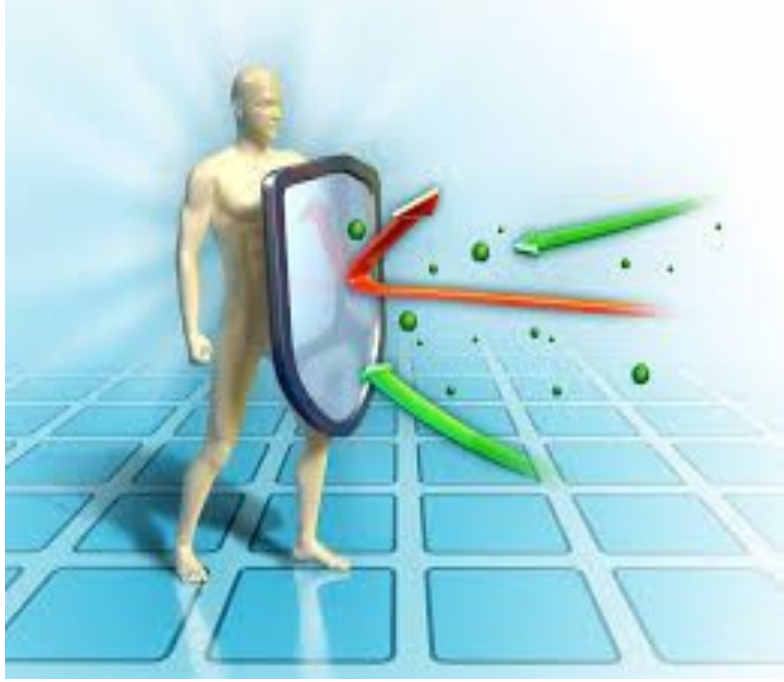
INFECTION IN THE IMMUNOCOMPROMISED HOST



Hazem.K.Alkhafaji •
-Lecture-3 •

Overview

Recognizing common atypical presentations of various infections and their complications (Everything is possible!!!)

In the immunocompromised patient , infection can be particularly challenging because symptoms are sometime quite subtle and atypical & sooner will be complicated. Prompt & aggressive treatment should be initiated as soon as possible without waiting the isolation of possible pathogens. Prophylactic measures are essential in many cases .to avoid institution of the infection

Infections in the Immunocompromised Host

INTRODUCTION

- An immunocompromised host is a patient who does not have the ability to respond normally to an infection due to an impaired or weakened immune system. This inability to fight infection can be caused by a number of conditions including illness (cancer and its treatment) and disease (Diabetes, HIV), malnutrition, and drugs.

Infections in Immunocompromised Patients:

- Infections usually chronic, severe and recurrent
- Partially responsive
- Organisms are often unusual (**opportunistis** or unusual)

Opportunistics organism: usually low virulence but become invasive in immunodeficient states e.g. atypical mycobacteria, Pneumocystis Jiroveci, staphylococcus epidermis

Components of immune system
Two types of immunity

Innate immunity(natural):- (already present in the body, not antigen-specific) **-1**

Anatomical barriers

Mechanical

Biochemical

Non-specific (e.g. Gastric acidity, natural killer cells,etc)

Adaptive-2 immunity(antigen-specific):Aquired

Pre-existing clones programmed to make a specific immune response (humeral/cellular)

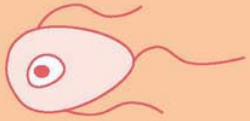
The immune system

Pathogens: Intimate Enemies

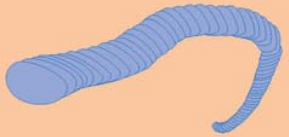
Viruses

Bacteria

Fungi



Protozoa



Parasitic worms

Prions

How Your Body Defends Itself

The Skin

- Break in skin must be penetrated.

Body Secretions

- Sweat and oil glands kill or repel invaders.
- Secretions such as
  - — wax (ears)
  - — tears (eyes)
  - — mucus (nose)

  include enzymes that destroy invaders at body entrances.
- Body temperature (fever) kills invaders.

Mucous Membranes

- They trap and engulf invaders.
- Cilia function to sweep invaders toward body openings.
- Enzymes prevent or slow reproduction of invaders.

Enzymes and Compounds in Blood

- They kill invader by
  - — causing it to burst
  - — destroying its cell membrane
  - — preventing/slowing reproductive cycle

Immune System

- It provides antigen/antibody response (humoral immunity).
- It triggers white blood cell action (cell-mediated immunity).
- It attempts to repel, destroy, or wall off foreign substances or invaders.

Interferon and Natural Substances

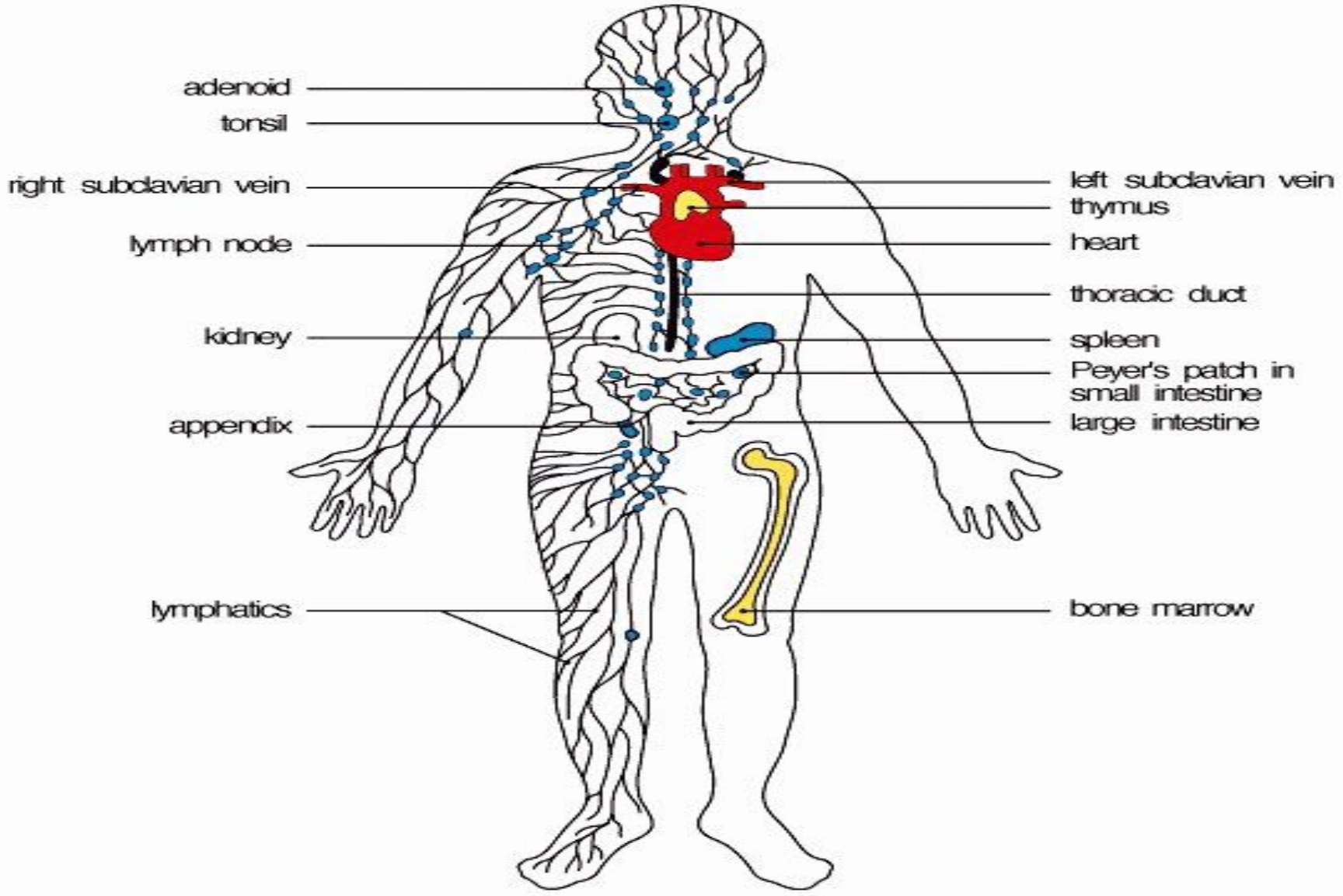
- When virus invades, a protein is produced that protects "healthy" cells.
- *Properdin* is a large protein that destroys gram-negative bacterial forms.
- *Polypeptides* have the same action as properdin.
- *Lysozyme* is a substance that kills bacteria.

PHAGOCYTES

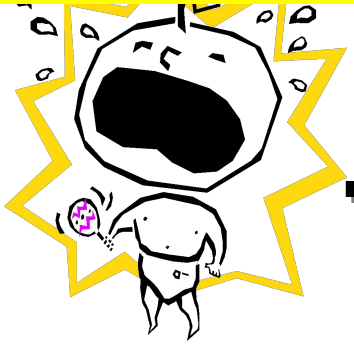
- They include neutrophils, monocytes and macrophages, and are crucial for defense against bacterial and fungal infections. Phagocytes express a wide range of surface receptors that allow them to identify microorganisms' -reactive protein (CRP), antibodies and complement bind both to the pathogen and to phagocyte receptors, acting as a bridge between the two and facilitating phagocytosis. If there is defect in phagocytosis , the patient more susceptible to infection **with**

- ***Staphylococcus aureus***
- ***Pseudomonas aeruginosa***
- **Atypical mycobacteria**
- ***Neisseria meningitidis***
- ***Neisseria gonorrhoeae***
- ***Haemophilus influenzae***
- ***.Streptococcus pneumoniae***

Distribution of Lymphoid Tissues



The role of blood in the immune system



Blood

\+ Plasma

Leukocytes, Platelets and RBC

Serum Proteins

- Immunoglobulins
- Complement
- Clotting factors
- Many others

Mononuclear Cells

- Lymphocytes (T cells, B cells & NK cells)
- Monocytes

Polymorphonuclear leukocytes (or Granulocytes)

- Neutrophils
- Eosinophils
- Basophils

IMMUNODEFICIENCIES

Definition

Defects in any of the components of the immune system(congenital or acquired) can compromise host protection and lead to increased susceptibility for infections. patients with immune deficiencies also are prone to develop certain types of .malignancies


“There is no better way to thank God for your sight than by giving a helping hand to someone in the dark.” Helen Keller

WARNING SIGNS OF IMMUNE DEFICIENCY

- respiratory tract infections/year in a child, 8 or > 4 respiratory tract infections/year in an adult
- infection requiring hospital admission or 1 < intravenous antibiotics
- Infections with unusual organisms
- Infections at unusual sites
- Chronic infection unresponsive to usual treatment
- Early end-organ damage (e.g. bronchiectasis)
- Family history of immune deficiency

WHO Classification of immunodeficiency

Primary Immunodeficiency-1

Inherited or genetics

Selective IgA deficiency*

Disorders

Common variable*
.immunodeficiency

X-linked agammaglobulinemia •
*** Immunodeficiency with normal serum globulins or .hyperimmunoglobulinemia**

Immunodeficiency with * • thymoma

Chronic granulomatous disease •

Secondary Immunodeficiency-2 •
Acquired •
Disorders •
:for example •
Corticosteroid therapy •
.Immunosuppressive drugs
Splenoectomy
Leukaemia •
.Diabetes mellitus •
Radiation(radiotherapy) •
AIDS •

Rare inherited immunodeficiency states

- Di George syndrome, associated with T cell defects (CMV, mycobacteria)
- Hypogammaglobulinaemia: B cell defects (pyogenic infections)
- Phagocyte disorders: Chronic granulomatous disorder (Staph aureus, fungal infections)
- Complement deficiency states (encapsulated bacteria)

Immunodeficiencies and Chronic or Recurrent Infections

Organism	Immune Defect
Encapsulated organisms: ***S.pneumoniae, H. influenza***	**Hypogammaglobulinemia** **neutropenia** **Complement deficiency** **Asplenia** **T-cell deficiency**
Fungal infections **Herpes zoster virus** ***Pneumocystis* pneumonia** **Mycobacterial infections even with atypical mycobacterium**	**T-cell deficiency**
***Neisseria* (N. meningidis)infections**	**Asplenia** **Complement deficiencies**

The spleen

- The spleen is the largest of the secondary lymphoid organs.
- Note:Primary lymphoid tissue are bone marrow & thymus,while secondary lymphoid tissue are lymph nodes , payer patches & the spleen.
- It is highly effective at filtering the blood:
- Important site of phagocytosis of -1 bacteria(particularly important for defense against encapsulated bacteria, *Streptococcus pneumoniae* and *H. influenzae* infection.
- It is also a major site of antibody synthesis -2

Splenectomy/hyposplenism

- :Auto splenectomy
- Sickle cell disease
- Splenic infarction
- Graft versus host disease(GVHD)
- Splenic irradiation
- Surgical removal:indicated in the following -:conditions
- Traumatic injuries
- ITP(immune thrombocytopenic purpura)
- .Congenital spherocytosis
- .Mylefibrosis

Management of the splenectomised patient

- Vaccination against Pneumococci,Haemophilus-1 influenza,meningococci,influenza virus should be sterted 2weeks prior to elective splenectomy or as soon as possible following urgent splenectomy(mostly traumatic)
- Life-long antibiotic prophylactic either -2 penicillin V 500mg twice daily or erythromycin if .the patient allergic to penicillin

Opportunistic Infection

an infection by a microorganism that normally does not cause disease but pathogenic when the body's immune system is impaired and unable to fight off infection

Prolonged Neutropenia → disseminated Candidiasis

Common Variable Immunodeficiency → recurrent bacterial infections.

cortico-steroid use → disseminated Herpes zoster & activation of latent tuberculosis.

HIV/AIDS, Bone marrow/Solid organ transplants → CMV

Some examples of opportunistic pathogens

- ***Legionella pneumophila*** **(pneumonia)**
- ***Candida albicans(disseminated)*** **o**
- ***Listeria monocytogenes*** **(meningitis)** **o**
- ***Atypical myco.tuberculosis*** **(pneumonia,** **o** **disseminated.)**
- ***Pneumocystis jirovecii*** **(pneumonia)** **o**
- ***Crypto. neoformans*** **(meningitis)** **o**
- ***Aspergillus fumigatus*** **(pneumonia.** **o** **Disseminated.)**
- ***Toxoplasma gondii*** **(pneumonia.** **o** **Encephalitis)**

Febrile Neutropenia

Definition •

A single oral temp ≥ 38.3 ° C • (F ° 101)

or

A temperature of ≥ 38 ° C • on two occasions (F 100.4) separated by 1 hour

Definition of Neutropenia

Normal ANC 1500 to 8000 cells/mm^3

Severe Neutropenia : Absolute Neutrophilic Count (ANC ≤ 500/ mm^3 or

mm^3 and predicted decline to ≤ 500/ mm^3 /1000 ≥ .over the next 48hours

?HOW WOULD YOU CALCULATE ANC

Total number of WBC) x (% of Neutrophils) = ANC
If WBC count 7000/ mm^3 & percentage of neutrophils is 60%

m^3

Clinical presentations of infections in neutropenic patient

- Febrile neutropenia: fever greater than .38^{0}C for 2 hours or longer
- There may be rigors, drop in blood pressure, septic shock
- Herpes: mouth ulceration which may be complicated by bacteraemia by oral bacteria
- *Candida* sepsis; *Aspergillus* lung infiltrates

Febrile neutropenia Investigations

Complete Blood Count (with Differential) •

White cells, haemoglobin, platelets-

Biochemistry •

Electrolytes, urea, creatinine, Liver function-

Microbiology •

Blood cultures (peripheral and all central line lumens)-

Oral ulcers or sores –send swabs (Viral Culture and-fungal culture)

Wound swabs-

Urine Cultures-

Stool Cultures and C . Difficle Toxin/PCR-

Radiology •

Chest X ray +/- CT abdomen/pelvis-

Management of High Risk Patients on Admission

:High risk patients require

IV fluids –

Regular pulse and BP monitoiring –

Regular medical review –

Specialist Oncology/Heamatology review within –
.24 hours of admission

- **prompt antibiotic therapy(Antibiotic therapy should be given WITHIN 4 hours of the patient entering the hospital)**

- **G-CSF (granulocyte colony stimulating factor) has no role in the acute management of uncomplicated neutropenic fever**

THREE approaches for IV EMPIRIC therapy

:IV MONO THERAPY: one of the following

Ceftazidime(superior for ever)

Meropenem(Carbapenem)

Piperacillin

Tazobactam

IV DUAL THERAPY:aminoglycoside

plus one of the monotherapy drugs

COMBINATION THERAPY •

Mono or dual therapy + VANCOMYCIN

What is the

Opportunistic Infection

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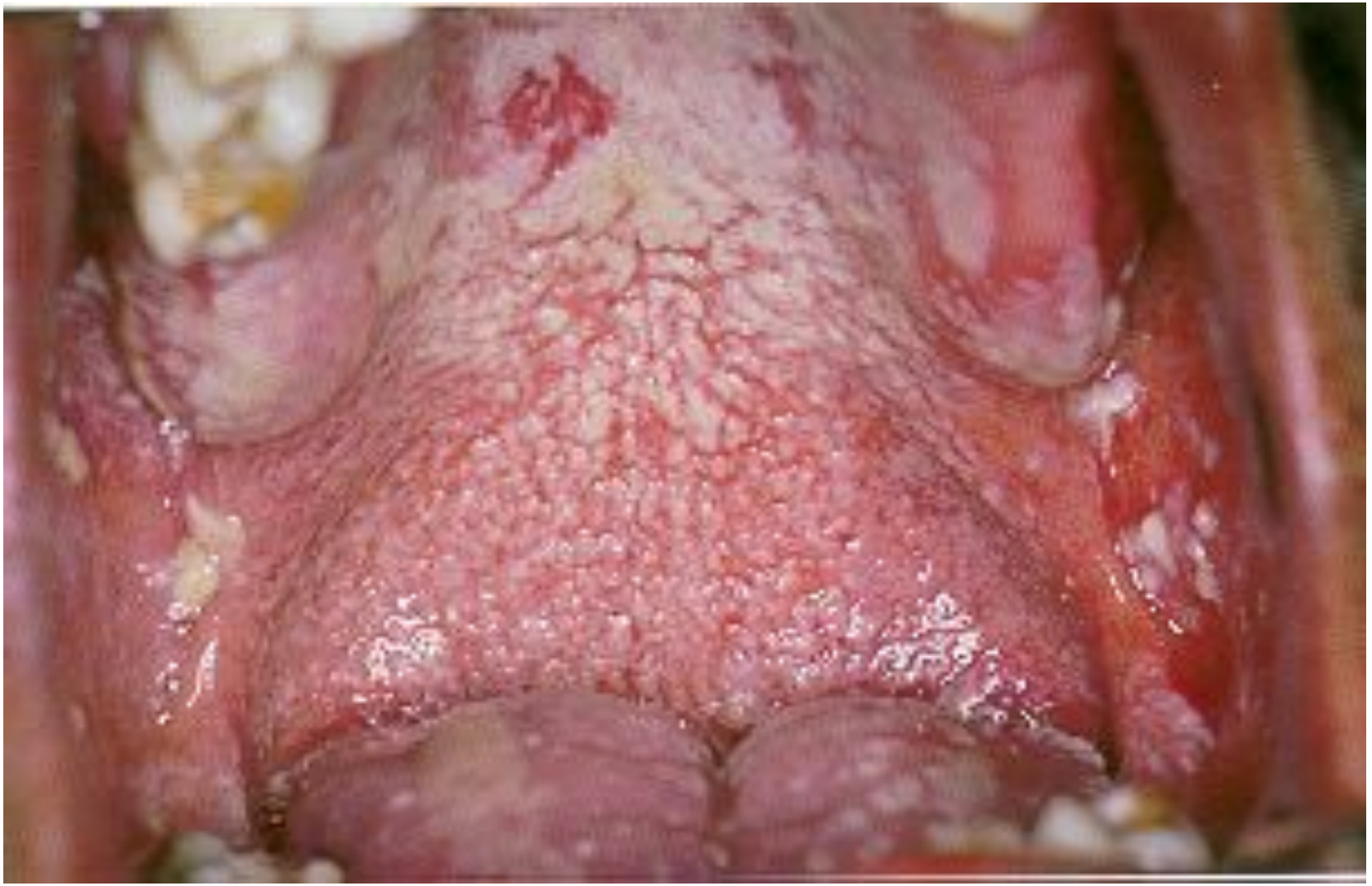

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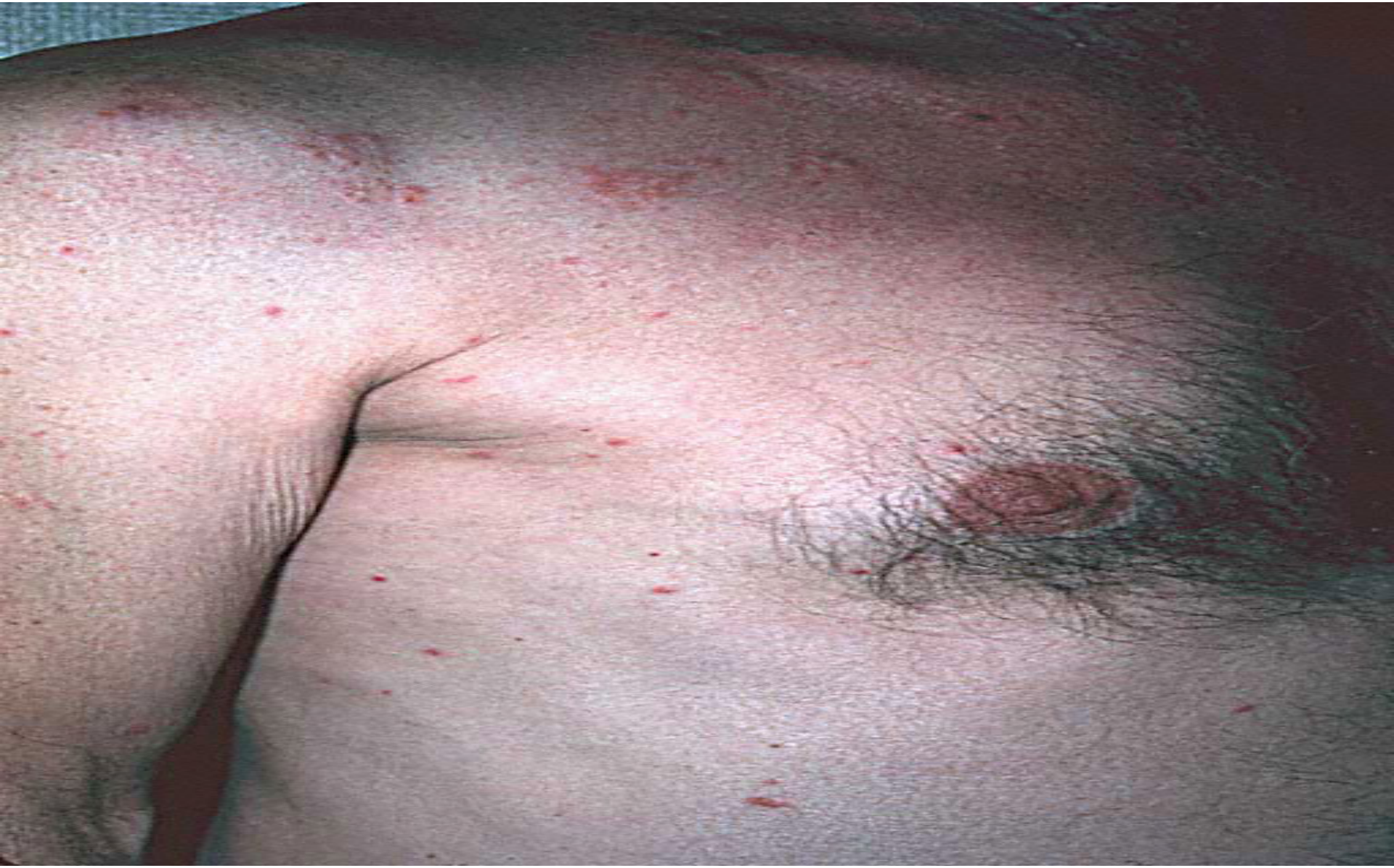

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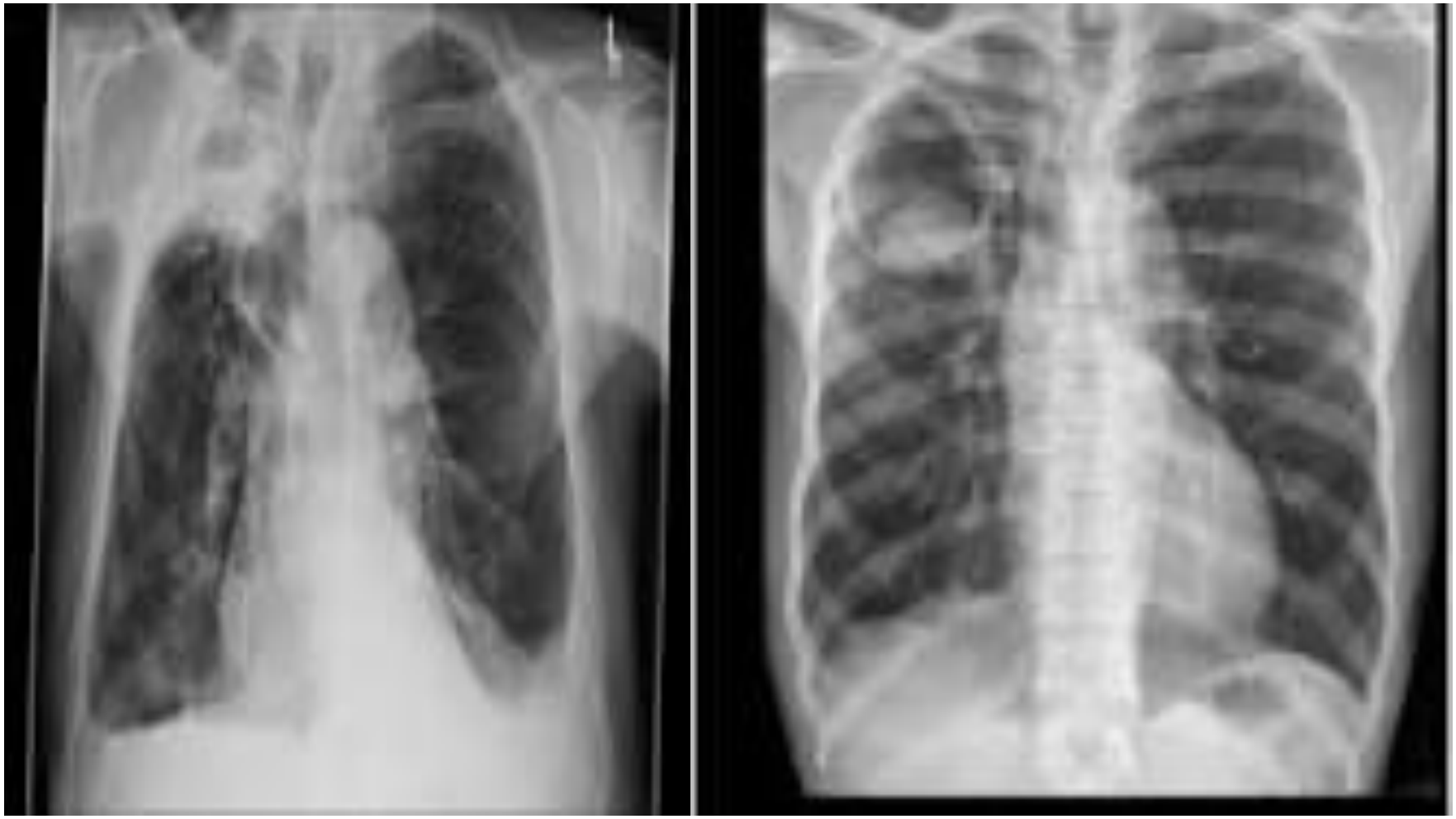

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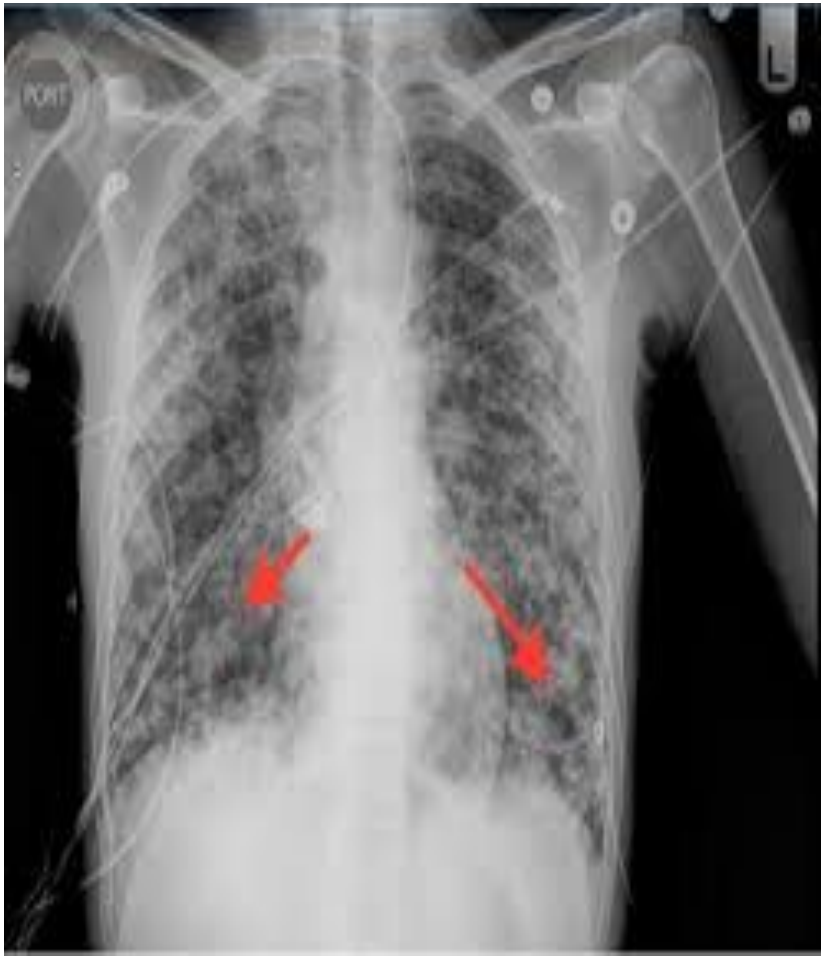

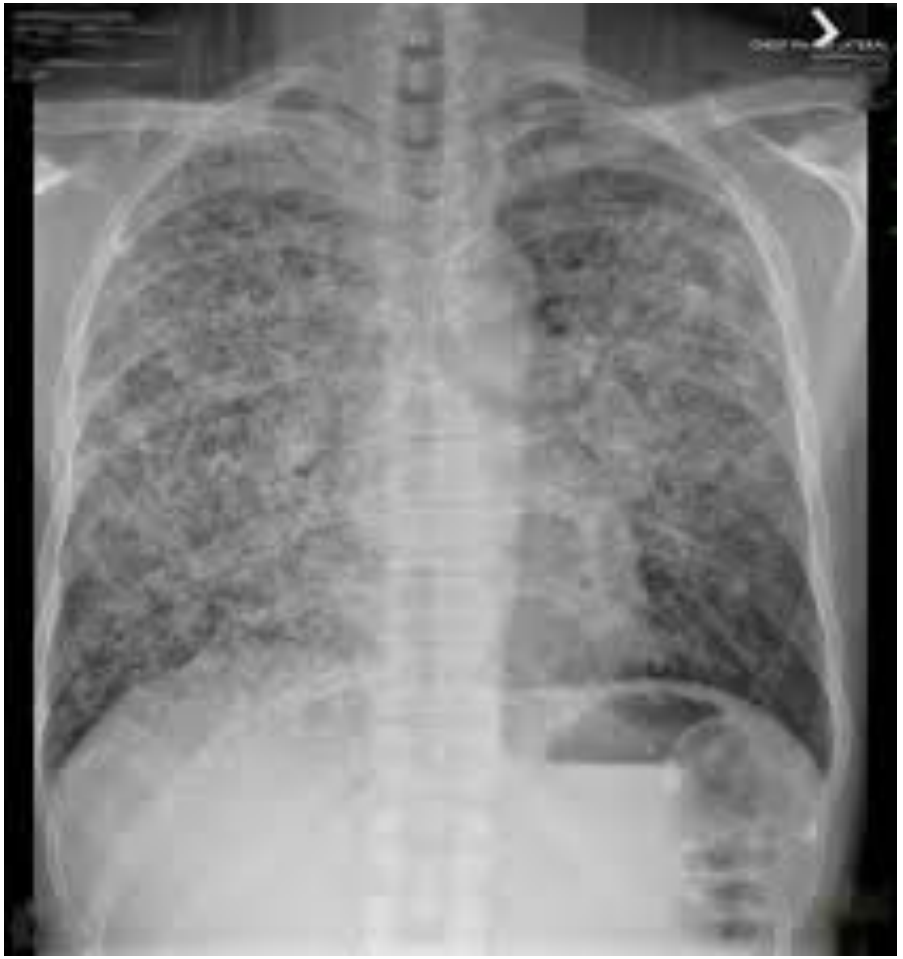


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