Clinical Features of Primary Immunodeficiency

David Kiptum

Introduction

- Primary Immunodeficiency diseases are a group disorders caused by genetic defects of the immune system
- Rare – 1:10,00 – 1:100,000
- Early detection is critically reducing morbidity and mortality
- Children with severe, recurrent, or unusual infections may have a PID

Parts of the Immune System

- B-Lymphocytes
- T-Lymphocytes
- Phagocytic System
- Complement System
- They each have specific roles, but work best in concert with the others

Rationale

- Early diagnosis is important so that appropriate therapy can be instituted before organ damage
- Early diagnosis is essential for making genetic information available to the families of affected individuals

Infectious Manifestations

- Increased susceptibility – Chronic, recurrent infections
- Infection with organism of low virulence (Aspergillus, Candida, Pneumocystis)
- Infection of unusual severity (Sepsis, Empyema, Fistula)
- Autoimmune or inflammatory disease Syndrome Complex

Prediction

- Cell Mediated Immunity deficiency- difficulty with viruses and fungi

- Antibody deficiencies - encapsulated bacteria and enteroviruses

Prediction

- Complement deficiencies - bacteremia, septic arthritis and meningitis, caused by encapsulated bacteria
- Phagocytic disorders - infections of the skin and reticuloendothelial system (lymph nodes, spleen and liver)

Autoimmune and Inflammatory Manifestations

- The basic abnormality leading to immunodeficiency may also lead to faulty discrimination between self and non-self, and thus to autoimmune disease
- May be limited to a single target cell or organ or may involve several different target organs
- Common in some PIDDs

Autoimmune and Inflammatory Manifestations

- A disorder that appears to be autoimmune in nature may, in fact, be due to a viral agent
- Target Cells
  - Hemolytic anemia
  - Immune thrombocytopenia
  - Thyroiditis

Autoimmune and Inflammatory Manifestations

- Target Tissues
  - Vasculitis
  - Systemic lupus erythematosus
  - Rheumatoid arthritis
- Associated Diseases
  - Common variable immunodeficiency
  - Selective IgA deficiency
  - Chronic mucocutaneous candidiasis
  - Complement pathway deficiencies

Immunodeficiency Diseases

- Immunodeficiency can also be one part of a constellation of signs and symptoms in a syndrome complex
- Recognition that a patient has a syndrome in which immunodeficiency occurs may allow a diagnosis of immunodeficiency to be made before there are any clinical manifestations of that deficiency

Immunodeficiency Diseases

- DiGeorge syndrome
  - Congenital heart disease
    Hypoparathryroidism
  - Abnormal facies
  - Thymic hypoplasia
- Wiskott-Aldrich syndrome
  - Eczema, Thrombocytopenia
  - Variable B- and T- lymphocyte dysfunction

Immunodeficiency Diseases

- Ataxia-Telangiectasia
  - Ataxia-Telangiectasia
  - Variable B- and T- lymphocyte dysfunction
- Ivemark syndrome
  - Bilateral 3-lobed lungs, Congenital heart disease
  - Asplenia

Immunodeficiency Diseases

- Polyendocrinopathy syndrome
  - Endocrine organ dysfunction
  - Chronic mucocutaneous candidiasis

10 Warning Signs of Immunodeficiency

- ≥ 4 new ear infections within 1 year
- ≥ 2 serious sinus infections within 1 year
- ≥ 2 months on antibiotics with little effect
- ≥ 2 pneumonias within 1 year
- Failure of an infant to gain weight or grow normally

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Safe Care BASIC HEALTHCARE STANDARDS

CHILDREN'S HOSPITAL ASSOCIATION

Gertrude's CHILDREN'S HOSPITAL Quality healthcare for children

10 Warning Signs of Immunodeficiency

- Recurrent, deep skin or organ abscesses
- Persistent thrush in mouth or fungal infection on skin
- Need for IV antibiotics to clear infections
- ≥ 2 deep-seated infections including septicemia
- A family history of PID

Most Useful Warning Signs

- Positive family history (RR = 18; 95% CI, 8 to 45 for any type of primary immunodeficiency disease);
- A diagnosis of sepsis treated with intravenous antibiotics (RR = 5; 95% CI, 1.4 to 15 for phagocytic disorders)
- Failure to Thrive

Initial Laboratory Work Up

- HIV Screening
- Haemogram
- Immunoglobulin Levels
- Complement Levels
- Further Testing – Guided by Clinical Features

Specific Tests

Screening Tests for Primary Immunodeficiency	
Suspected Abnormality	**Diagnostic Tests**
Antibody	Quantitative immunoglobulins (IgG, IgA, IgM) Antibody response to immunization
Cell Mediated Immunity	Lymphocyte count T lymphocyte enumeration (CD4, CD8) HIV serology Delayed type hypersensitivity skin tests
Complement	Total hemolytic complement (CH50)
Phagocytosis	Neutrophil count Nitroblue tetrazolium (NBT) dye test

Resources

- European Society for Immunodeficiencies http://www.esid.org
- Immune Deficiency Foundation/The National Patient Organization for Primary Immunodeficiency Diseases http://www.primaryimmune.org
- U.S. Immunodeficiency Network http://www.usidnet.org

Management

- Manage Infections
  - Prevent, Treat
  - Treat Symptoms
- Boost Immune System
  - Immunoglobulin Therapy
  - Interferon Gamma Therapy
  - Growth Factors
- Stem Cell Transplant