Infections in the Immunocompromised Host

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A 29-year-old female patient, 2 years after kidney transplant, on mycophenolate, sirolimus, and prednisolone, presented with semiconsciousness, ulcerating lesions around right elbow, and oliguria for the past 6 h.

Managing infection in an immunocompromised patient is a challenge to any ICU physician, as the presentation is varied and subtle and needs high index of suspicion for diagnosis and multiple possible etiologies. A methodological approach to investigation and choice of empirical therapy is warranted in these patients. Complexity of the problem necessitates close liaison between the microbiologist, infectious disease consultant, and hemato-oncologist.

Step 1: Resuscitate

- If assisted respiration is required, initially High Flow Nasal Oxygen (HFNC) or noninvasive ventilation should be tried.
- The patient should be closely monitored, and if no improvement or deterioration occurs in 2 h, invasive ventilation should be initiated.
- Urinary catheters and central lines should be avoided as these patients are coagulopathic and neutropenic and have a high risk of line sepsis.
- If absolutely necessary, invasive catheters and lines should be placed with utmost aseptic precautions by an experienced person.
- Careful maintenance of the peripheral line is extremely vital in these patients.
- Use of Chlorhexidine patch at the central line insertion site is recommended.

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Table 56.1 Syndromic approach to infection in immunocompromised patients

Pneumonia
Focal/nodular infiltrate
Bacteria, *Aspergillus*, mycobacteria, *Nocardia*, *Histoplasma*
Diffuse infiltrate
Virus (cytomegalo, herpes), *Pneumocystis*, *Strongyloides*
Meningoencephalitis
Bacteria: *Neisseria, Hemophilus, Pneumococcus, Listeria*
Mycobacteria: Typical and atypical
Fungus: *Cryptococcus*
Focal CNS lesions
Toxoplasma
Tuberculoma
Nocardia
Severe sepsis or septic shock
Gram-positive and gram-negative bacteria
Candidemia
Gastroenteritis
Strongyloides
Cryptococcosis
Amebiasis

Step 2: Take a Focused History (Table 56.1)

- This should be done to determine the type and duration of the immunocompromised state.
- Disease states such as hematological malignancy (leukemia and lymphoma), solid organ tumor, and conditions associated with neutropenic state should be looked for.
- History of any organ transplant and duration since transplant should be taken.
- HIV status should be determined, with proper consent.
- History of chemotherapy or radiotherapy should be taken.
- Detailed drug history should be elicited.
- Neurological, respiratory, gastrointestinal symptoms need to be elicited to narrow down differential diagnosis of opportunistic infection.

Step 3: Perform Focused Physical Examination (Table 56.1)

- Any breach of skin or mucosal abrasion, skin ulcer, oral ulcer, oral thrush, and perianal lesion should be searched for.
- Look for skin rash.
- All insertion sites of invasive lines should be inspected for tenderness or discharge.
- All suture lines and drain sites should be inspected in postoperative patients after removing the dressing.
- Look at the back for decubitus ulcer.
- Do neurological, respiratory, and gastrointestinal system examination to determine organ system involvement.

Step 4: Send Basic Investigations

- There is a broad differential diagnosis of opportunistic infection—bacterial, viral, or fungal—in immunocompromised patients.
- These patients are also prone to infections which are common in non immunocompromised patients.
- In these patients, infection mimics drug reaction, transfusion reaction, radiation-induced complications, and disease-associated problems, which all need to be properly investigated.
- Focused investigation, initially noninvasive and then invasive, should be performed to confirm the causative organism in order to narrow down anti-infective agents.

Step 5: Identify Underlying Immune Deficiency States and Suspected Pathogens (Table 56.2)

- Based on history, physical examination, and basic investigation, an approximation of underlying immunodeficiency states needs to be recognized.
- Specific immunodeficiency states are associated with alteration of natural defense system (neutrophils, T cell, B cells).

Table 56.2 Immunodeficiency states

T-lymphocyte deficiency
Causes
HIV/AIDS
Lymphoma
Corticosteroids
Drugs (methotrexate)
Organisms
Intracellular bacteria (mycobacteria, *Legionella*)
Virus (herpes, cytomegalovirus)
Fungi (*Pneumocystis*, *Cryptococcus*, *Histoplasma*)
Parasites (*Strongyloides*, *Toxoplasma*)
Nocardia
B-lymphocyte deficiency
Causes
Multiple myeloma
Acute leukemia
Drugs (corticosteroid, azathioprine, mycophenolate)
Plasmapheresis
Burn
Organisms
Encapsulated bacteria (*Neisseria, Pneumococcus, Hemophilus*)
Salmonella
Campylobacter
Giardia
Neutropenia
Causes
Chemotherapy
Hematological malignancy
Myelodysplasia
Severe viral infection

(continued)

Table 56.2 (continued)

Hypersplenism
Organisms
Gram-negative bacilli (enteric and nonenteric)
Staphylococcus aureus
Coagulase-negative *Staphylococcus*
Streptococci, enterococci
Fungi (*Aspergillus* spp., *Candida* spp.)
Neutrophil dysfunction
Causes
Diabetes
Uremia
Alcoholism
Cirrhosis
Burn
Organisms
Staphylococcus aureus
Streptococci
Mucor (Zygomycoses)
Gram negative bacilli (enteric and non-enteric)
Coagulase negative staphylococcus
Fungi (Aspergillus spp., Candida spp.)

- Patients with specific defense system alteration have propensity to be infected with certain groups of organisms, which need to be recognized.

Step 6: Initiate Empirical Anti-Infective Agents (Table 56.3)

- Guided by the type and duration of immunosuppression and primary organ system involvement, broad-spectrum anti-infective agents should be initiated against suspected organisms.
- These agents need to be deescalated once an organism is confirmed.
- The dose of these agents needs to be modified depending on renal and liver function tests.
- The duration of therapy with these agents depends on clinical response of the patient.

Step 7: Beware of Infection Mimics in Immunocompromised Patient

- Immune reconstitution response Syndrome (IRIS) is a paradoxical response noted in HIV patient when HAART is started along with the treatment of an opportunistic infection like cryptococcosis or tuberculosis.

Table 56.3 Diagnostic test and treatment of opportunistic pathogens

Organism	Test	Treatment
Bacteria		
Gram-positive/ negative	Gram stain: BAL, fluid, urine cultures (aerobic and anaerobic): Blood, BAL, fluids, urine	Vancomycin/teicoplanin/daptomycin (Gm+) Carbapenem, piperacillin–tazobactam (Gm−)
Mycobacterium tuberculosis	Induced sputum/BAL/AFB stain	Four-drug therapy
Nontuberculosis mycobacteria	Induced sputum/BAL/AFB stain	Variable
Nocardia spp.	Sputum/biopsy/modified AFB stain	Trimethoprim-Sulphamethoxazole (TMP-SMX)
Legionella	Sputum/BAL culture/urine antigen	Macrolide / respiratory fluoroquinolone
Fungi		
Candida	Blood culture/biopsy/Fundoscopy	Echinocandin, amphotericin B, azoles
Aspergillus	BAL/TBB/sputum fungal stain, galactomannan, H & P/HRCT chest/PCR	Amphotericin B/voriconazole
Pneumocystis jiroveci	Induced sputum/BAL/DFA	TMP-SMX/corticosteroid (pao2 < 70)
Cryptococcus	Serum/CSF antigen/blood culture/lateral flow assay	Ampho B/flucytosine
Histoplasma	Urine antigen/histology/fungal culture/Galactomannan	Ampho B/itraconazole
Parasites		
Toxoplasma	CSF/blood PCR	Pyrimethamine/sulfadiazine
Virus		
Cytomegalovirus	Blood CMVPCR/PP65 antigen/ BAL Biopsy—H & P, culture	Ganciclovir/foscarnet
Varicella zoster	BAL/CSF PCR, histology	Acyclovir
Herpes simplex	CSF/blood PCR	Acyclovir
Influenza	Nasopharyngeal swab/BAL DFA/ culture	Oseltamivir/zanamivir
Epstein–Barr	CSF PCR	Lymphoma chemo
RSV	Nasopharyngeal swab/BAL DFA	Palivizumab

For doses, see Appendix A

- Features resembling an exacerbation of underlying infection (e.g recurrence of pleural effusion, increase in the size of lung or brain lesion) occurs which can be confused with relapse of the opportunistic infection.
- This may be avoided by delaying HAART therapy after a few weeks of starting treatnent of the opportunistic infection.
- The IRIS phenomenon responds well to steroid treatment which needs to be tapered over a few weeks.

Step 8: Beware of Breakthrough Infection

- Antibiotic or antifungal prophylaxis is routinely used in many immunosuppressed patients before initiation of chemotherapy. Breakthrough infections can occur with organisms which are resistant to the prophylactic agent used (e.g. Aspergillus infection in patients prophylaxed with fluconazole, or mucor infection in patients prophylaxed with voriconazole).

Suggested Reading

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Website

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Free text available on many references on the subject.