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**Healthcare Associated
Infections: A Case-
based Approach
to Diagnosis and
Management**

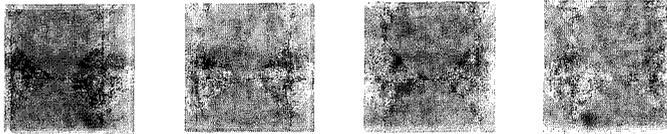
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Chapter 7a

Healthcare-Associated Infection after Solid Organ Transplant

Charlesnika T. Evans and Michael G. Ison

Case Presentation

The patient is a 48-year-old African American male who underwent cadaveric renal transplant 1 week prior to presentation. He has a history of hypertension, diabetes mellitus, coronary artery disease, hypercholesterolemia, and morbid obesity (BMI = 43). He is currently taking tacrolimus, mycophenolate mofetil, valganciclovir, trimethoprim-sulfamethoxazole, clotrimazole troches, insulin, aspirin, simvastatin, and metoprolol. Additionally, he received alemtuzumab and methylprednisolone for induction immunosuppression perioperatively. Clinically he did well after transplantation, rapidly made urine, and had a decline in his creatinine from 6.4 mg/dl immediately pretransplant to 2.2 on postoperative day 2. He returns now for routine postsurgical follow-up and is noted to have erythema, pain, and induration around the inferior one-third of the incision; he has had no fevers. No purulent drainage is expressed on palpation and his white blood cell count is 3.2; creatinine is 1.1 mg/dl. Two staples are removed from the incision and he is started on an oral first generation cephalosporin.

Differential Diagnosis and Initial Management

Solid-organ transplantation (SOT) is now considered the definitive management option for most patients with end-stage organ failure. Improvements in surgical techniques, immune suppression, and antimicrobial prophylaxis have reduced the frequency of rejection and prolonged graft survival after SOT. However, infections, whether they are healthcare-associated, opportunistic, or community-acquired remain a significant and frequent cause of morbidity and mortality following SOT. In general, infectious complications occur in three major time periods: early (0–30 days posttransplant), during peak immune suppression (31–180 days post-transplant), and late (181+ days posttransplant). Although healthcare-associated infections can occur at any time, most occur during the early posttransplant period and are typical of other healthcare-associated infections recognized after elective surgery. Presentation, though,

is often modulated by the use of immune suppression; as a result, signs and symptoms may be muted.

The development of pneumonia, bloodstream infection (BSI), surgical site infection (SSI), and urinary tract infection (UTI) occur in all types of transplantation, although they vary by solid organ received. For example, there is a higher rate of pneumonia among lung transplant recipients and a higher rate of UTI among renal transplant recipients. Reported rates of pneumonia, BSI, and UTI episodes in heart and lung transplantation range from 14 to 138 infections per 100 patients for pneumonia, 4.1 to 29 infections per 100 patients for BSI, and 2.6 to 21.6 infections per 100 patients for UTI. Most HAIs occur within the first 30 days posttransplantation and SSIs are the most frequent within this time period, although post-transplant wound infections can occur up to a year after surgery. These infections are highest in abdominal transplantation (kidney and liver), with estimates from the literature up to 18.6% in kidney transplantation and up to 37.6% for liver transplantation. The Centers for Disease Control and Prevention (CDC) National Healthcare Safety Network (NHSN) collects data on HAIs in over 1,000 medical facilities; however, only 9 are transplant centers. The limited NHSN data suggest that SSIs in high-risk kidney transplant (6.6/100 operations) and liver transplant recipients (20.1/100 operations) are higher than in comparable nontransplant procedures (4.5 and 13.7, respectively). The most common risk factors for SSI have included patient demographic and medical characteristics such as age, body mass index, severe hyperglycemia, and surgery characteristics such as duration of operation and previous surgery.

Initial management of individual HAIs should be consistent with local standard-of-care practice and antimicrobial resistance patterns and detailed management guidelines are available from the American Society of Transplantation's Infectious Diseases Community of Practice. Some important points to note include: (1) Renal function is often abnormal in most transplant recipients; as such, any prescribed antimicrobial should be adjusted based on the individual patient's estimated creatinine clearance. (2) Drug interactions between frequently prescribed antimicrobials and antirejection medications complicate the management of such patients and may result in either over- or under-immunosuppression. (3) Foreign bodies (i.e., ureteral stents, biliary T-tubes) may be placed during the transplant procedure and should be taken into consideration in determining the duration of antimicrobial therapy. Discontinuation of antimicrobial therapy before removal of such foreign bodies may allow the infection to relapse. (4) Involvement of the transplant team (especially Transplant Infectious Diseases clinicians if available) at your center is critical. They may often be aware of unique surgical or host characteristics useful for diagnosis and management of the infection. (5) It is critical to consider the donor as the source of any early post-transplant infections presenting in the recipient. A careful review of all donor cultures should be conducted to help inform concern about a potential disease transmission. If a donor-derived disease transmission is considered, this should be reported immediately to the leadership at your transplant center, to your local organ procurement organization, and the national Organ Procurement and Transplant Network (currently the United Network for Organ Sharing). This is critical because it

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may avert morbidity and mortality in other recipients and is currently required by OPTN policy.

Case Presentation (continued)

The patient returned three days later with worsening erythema, pain, and induration despite being compliant with his antibiotic. He also noted low-grade temperature (to 100.5°F) at home and his peripheral WBC was 5.4. He was admitted and started on vancomycin and meropenem. CT imaging revealed a fluid collection deep to the wound and aspirated fluid grew an extended spectrum β -lactamase (ESBL) producing *Klebsiella pneumoniae*. Blood cultures remained negative.

Discussion and Management

Risk factors for infections with antibiotic-resistant microorganisms include comorbidities and underlying illness, hospitalization, invasive instrumentation (i.e., indwelling devices, mechanical ventilation), and previous antibiotic exposure. The latter, antibiotic exposure, has been associated with acquiring a variety of antibiotic-resistant microorganisms, such as methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), and multidrug-resistant gram negatives. The prevalence of these resistant organisms varies by region and many of these organisms have been increasing in transplant recipients and can cause significant morbidity and mortality.

Methicillin-resistant *S. aureus* is responsible for 2.7% to 24% of SSIs in SOT recipients and 5.9% of BSIs. Colonization with MRSA in liver transplant recipients is associated with a high incidence rate of MRSA infection (31% to 87%). Reports have indicated that VRE may cause 5% to 11% of infections in liver recipients. Resistance in gram-negative organisms, such as ESBL-producing or carbapenem-resistant *Klebsiella* or *Pseudomonas*, are also increasing among SOT recipients. One study found that in SSIs, 80% of *K. pneumoniae* were ESBL-producing and 33.3% of *P. aeruginosa* isolates were carbapenem-resistant among kidney recipients.

Because both resistant pathogens and unusual infections (i.e., Mycobacteria, fungi) may be responsible for infections that fail to respond to initial therapy, routine cultures of the affected organ system are critical and should be obtained whenever possible before antimicrobial therapy is instituted. Likewise, known colonization of the recipient with resistant pathogens (such as MRSA or VRE) may help guide initial therapy while cultures are still pending.

Prevention and Next Steps

Both the CDC and the American College of Surgeons, through the National Surgical Quality Improvement Program, have extensively studied and developed guidance to minimize post-surgical HAIs in nontransplant settings (Table 7.1).

TABLE 7A-1 Summary of CDC Recommendations for Prevention of Surgical Site Infection

Recommendation	Level of Evidence for Recommendation*
Preoperative	
Preparation of the patient including: treating all current infections, hair removal, obtaining appropriate chemistry/hematology tests, and preoperative maintenance of surgical area	Category IA-IB, Category II
Hand/forearm antiseptics for surgical team members including cutting and cleaning nails and scrubbing arms	Category IB, Category II
Management of infected or colonized surgical personnel through education and encouragement of reporting of symptoms and developing policies related to personnel responsibility, work restrictions, and clearance to resume work	Category IB
Appropriate antimicrobial prophylaxis	Category IA-IB
Intraoperative	
Maintenance of appropriate ventilation in operating room	Category IB, Category II
Cleaning and disinfection of environmental surfaces	Category IB, Category II
Performance of environmental microbiologic sampling only in cases of epidemiologic investigation	Category IB
Appropriate sterilization of surgical instruments	Category IB
Use and changing of surgical attire (masks, gloves, gowns), when appropriate	Category IB
Adherence to aseptic technique	Category IA-IB, Category II
Postoperative incision care	
Protection of incision with sterile dressing and use of sterile technique and washing hands when changing dressings	Category IB, Category II
Education of patients and family about proper care of incision and potential symptoms of infection	Category II
Surveillance	
Use CDC definitions for SSI case finding; conducting both surveillance in the inpatient setting and postdischarge.	Category IB, Category II
Document surgical wound classification and variables known to be associated with SSI risk	Category IB, Category II
Calculate and review SSI rates periodically.	Category IB

* *Category IA.* Strongly recommended for implementation and supported by well-designed experimental, clinical, or epidemiological studies. *Category IB.* Strongly recommended for implementation and supported by some experimental, clinical, or epidemiological studies and strong theoretical rationale. *Category II.* Suggested for implementation and supported by suggestive clinical or epidemiological studies or theoretical rationale.

Recommendations for prevention of SSI focus on preoperative patient and surgical team factors, intraoperative issues related to the environment of the operating room and aseptic technique, postoperative incision care, and conducting appropriate surveillance for SSIs in the inpatient setting as well as postdischarge. However, little work has been performed in transplantation. Additional work

needed to improve the current surveillance for HAI in SOT and develop interventions to reduce the rate of HAI.

Case Conclusion

After initial clinical improvement and appropriate drainage of the fluid collection, the patient's antibiotic regimen was reduced to meropenem and he received a total of 14 days and was discharged from the hospital. He was seen in follow-up 7 days later and had resolution of his infection. He continues to do well.

Suggested Reading

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