Sepsis in Immunocompromised Patients

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Introduction

- The advances in care for patients with an immunocompromised status have been remarkable over the last 2 decades, but sepsis continues to be a major cause of death

- The detection of serious infections may be more challenging owing to patients' lower ability to mount the clinical symptoms that usually accompany sepsis

Introduction

- Immunocompromised patients are also susceptible to a broader range of pathogens than nonimmunocompromised patients, and certain infections are more common relative to the duration and type of immunosuppression.

- SEPSIS IN SOT RECIPIENTS
- SEPSIS IN NEUTROPENIC PATIENTS AND HSCT RECIPIENTS
- BIOMARKERS IN SEPSIS OF IMMUNOCOMPROMISED PATIENTS

SEPSIS IN SOT RECIPIENTS

- Transplant recipients are more frequently admitted than other patients and they experience more frequent nosocomial infections and sepsis

- classic features of sepsis, such as leukocytosis and fever, may be absent, whereas thrombocytopenia and organ failure may be more pronounced

- Bacterial infections in these patients display more antibiotic resistance, likely owing to more frequent hospitalization and repeated antibiotic exposure

SEPSIS IN SOT RECIPIENTS

- Candida spp. are the most common cause of fungal infections in SOT recipients and the most common cause of fungemic sepsis

- These patients are also at increased risk for opportunistic viral infections, particularly cytomegalovirus (CMV) infections

Risk Factors

- CMV serologic mismatch
- because of CMV reactivation, through immunomodulatory mechanisms, the risk of subsequent bacterial and fungal infections is increased
- Type of surgical procedure
- Cold ischemia time
- length of surgical procedure
- Amount of blood loss and transfusions during transplant
- The net state of immunosuppression
- The use of T-cell–depleting antibodies for induction or rejection
- The use of previous myeloablative regimens

Types and Timing of Infections After SOT

- During the first month after transplantation, nosocomial pneumonia, including hospital-acquired or ventilator-associated pneumonia, is relatively common in SOT recipients

- Infections due to Candida spp. are primarily noted within 30 days after transplantation

Types and Timing of Infections After SOT

- Between 1 and 6 months after transplantation, Community-acquired pathogens and opportunistic infections also start playing a role

- After 6 months, with decreasing immunosuppression, community-acquired infections predominate, although opportunistic infections are still seen

Management of Sepsis After SOT

General management principles for sepsis in SOT recipients do not differ significantly:

- Rapid initiation of intravenous antibiotics
- Early resuscitation to restore adequate circulatory volume, use of organ support (eg, ventilator support, vasopressors, and hemodialysis)
- Attempts at rapid diagnosis of the offending pathogen
- Source control
- A thorough evaluation for diseases that can mimic sepsis

Effects of SOT Status on Outcomes in Sepsis

- Evidence suggesting that SOT recipients have no greater mortality risk
- Immunosuppression in transplant recipients may attenuate an otherwise harmful immune response and thereby be of some benefit in sepsis.

- A large prospective study comparing immunocompromised and nonimmunocompromised patients and measuring clinical and biochemical parameters throughout the time course of sepsis would be highly informative

Kidney Allograft Recipients

- Early infections after kidney transplantation are commonly related to anastomotic leaks, urinary catheters, or retained ureteral stents

- Given that the urinary tract is the most common site of infection and source of sepsis in kidney transplant recipients **abdominal ultrasonography** should be considered in any kidney transplant recipient presenting with sepsis to assess for pyelonephritis, perinephric abscess, fungal ball, or ureteral obstruction

Liver Allograft Recipients

- Risk factors for the development of sepsis in these patients are related to:

- Biliary and enteric procedures,
- Poor baseline status,
- Prolonged transplant procedure,
- Extended stay in the postoperative intensive care unit

Liver Allograft Recipients

- Up to 30% of liver recipients develop sepsis in the first 3 months after transplantation, with intra-abdominal infections the most common source

- Pneumonia is another common source of infection in liver transplant recipients, especially in the first month after transplantation

Heart Allograft Recipients

- Infections in heart transplant recipients in the first 30–60 days after transplant are more likely to be caused by nosocomial organisms, such as :

Acinetobacter baumannii, Pseudomonas aeruginosa, Klebisella pneumonia, Escherichia coli, and S. aureus.

Heart Allograft Recipients

- Mediastinitis is diagnosed in 5%–10% of heart transplant recipients and is a major concern

- Pneumonia is another important infectious complication

Lung Allograft Recipients

- In lung allografts, the pulmonary lymphatics are necessarily disrupted during surgery thereby altering the lymphatic drainage and the immune system's ability to interact with the graft.

- In addition, denervation diminishes the cough reflex and impairs mucociliary clearance.

- Together, these changes increase the risk for severe infection of the allograft.

Lung Allograft Recipients

- Knowledge of colonization and previous infections in the lung recipient, especially resistance patterns for multidrug-resistant organisms can be helpful in the management of sepsis.

- The lung is the most common site of infection in these patients, with bacterial infections the most common cause of pneumonia and sepsis. Fungal infections are more common in the first 2–3 months after transplantation

SEPSIS IN NEUTROPENIC PATIENTS AND HSCT RECIPIENTS

- Prolonged neutropenia (≥7 days) identifies patients at greatest risk for infection and sepsis
- Neutropenic patients may lack the classic signs of inflammation,complicating the early diagnosis of infection and sepsis
- If neutropenic patients are febrile, antibiotics should be initiated early, and infection should be suspected until proved otherwise

Types and Timing of Infections After HSCT

- In HSCT recipients, the **pre-engraftment period** (<15–45 days after transplantation) carries significant risk for **nosocomial infection**, as well as infection due to *Aspergillus, Candida,* herpes simplex virus, and other respiratory and enteric viruses.

Types and Timing of Infections After HSCT

- Between 30 and 100 days after engraftment, (**Post-engraftment period**) herpesviruses, and particularly CMV, may predominate, in addition to *Pneumocystis* and *Aspergillus*

- Beyond 100 days (**Late period**), the risk for CMV, varicella zoster virus, and *Aspergillus* remains high, with community-acquired pathogens becoming more common

DDX & Evaluation

- Catheter related BSI
- Enterocolitis and typhlitis
- Pneumonia
- IFI (mold, candida)
- Other sites
- Unknown origin

Management of Sepsis in Neutropenic Patients

- In general, empiric antibiotic selection in septic HSCT recipients should be guided by local resistance patterns, recent antibiotic exposure, colonizing organisms, recent culture data, and the most likely organism at the suspected site of infection.

- Monotherapy with bactericidal antibiotics covering gram-negative bacilli, such as **antipseudomonal β -lactams** (cefepime, piperacillin-tazobactam, or carbapenems) is recommended in neutropenic patients without sepsis signs.

Management of Sepsis in Neutropenic Patients

- If gram-positive infections are likely, such as those that would be suspected in vascular catheter–related infection, skin and soft-tissue infection, or staphylococcal or streptococcal toxic shock syndrome:

The addition of empiric coverage for resistant gram-positive infections may be warranted

Management of Sepsis in Neutropenic Patients

- Combination antimicrobial therapy with the addition of a fluoroquinolone, aminoglycoside, or other broad-spectrum antimicrobial agent may be used in patients with a high likelihood of multidrug-resistant pathogens or those presenting with septic shock.

- **Empiric antifungal therapy**, should be started in all neutropenic patients, presenting with septic shock

- Empiric antifungal therapy should be considered in high-risk patients with persistent unknown origin fever >4 days who are not responding to antibacterial therapy.

Management of Sepsis in Neutropenic Patients

- Biomarkers that suggest invasive fungal infections, including galactomannan and β-D-glucan, may be useful, especially in those with prolonged neutropenia

- False-positive β-D-glucan results have been seen in certain situations, including cellulose membranes used for hemodialysis and use of intravenous immunoglobulins, and with certain bacterial infections, including *P. aeruginosa*

Management of Sepsis in Neutropenic Patients

- Another evaluation and management challenge in this population relates to the numerous new cancer therapeutics (target therapy and monoclonal Ab)that have become available in recent years.

- Each agent must be considered for its own adverse effect profile, some of which can mimic infection.

- The cytokine release syndrome in chimeric antigen receptor T-cell therapy is one notable example

Effect of Severe Neutropenia on Outcomes in Sepsis

- When assessing the mortality rates associated with sepsis in neutropenic patients, some studies have found rates similar to those seen in nonneutropenic patients without cancer

- The lack of neutrophils in neutropenic patients may abate some of the endothelial injury caused by neutrophilinduced proteolytic and oxidative stress that nonneutropenic septic patients would otherwise endure

BIOMARKERS

- Procalcitonin (PCT) is a propeptide biomarker that is released by a host of human tissues in response to inflammatory cytokines and endotoxin
- After transplant surgery, PCT levels expected to peak on the first or second day, with reduction over the next week if the course is uncomplicated Although the peak does not seem to correlate with complication, a PCT level that fails to decrease during the first postoperative week should prompt suspicion of infection
- Thus, the kinetics of PCT may be more useful than a measurement at a single point in time

BIOMARKERS

- Antithymocyte globulin for induction or rejection therapy has been associated with significantly elevated PCT levels, whereas interleukin 2 antagonists and steroids do not affect PCT levels
- Among patients who are chronically immunosuppressed, baseline PCT levels are not thought to be altered in the absence of infection

- Another host biomarker that is being evaluated at the current time is the individual patient's immune profiling


Thank You!