Immunodeficiency Diseases

Objectives

- Outlines different types of autoimmune deficiencies
- Differentiates primary and secondary autoimmune deficiencies
- Discus the common characteristics and the major clinical diseases of

1. B cell deficiency
2. T cell deficiency
3. Combined deficiency
4. Phagocytic deficiency
5. Compliment deficiency

Introduction

- Deficiencies of host defense systems result in an immunologic imbalance that can lead to a susceptibility to infection, an autoimmune disease, or a predisposition to malignancies.

Types of immunodeficiency disorders:

Primary: Causes in immune system component:

a. According of component:

- Complements.
- Phagocytic.
- B cells.
- T Cells.

b. According to the etiology:

- Congenital (X-linked disease)
- Acquired (AIDS)
- Embryogenesis (Digoerge syndrome).
- Idiopathic

Secondary: Non Immunogenic causes:

- Prematurity.
- Mal nutrition.
- Hodgkin`s and others malignancy.
- Injury, Burns, Splenectomy.
- Drugs.

1. B-cell defect

- Causative agents are most commonly extracellular organisms, namely pyogenic and enteric bacteria, because patients are deficient in serum antibodies necessary for phagocytosis.
- Recurrent infections with encapsulated bacteria
- Chronic sinupulmonary infections
- Sites of infection include the skin, sinuses, meninges, and the respiratory, urinary, and gastrointestinal tracts.

Bruton's Agammaglobulinemia

- Immunology:
  - No B cells or non functional B cells including defective signaling or defective BCR
  - Markedly low levels of Immunoglubulines
- Clinical:
  - Child clinically well for first 6 months of life
  - Recurrent upper/lower respiratory tract infections with encapsulated bacteria (S. pneumonia)
  - Sepsis, meningitis, skin infections
  - Short life span
- Treatment: IVIG, antibiotic therapy

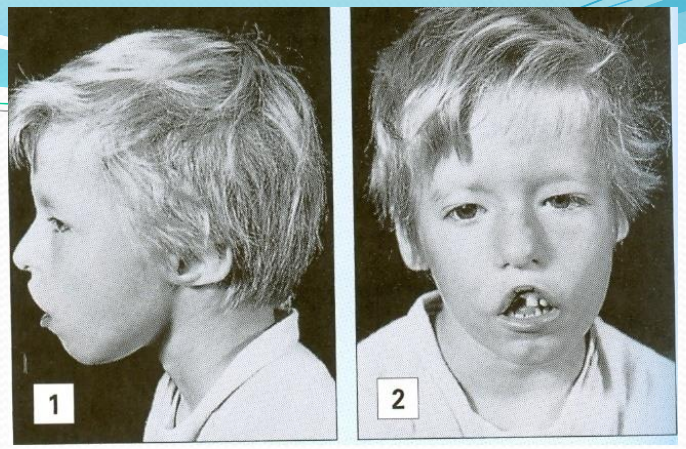
IgA deficiency

- Immunology:
  - Most common humoral antibody deficiency
  - Isolated low IgA level
- Manifestation:
  - 50-80% asymptomatic
  - Recurrent sinopulmonary infections most frequent manifestation
  - May have severe malabsorption (chronic diarrhea)
  - Increased risk of autoimmune disorders
- Treatment: Broad spectrum antibiotics

2. T-cell deficiency disorders

- Also known as cell-mediated (cellular) immuno-deficiencies, result from abnormalities in T-cell functions.
- Antibody production is also likely to be affected in patients with severe T-cell abnormalities because T cells are important immunoregulators of B-cell differentiation and function.
- Recurrent infections --Causative agents are intracellular pathogens (e.g., herpesviruses, mycobacteria, fungi (Candida), and protozoa (Pneumocystis carinii, Toxoplasma).

DiGeorge Syndrome



- Immunology:
  - Poorly developed or functioning thymus
  - Depression of T cell numbers
  - Absence of T cell response
  - Humoral response to T independent antigens only
- Clinical: Overwhelming infections with viruses, fungi, bacteria
- Treatment: correct hypocalcemia, cardiac defects, fetal thymus transplant

3. Combined Deficiencies

- Immunological abnormalities are combined to B cells and T cells

Sever Combined Immune Deficiency (SCID)

- Immunology:
  - Defects in stem cell maturation with various genetic defects
  - No TCR or defective TCR
  - Defective cell signaling
  - Defective IL 2
- Manifestations seen in first 3 months of life
  - Recurrent, severe bacterial, viral, fungal, and protozoan infections (usually respiratory infections)
  - Failure to thrive, diarrhea, dermatitis, candidiasis
  - Death at early age
- Treatment: isolation, treat underlying infections, bone marrow transplant

Wiskott Aldrich Syndrome

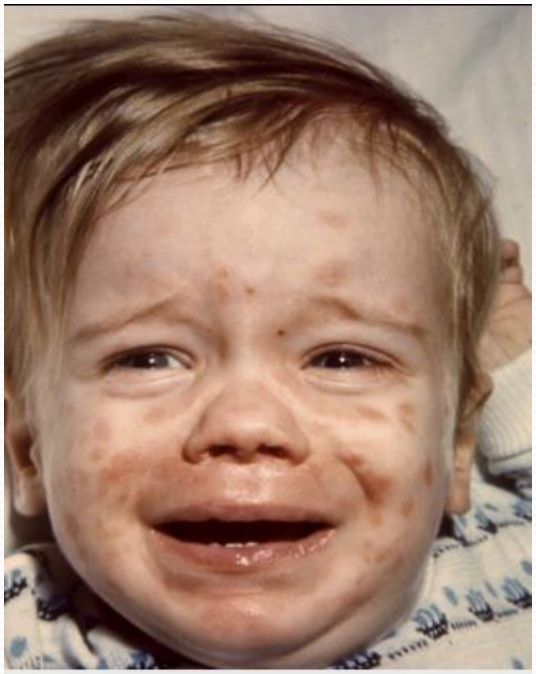
- Immunology:
  - X linked disorder
  - Affects platelet numbers/function
  - Affects T cell function
  - Cytoskeleton of lymphocytes affected
  - Lower amounts of IgM
  - characterized by eczema, thrombocytopenia (low platelet count), immune deficiency, and bloody diarrhea (secondary to the thrombocytopenia).
- Symptoms in infancy
  - Recurrent, severe infections
  - Eczema
  - Thrombocytopenia (petechiae)
- Treatment: manage bleeding/infections, BMT

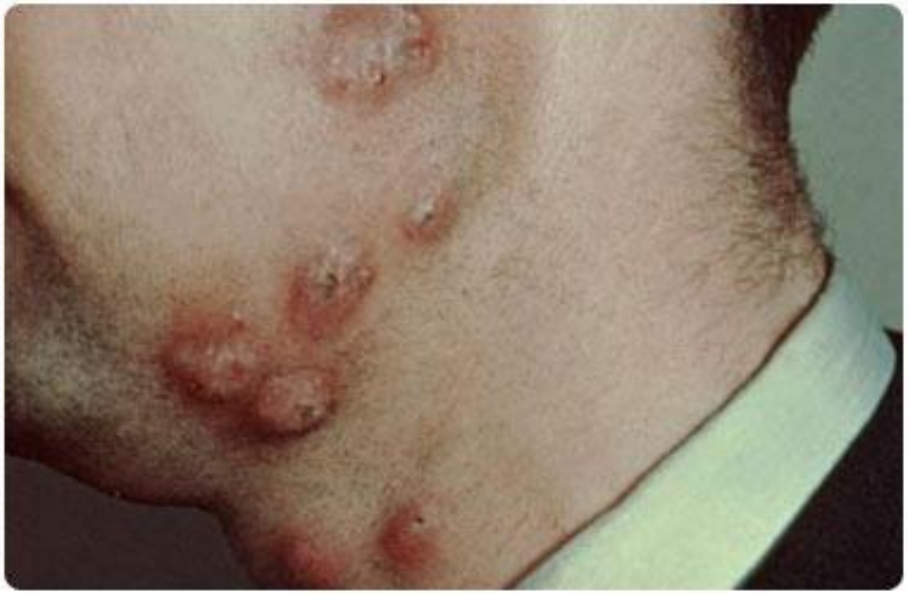
4. Phagocyte disorders

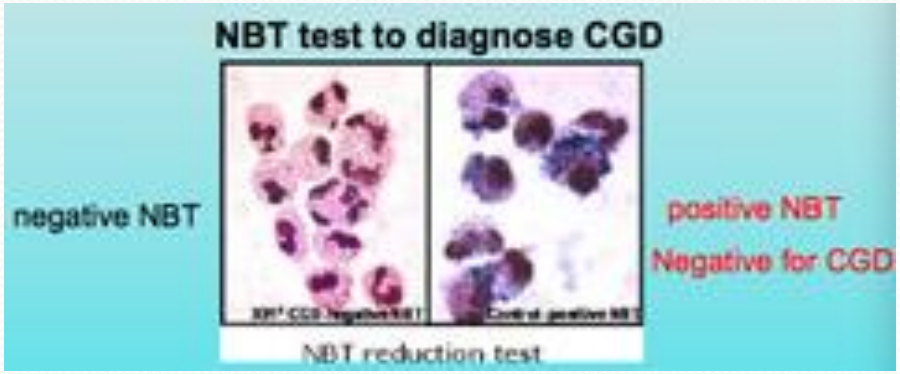
- Clinical features: Affected individuals are prone to infections with low-grade bacteria such as Staphylococcus aureus and gram-negative enteric bacteria.

Chronic Granulamatous Disease (CGD)

- Immunology:
  - Non functional phagocytes
  - Defective NADPH oxidase
- 75% X-linked recessive, 25% autosomal recessive
- Manifestation:
- Severe, recurrent staph aureus infections of lymph nodes, skin, and lung
- Dx: Nitroblue tetrazolium (NBT) test
- Treatment: antimicrobial prophylaxis, IFN-gamma, BMT






NBT test to diagnose CGD
negative NBT
positive NBT
Negative for CGD
NBT reduction test

5. Complement Disorders

- Deficiency of early complement components (C1, C4, C2) results in a symptom complex resembling collagen vascular disorders (e.g., systemic lupus erythematosus (SLE)] and increased susceptibility to pyogenic infections.
- C3 deficiency results in severe pyogenic infections. Several patients have also had SLE and glomerulonephritis.
- Deficiency of late complement components (C5, C6, C7, C8) results in systemic Neisseria infections such as meningococcal sepsis and meningitis, and disseminated gonococcal infections.

Diagnosis of immunodeficiency disease

- laboratory investigation:
  - CBC: increase PMNL suspect phagocyte deficiency
  - Culture: to know the organism and choose the antibiotics.
  - ESR and CRP: inflammation markers for follow up.

- Specific tests:

1. B-cells:
   - Total lg
   - Selected lgA and lgG
   - Antibodies for pervious vaccination
2. T cells:
   - Lymphocyte count.
   - Delayed hypersensitivity reaction
   - T cells and macrophage function test.
3. Phagocyte:
   - Neutrophil count
   - NBT test for screening.
   - Macrophage function test
4. Complement: Total and specific complement count.