Principles of antibiotics use in immunocompromised patients

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GENERAL PRINCIPLES IN THE USE OF ANTIBIOTICS

- ١- perception of need - is an antibiotic necessary ?
- ٢- choice of antibiotic - what is the most appropriate antibiotic ?
  - Etiological agent
  - Patient
  - antibiotic
- 3- choice of regimen : what dose, route, frequency and duration are needed ?
- 4-monitoring efficacy : is the treatment effective ?

Principles of use of antibacterial agents

- Identify the pathogen
- Site of infection
- Pharmacokinetic and pharmacodynamic of agent
- Potential toxicity to the patients
- Possible drug interaction
- Cost
- Convenience of administration

Principles …

- Immunocompromised patients have alterations in
  - Phagocytic
  - Cellular
  - humoral immunity
- That increases:
  - risk of infection and
  - ability to combat infection.
- Patient immunity may be impaired:
  - temporarily
  - permanently

Principles …

- High-risk:
  - Haematological malignancies
  - AIDS patients with low CD4+ counts
  - Bone marrow transplantation
  - Splenectomy
  - Genetic disorders such as severe combined immunodeficiency.

Principles …

- Intermediate-risk:
  - Solid tumours (particularly after cytotoxic chemotherapy)
  - HIV/AIDS
  - Solid organ transplant

Principles …

- Low-risk:
  - Long-term corticosteroid use (such as patients with rheumatoid arthritis)
  - Patients with areas of locally reduced immune function
  - Diabetics.

Principles ….

- **Patients who are**
  - **profoundly *neutropenic* (ANC<500 mm3)**
  - ***asplenic* or dysfunctional spleen : are at special risk and infections in these patients <u>should be treated as a medical emergency.</u>**

Aetiology of infection in the immunocompromised patient

- very wide range of organisms.
- Opportunistic pathogens .
- more than one infection and different organisms
- Commensals
- secondary fungal infections.
- nosocomial infections
- Neutropenic patients .
- Diabetic patients

Diagnosis of infection

- The wide-range of potential pathogens means that standard culture media may not cover all the possibilities and the microbiology department should be alerted to the patient's clinical history and extent of immunosuppression. Initiation of treatment should not be delayed pending laboratory results, but treatment should be tailored once the results are obtained.

Laboratory evaluation

- Specimens should be selected based on the signs and symptoms presented and should reflect the disease process. Blood samples should always be taken and both bacterial and fungal cultures should be assessed. Blood counts may also be useful to assess the degree of neutropenia. Cultures may also be obtained from:
- Cerebrospinal fluid
- Urine and stool samples, which may indicate a UTI or gastrointestinal infection
- Nose and throat swabs or a sputum sample if the signs present in the oropharynx
- If a viral infection is suspected, a cytomegalovirus antigen test may be performed, particularly in transplant and HIV/AIDS patients.

Principles for management

- Generally, the treatment should target the pathogen most likely to be involved, depending upon the host condition and duration of immunosuppression. Resistant or opportunistic organisms should always be considered. The core regimen should include:
- A combination of broad-spectrum antibiotics at high-doses to combat Gram-positive and Gram-negative aerobes, plus antifungal therapy from the outset of treatment to prevent secondary fungal infection
- Administration via IV for rapid onset of action
- Consideration of local factors ie. underlying disease state, presence of an intravascular device, local bacterial ecology and known resistance patterns.
- Once results of the culture and sensitivities are known, consult the hospital microbiologist and tailor antibiotic treatment accordingly.

Empirical therapy

- **Consult your microbiologist or local treatment guidelines for initial empirical therapy**
- **The immunocompromised patient with fever should be examined every day while fever persists**

Treatment regimens

- **Patients with HIV or AIDS should be managed by a specialist team. The possibility of TB or other diseases common in AIDS, such as *Pneumocystis carinii* pneumonia should be considered.**
- Neutropenic patients
- Transplant patients
- Asplenic patients
- Rheumatoid arthritis
- Diabetic patients

Reasons for treatment failure

- 1. Delay in diagnosis or therapy
- 2. Wrong or incomplete diagnosis No infection Nonbacterial infection Polymicrobial infection
- 3. Errors in antimicrobial susceptibility testing
- 4. Inadequate concentration of antibiotic at the site of infection Improper dose Decreased absorption from food or drug interaction Increased elimination of agent High protein binding Poor delivery (eg, vascular disease)
- 5. Decreased activity at the site Chemical factors (pH and others) Antibiotic antagonism
- 6. Other factors at the site of infection Collection requiring drainage Necrotic tissue Foreign body
- 7. Other host factors Impaired immune defenses Infection in a protected site (ie, requiring bactericidal drug or combination)
- 8. Development of resistance to antimicrobial agents
- 9. Superinfection

Source of infection

- Oropharynx
- Lungs
- Skin
- Perirectal area
- Perianal region

Principles of microbiologic diagnosis

- Blood culture
  - Repeat 3-4 days after empirical therapy
  - IVC culture
    - Coag- staph.
    - Coag+ staph.
  - Damaged mucosa:
    - Viridance strep.
    - Clostridium perfringens
    - C.septicum
  - Oral lesions:
    - Candida
    - Herpes simplex

Principles of microbiologic diagnosis

- Lung:
  - BAL
  - Nasopharyngeal swabs
  - Nasopharyngeal wash
    - Aspergillus
    - RCV
    - CMV
    - Adenovirus
    - Influenza
    - Pneumocystis jiroveci
    - Acid fast bacilli
    - Nocardia
    - Legionella

Principles of microbiologic diagnosis

- Skin lesions
  - Punch biopsy
    - Candida spp.
    - Trichosporon spp.
    - Fusarium spp.
    - Mucormycosis
    - P.aeroginosa
- Vascular devices

Principles of microbiologic diagnosis

- Gastrointestinal tract
  - Endoscopy:
    - HSV
    - CMV
    - Candida
    - VRE
    - P. aeroginosa
    - K.pneumoniae
    - C.difficile
    - C.septicum

Principles of microbiologic diagnosis

- Urinary tract
- Noncultural techniques
  - Antigen detection
    - Legionella pneumophila type 1
    - CMV(PCR)
    - HHV6
    - BK virus
    - EBV
    - Aspergillus(Elisa)

Principles for prophylaxis

- Immunisation
- Chemoprophylaxis