disagree that monitoring for parasitic and other infections by exam-