Commentary (Sendowski/Segal): Management of Health-Care–Associated Infections in the Oncology Patient

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Infections are major causes of morbidity and mortality in patients with cancer. In certain instances, the malignancy itself can predispose patients to severe or recurrent infections. For example, acute leukemia may cause neutropenia and ensuing bacterial or fungal infection. Hypogammaglobulinemia of chronic lymphocytic leukemia may be complicated by infections due to encapsulated bacteria. Patients with Hodgkin's lymphoma may suffer from recurrent varicella-zoster infections. Solid tumors may obstruct the lumens of respiratory, digestive, and urinary tracts, leading to bacterial infections. Nevertheless, the principal risk of infectious complications is related to the intensity and duration of immunosuppressive chemotherapy. Patients with cancer constitute a highly varied population, both in terms of the underlying malignancy and in terms of their immunosuppression. In addition, a single patient may have multiple predisposing factors, thus increasing the spectrum of likely pathogens. When evaluating a patient with cancer for a possible infection, it is essential to develop a conceptual framework of quantitative and qualitative immune defects the patient is likely to have, and then to stratify the risk for specific pathogens in the context of the history, physical exam, and laboratory data.[1]

Areas Deserving More Attention

The review by Guinan et al clearly defines the scope of health-care- associated infections (HAIs) on a national level in terms of added patient mortality and cost of care. Based on Centers for Disease Control and Prevention estimates, in the United States, HAIs occur in 2.4 million patients annually at a cost of $4.5 billion. Moreover, HAIs are the primary cause of (or a contributing factor in) the death of approximately 100,000 patients each year. The authors provide a rank order of the most common sites of infection, and note that the specific goals of their paper are to review the risk factors for HAI in oncology patients, HAI outbreaks, and preventive measures. The review would be considerably more useful if the section headed "Compromised Immune System" was better organized and prioritized the major categories of immune suppression encountered in oncology. The concept that the degree and duration of neutropenia have a critical impact on the risk of, and likelihood of recovery from, serious infection should be developed at the outset of the article. Additional factors such as compromised T-cell and humoral immunity, splenectomy, and defects in mucosal immunity following mucotoxic chemotherapy and radiation therapy should be more fully developed.

The role of corticosteroids, frequently used as chemotherapeutic agents, is largely ignored. In addition, issues of performance and nutritional status-important factors that interact with both the underlying malignancy and toxicity of treatment- are not given appropriate attention as risk factors.
for infectious complications. A table summarizing immune defects and the specific pathogens to which they predispose would be very useful. With this groundwork established, the reader would be better equipped to understand the interface between the patient and the hospital environment, which leads to specific infectious syndromes such as pneumonia, bloodstream infection, and postoperative infections.

**Spectrum of Pathogens**

This article also does not adequately discuss and prioritize the spectrum of pathogens that afflict patients with cancer. The authors correctly point out that there has been a shift in the relative prevalence of specific pathogens in cancer patients. Whereas in the 1960s and 1970s, gram-negative bacterial pathogens (Enterobacteriaceae and *Pseudomonas aeruginosa*) were the principal causes of bacteremia, over the past 20 years, grampositive pathogens have become predominant.[2] This shift is likely due to the widespread use of indwelling central catheters and prophylaxis with quinolones.

In this review, antibiotic resistance among nosocomial bacteria, including oxacillin-resistant *Staphylococcus aureus*, extended-spectrum beta-lactamase and cephalosporinase-producing gram-negative rods, and quinolones-resistant gram-negative rods receive little or no attention. The authors use the term "vancomycin-resistant infections" in the "Environment" section. It would be more useful to clearly delineate between vancomycin-resistant *Enterococcus* and vancomycin-intermediate and vancomycin-resistant *S aureus*. Nosocomial acquisition of *Clostridium difficile* is also not mentioned.

*Candida* spp are the fourth most common cause of nosocomial bloodstream infection[3] but receive virtually no attention in this paper. Candidemia is a major cause of mortality in patients with cancer, associated with a mortality rate of 40% to 60%.[4] Central-line catheters are an important source of nosocomial candidemia. In patients receiving induction/remission chemotherapy, candidemia and disseminated candidiasis are most closely related to gut mucotoxicity. Azole-resistant *Candida* spp are an important concern, particularly in transplant centers in which fluconazole (Diflucan) prophylaxis is widely used.[5]

**Risk of Aspergillosis**

The authors appropriately note the importance of invasive aspergillosis in highly immunocompromised patients with cancer. The risk of aspergillosis in patients with cancer is strongly related to the degree and duration of neutropenia. The more frequent use of allogeneic hematopoietic transplantation has expanded the risk factors for aspergillosis. Late aspergillosis occurring after neutrophil recovery and in the setting of potent immunosuppressive therapy for graft-vs-host disease has become a major cause of mortality in this patient population.[6]

The authors correctly note the association between hospital construction/renovation and an increased risk of *Aspergillus* infection. However, most cases of invasive aspergillosis and other filamentous fungal infections occur in the absence of a clearly identified environmental source. It would be interesting to know the authors' views on high-efficiency particulate air (HEPA) filtration and laminar air flow rooms as a means of preventing infections by molds in high-risk patients with hematologic malignancies and in hematopoietic transplant recipients.[7]

**Preventive Measures**

In the "Prevention and Future Developments" section, the authors devote significant attention to the importance of using appropriate antibiotic therapy for established infections. However, there is no discussion of policies that foster appropriate use of antibiotics as a means of preventing the emergence of resistant nosocomial pathogens. An example would be the institution of specific infection control measures (such as oversight of prescribing antimicrobial agents by an infectious diseases specialist) to reduce the frequency of vancomycin-resistant enterococcal infection.[8] Also of value would be a brief discussion of molecular techniques used to identify nosocomial outbreaks of infection.

Finally, there have been recent reports of two clinical infections by vancomycin-resistant *S aureus* occurring as a result of transfer of the vanA gene from *Enterococcus*. The potential for transfer of this gene in nature has been anticipated for several years. Given the intrinsic virulence of *S aureus* and its propensity to cause serious nosocomial infections, this mode of acquiring vancomycin resistance could be of particular concern in oncologic and surgical patient populations.
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