Sepsis and Challenging Infections in the Immunosuppressed Patient in the Intensive Care Unit

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KEYWORDS

• Sepsis • Infection • Critically ill • Immunosuppressed

KEY POINTS

- The clinical approach to both diagnosis and treatment of infections in the critically ill immunosuppressed patient is highly dependent on the specific cause of the immunosuppression.
- The opportunistic infections affecting patients with human immunodeficiency virus (HIV) are different from those affecting patients with solid organ transplantation, which in turn are also different from those affecting patients with hematopoietic stem cell transplantation.
- Furthermore, important epidemiologic questions, such as how advanced the HIV disease is, how far the patient with solid organ transplantation is from the surgical procedure, and what type of stem cell transplant was performed, are all important to guide the clinician toward the most probable infection etiology that could be causing the critically ill status.
- The general treatment approach is dependent on the precision of the diagnostic approach and consists of rapid initiation of antimicrobials, source control, and minimization of immunosuppression by either reducing immunosuppressive drugs, or reconstituting the immune system with antiretroviral drugs for patients with HIV.

INTRODUCTION

Sepsis remains a major public health problem, one of the top causes of death among immunosuppressed critically ill patients who have undergone solid organ transplantation (SOT) and hematopoietic stem cell transplantation (HSCT).[1,2] These are small but unique and growing populations that are often excluded from randomized controlled trials evaluating therapies for sepsis and infection.[3] The incidence of sepsis is 20% to

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60% of all SOT recipients, with an in-hospital mortality of 5% to 40%.[4,5] Severe sepsis in HSCT recipients is approximately 5 times more frequent when compared with the nonimmunocompromised population, with a twofold higher mortality for allogeneic HSCT recipients than autologous recipients; reported in-hospital mortality is 55% to 70% for allogeneic and 30% to 58% for autologous HSCT recipients.[6] Most infections and sepsis in patients with HSCT are related to neutropenia (neutrophil count $\leq$500/mm^3 or $\leq$1000/mm^3 with a predicted decrease to $\leq$500/mm^3) and mucositis induced by cytoablative chemotherapy, or delayed engraftment following HSCT.[7] Patients with solid tumors usually undergo less intense chemotherapy and rarely become neutropenic.

Detailed epidemiologic information and clinical history are vital to understand the risk of different infections in immunocompromised patients. Exposures to contacts with respiratory illness would suggest influenza, parainfluenza, respiratory syncytial virus (RSV), and adenovirus infections; exposure to construction sites or environmental sources would make us suspect *Histoplasma*, *Aspergillus*, or *Nocardia* infections; exposure to water sources can be followed by *Legionella* or atypical mycobacterium infections; travel to certain areas might raise suspicion for endemic fungal infections (histoplasmosis, cryptococcosis, coccidioidomycosis).[8,9] The risk for certain opportunistic infections (invasive aspergillosis, cryptococcosis, nocardiosis, *Pneumocystis* pneumonia, cytomegalovirus [CMV] disease) depends on the net state of immunosuppression, a direct reflection of previous use of T-cell depleting antibodies for induction or rejection, myeloablative regimens, and the chronic immunosuppression.[10,11] SOT and HSCT recipients with infections and sepsis frequently are afebrile, but tend to have more thrombocytopenia and develop organ failure.[12]

CLINICAL SYNDROMES

Vascular Access Device–Related Infections

Please refer to the article by Taison Bell and Naomi O'Grady, "Prevention of Central Line-Associated Bloodstream Infections," in this issue.

Prolonged vascular access may be needed for longer periods for renal replacement therapy, total parenteral nutrition, treatment of acute rejection, or graft-versus-host disease (GVHD).[13–15] Vascular access device (VAD) infections can originate from the skin flora or from severe gastrointestinal mucositis (due to chemotherapy or bowel ischemia).[13–15] To determine the role of VAD in the etiology of bloodstream infections, the time-to-positivity between peripherally and centrally drawn blood cultures should be compared; a centrally drawn blood culture that is positive at least 120 minutes earlier than a peripherally drawn blood culture is highly sensitive and specific for VAD-related infection. Most VAD exit site infections can be treated with anti-infective therapy without line removal. However, VADs should be immediately removed in patients with septic shock, septic phlebitis, and tunnel or port pocket infection. VAD should be removed in patients with infections caused by *Staphylococcus aureus*, *Bacillus* spp, *Acinetobacter*, *Pseudomonas aeruginosa*, *Stenotrophomonas maltophilia*, *Corynebacterium jeikeium*, nontuberculous mycobacteria, yeasts, and molds. Management of VAD should follow the published guideline.[15,16]

Pneumonia

The respiratory tract remains one of the most frequent portals of entry for community-acquired, nosocomial, or opportunistic pathogens. In SOT, during the first month after transplantation, nosocomial infections, including hospital-acquired or ventilator-associated pneumonia are common, whereas pulmonary aspergillosis and viral