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Medi Quest BRS Hospital

A monthly News letter from BRS Hospital

Primary Immunodeficiency Disorders - PART I

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Excerpted from Primary Immune Deficiencies Made Simple by Dr Sagar Bhattad

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This is the first of series of articles which would high light primary immune deficiency disorders (PID) also known as in born errors of immunity (IEI)

Secondary immune deficiency disorders due to AIDS, chemotherapy, or chronic steroid therapy will not be covered.

PID

The International Union of Immunological Societies (IVIS) publishes revised classification of PID/IEI every other year. The 2019 version has 416 inborn errors of immunity.

What does the term primary mean?

The term primary in PID – means they are Genetic Diseases.

What are the functions of a healthy Immune system?

1. Protection from invading microbes
2. Deletes auto reactive cells and prevents auto immunity
3. Keeps a cheek of mutant cells and prevents cancers – cancer surveillance

A defect in immune system would therefore predispose an individual to

1. Increased risk of infections
2. Increased auto immune disease
3. Increased predisposition for malignancy

What are the warning signals of Immune deficiencies?

1. Four or more new ear infections in a year
2. Two or more serious sinus infection in a year
3. Two or more pneumonias in a year
4. Two or more months on antibiotics with no improvement or little effect
5. Recurrent deep skin or organ abscesses
6. Failure to thrive from early infancy
7. Two or more deep seated infections eg. endocarditis , osteomyelitis , septic arthritis , epidural abscess
8. Persistent oral thrush mouth or cutaneous fungal infection
9. Need for IV Antibiotics to clear infection
10. Family history of PID

Presence of two or more warning signals should necessitate an evaluation for an underlying immunological disorder.

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Other features in PID
1.Chronic Diarrhoea
2.Complication from live viral vaccines

Basic components of Immune system

A. When a microbe enters the body /tissues
tissue macrophages engulf the organism – phagocytosis

B. Neutrophil present in blood stream leave the blood vessel to reach tissue – site of infection and engulf the organism

C. After Phagocytosis, microbes are killed by macrophages and neutrophils

Clinical Implications:

a) If neutrophils are absent, it would predispose individual to bacterial and fungal infections.
Eg: Severe congenital neutropenia

b) If neutrophils cannot adhere to endothelium they would not be able to reach infected tissues. This would lead to recurrent infections eg: leucocyte adhesion deficiencies

c) Intracellular killing is defective eg: NADPH oxidase deficiency this would lead to persistent infections eg: CGD

T and B cells

a) B cells produce immunoglobulin which neutralizes various pathogens (pre dominantly extra cellular bacteria) – Humoral Immunity
b) T.Cells – CD8 T cells kill viral infected cells and play an important role in handling intra cellular infection - Cell mediated immunity.

Clinical Implication:
1.Recurrent bacterial infections – think of B cell defect
2.Viral / Fungal infection – think of T cells defect

Clinical classification of IEI

1) B cell defect
2) Combined defect
3) Phagocytic defect
4) Compliment defect

1. B cell defect

1.Recurrent mucosal infections
Recurrent sinusitis
Recurrent pneumonia
Recurrent diarrhoea

2.Onset of symptoms beyond 6 months of age

Evaluation
S.Immunoglobulin
B cell counts
Antibody response to vaccine

2. T Cell / combined defect

Fungal or viral infect (eg: aspergillus, candida, CMV)
Severe forms of T cell defects have an onset in early infancy (eg: SCID)

Milder forms have an onset in later life eg: (combined immune defect due to LRBA def)

Evaluation
T cell count and S.Immunoglobulin

3. Phagocyte defects

Suppurative infections
Compliated pneumonias
Lung Abscess
Liver abscess
Suppurative lymphadenitis

Onset : Severe forms present in infancy while milder forms may present in later in life.

Evaluation:
Look at absolute Neutrophil counts
Neutropenia may point towards severe congenital neutropenia / cyclic neutropenia
High Neutrophil count must make one think of CGD (NBT and Dihydrorhodamine test are the screening tests for CGD).
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Complement deficiencies

Recurrent infections with encapsulated Bacteria (S.Pneumoniae, H. Inluenzae can be noted in complement def)
Early onset of auto immune diseases can be features of complement deficiency (eg. Onset of lupus before the age of 5years is seen in complement C1q def)
Individuals with recurrent infections with Neisseria meningitidis must be evaluated for terminal complement defects (C5 to C9 def)

Evaluation suggested

CH 50 assay -> functional assay for classical complement pathway
AP 50 assay -> functional assay for alternative pathway. If either or both of those assays is abnormal individual complement components can be assessed based on clinical suspicion.

Clinical approach to Immune deficiency

What are the questions to be answered in a patient with suspected immune deficiency

1. Is it a immune deficiency ?
Presence of warning signals given above
2.What is the type of immune defect
B cell / combined/ phagocytic syndrome
3.What are the organisms?
Bacterial / viral / Fungal / Parasites Is it the same group of organisms causes recurrent infection ? or is the spectrum of infection very broad
4.Family history:
Consanguinity, sibling deaths recurrent infection in parents, issues in maternal uncles , male relatives
5.Close look at all previous nomograms
Look at ALC and ANC (congenital Neutropenia, cyclical Neutropenia can be diagnosed with hemograms)
6.Look at thymic shadow
If absent points towards severe combined immune def
7.Relevant immunological tests
Immunoglobulins, Lymphocytes subsets (T.B and NK cell counts) nitroblue tetra zolium test, Dihydrorhodamine assay genetic tests.

In the next issue

Common immune deficiency syndromes in clinical practice

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would like to wish you

Happy Diwali


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