433 Teams

MEDICINE

28|Infections in Immuno-compromised hosts

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Objectives:

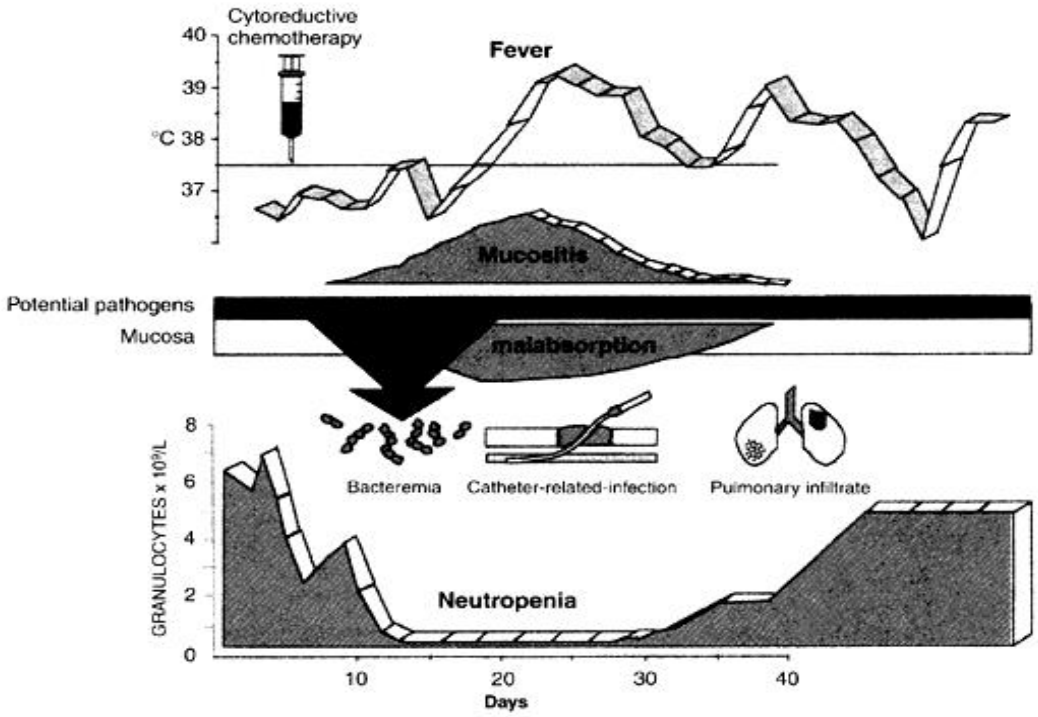
1. Have an overview of components of host defences and the different kinds of immunodeficiency that can occur.
2. Know which infections to expect in patients with different kinds of immunodeficiency i.e pathogens associated with the specific host defect.
3. Define febrile neutropenia and describe its management.
4. Describe infections in solid organ transplant patients.

Types of Immunocompromised hosts

Types of defects of immunity:	Pathogens that cause infection is such a defect:	Causes of immune deficiency:	Why is it important?
Granulocytopenia (Neutropenia)	•Staph. Aureus. •Coagulase -ve Staph. •Viridians strep. • Enterococci. • E. coli. •Pseudomonas aeruginosa. •K. pneumoniae. • Aspergillus spp.	1) **Primary**(Congenital): Rare, more common in children e.g chronic granulomatus disease, combined immunodeficiency syndrome, specific Ig deficiency. 2) **Secondary**(Acquired): - Aging, - Pregnancy, - HIV, - Malignancy, - Chemotherapy, - Transplant, - Steroids, - Burns, - Trauma, - Procedures, - Connective tissue disease, - Chronic diseases.	•Increasing numbers of immunocompromized patients. •Seriousness of infections in those patients. •Infections with unusual, nonpathogenic microorganisms. •Atypical presentation of infections by common pathogens.
Damaged mechanical barrier. (mechanical barriers such as skin, mucous membrane.)	•Coagulase -ve Staph. •Staph. Aureus. •Pseudomonas aeruginosa. •Camdida spp. •Viridans strep. •Herpes simplex virus.		
Cell-mediated immunity defects.	•Herpes simplex virus. •Cytomegalovirus. •Epstein-Barr virus. •Varicella zoster virus. •Respiratory syncytial virus. •Microbacterium TB. •Aspergillus spp. •Toxoplama Gondii.		
Humoral immunity.	•Strep. Pneumonia. •H. Influenza.		
Complement deficiency.	•Neisseria Meningitides. •Neisseria Gonorrhea.		
Spleen dysfunction.	•Strep. Pneumonia. •H. Influenza. •Neisseria Meningitides.		

1) Neutropenia: -

- Neutrophils count of **< 500 cells/mm^3**
- Neutropenia is associated with fever, which is defined **as Oral temperature of 38c for more than two hours or single temperature of 38.3c or more.**
- Neutropenia is common after chemotherapy, and may be prolonged in patients with hematologic malignancies and hematopoietic stem cell transplantation.
- Other drugs that cause neutropenia: - β-lactam antibiotics. Antipsychotics, antiepileptic's, NSAIDs, hydralazine, sulfonamides.
- Because some chemotherapy agents cause mucositis and other breaches of protective barriers, bacterial infection predominate.
- Pseudomonas species are associated with the highest mortality rate in neutropenia, and because of this empirical therapy (Vancomycin) for fever in the neutropenic patients should always cover this organism.



After receiving the cytoreductive chemotherapy there is a period of normothermia, as the neutrophils count decrease the infections start to develop (**from bacteremia, catheter related infection or primary pulmonary infiltrate**), and the temperature goes up.

How to approach the patient?

- History & examination.

- Investigations: Blood culture, urine culture and CXR.

- PCR for viruses.
- Serum Galactomanan and β-D-glucan assays may suggest a diagnosis of invasive infection with molds such as Aspergillus.
- Biopsy of skin lesions, bone marrow, or liver provide a diagnosis when other tests don't.
- In neutropenic patients with fever, elevated procalcitonin suggest bacteremia.

TREATMENT:

The treatment depends on how at-risk the patient in.

Low-risk neutropenic patients.

Scoring index for identification of low-risk febrile neutropenic patients.	**Factors that favor a low risk for severe infection among patients with neutropenia.**
No Symptoms - (5) Mild Symptoms - (5) Moderate Symptoms - (3) No Hypotension - (5) No COPD - (4) Solid Tumor - (4) No fungal infection - (4) No dehydration - (3) Outpatient at onset of fever - (3) Age < 60 years - (2) **A risk index score >21 indicates that the patient is likely to be at low risk for complications and morbidity.**	Absolute Neutrophil count of > 100 cells/mm^3. Absolute Monocyte count of > 100 cells/mm^3. Normal Chest x-ray. Nearly normal Liver and Renal function tests. Duration of neutropenia <7 days. No I.V. catheter-site infection. Early evidence of bone marrow recovery. Malignancy in remission. Peak temp. of <39.0°C No neurological or metal changes. No appearance of illness. No abdominal pain. No comorbidity complications.

- **Antibacterials**:

Piperacilline-tazobactam + aminoglycoside.

Cefepime + aminoglycoside.

Imipenem

Vancomycin, if indicated.

- **Antifungals**:

Amphotericin, Fluconazole.

- **Antiviral**:

Acyclovir.

- Administration of Granulocyte colony-stimulating factor with chemotherapy can prevent neutropenia.

- Prophylaxis should be administered in patients who have neutropenia for 7 days or more:

  - Quinolones and penicillin for bacteria.
  - Voriconazole and Psoaconazole as an antifungal.

Acyclovir primarily for Herpes Simplex Virus.

MCQs

1. A 36-year-old man with history of acute myelogenous leukemia is admitted to the ICU with neutropenic fever and low blood pressure that requires norepinephrine drip. The patient finished his first cycle of chemotherapy 10 days ago. He denies respiratory, gastrointestinal, or urinary symptoms. CBC reveals mild thrombocytopenia and an absolute neutrophil count of 100/µL. Urinalysis is within normal limits and chest x-ray does not show any infiltrate. Awaiting culture results, which of the following antibiotic regimens is most appropriate?

a. Imipenem.

b. Vancomycin.

c. Vancomycin, cefepime, and tobramycin.

d. Piperacillin/tazobactam, levofloxacin, and amphotericin B.

e. Continue supportive measures awaiting culture results

2. A 22-year-old male patient complains of fever and shortness of breath. There is no pleuritic chest pain or rigors and no sputum production. A chest x-ray shows diffuse perihilar infiltrates. The patient worsens while on azithromycin. A methenamine silver stain shows cystlike structures. Which of the following is correct?

a. Definitive diagnosis can be made by serology.

b. The organismwill grow after 48 hours.

c. History will likely provide important clues to the diagnosis.

d. Cavitary disease is likely to develop. e. The infection is unlikely to recur.

Answer: 1-C 2-C

1. The answer is c. Neutropenic fever is a medical emergency. Infections, most commonly gram-negative bacteria such as P aeruginosa, are responsible for most cases. Prompt empiric antibiotic therapy with two antibiotics from two different antibiotic classes (double coverage) that have anti-pseudomonal activity is most appropriate. Adding an antibiotic with anti–methicillinresistant Staphylococcus aureus (MRSA) activity to the initial antibiotic regimen is indicated if the patient was on antibiotic prophylaxis before the onset of the neutropenic fever or if he has any of the following conditions: skin infection, moderate to severe mucositis, central venous catheter, or shock (as in this vignette). Imipenem alone is not enough because it lacks anti-MRSA activity. Vancomycin does not provide gram-negative coverage and should never be used alone in the treatment of neutropenic fever. Awaiting culture results without initiating empirical antibiotic coverage is inappropriate because it increases the patient's mortality risk. Antifungal therapy is often added in the subsequent days if the patient fails to respond to broad-spectrumantibiotics

2. The answer is c. Patients with Pneumocystis jiroveci (formerly carinii) frequently present with shortness of breath and no sputum production. The interstitial pattern of infiltrates on chest x-ray distinguishes the pneumonia frommost bacterial infections. Diagnosis is made by review of methenamine silver stain. Serology is not sensitive or specific enough for routine use. The organism does not grow on any media. Cavitation is quite unusual. The history is likely to suggest a risk factor for HIV disease. The disease commonly recurs in patients with CD4 counts below 200/µL unless prophylaxis (usually with trimethoprim-sulfamethoxazole) is employed.

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