UNIVERSITY OF NAIROBI

SCHOOL OF MEDICINE

DEPARTMENT OF CLINICAL IMMUNOLOGY

Dr. Gontier Monday June 28th, 2010

TYPE 1 HYPERSENSITIVITY REACTION

INTRO

- in various conditions as a result of injection; IM or IV.
- Reactions to certain drugs
- drug history important
- post injection pt monitoring- 15- 30 min

definition

- type 1 hypersensitivity is a rapidly developing immunologic reaction occurring within minutes after the combination of an antigen with antibody bound to mast cells in an individual previously sensitized to that antigen.
- Divided into 2 phases
    1. immediate responses that occurs within 5 – 30 minutes
    2. late phase that can extend from hours to days
- Pathogenesis is the same while signs and symptoms are dependent on the systems involved.

Immunopathogenesis of type 1 reactions

1. when an antigen gains access to a mucosa either via inhalation, ingestion, or by contact it will be recognized by an antigen presenting cell.
2. The antigen presenting cell will take up the offending antigen, process it and exhibit it together with MCH II to a TH2 helper cell.
3. The TH2 helper cell will secrete various cytokines (proallergic cytokines); IL2, IL4, 5 & 13.
    - IL2 is responsible for recruiting, differentiation and proliferation of other lymphocytes esp. B lymphocytes.
    - IL4 is responsible for undertaking the switch over of IgG to IgE in the B cell.
    - Il5 activates and maintains eosinophils in the area of the allergic reaction.
    - IL13 promotes IgE production and acts on epithelium to produce secretions.
4. in addition th2 cell and epithelial cells produce chemokines that attract more th2 cells as well as eosinophils and basophils.
5. The IgE molecules produced bind to Fc receptors on mast cells and basophils

- secondary exposure is vital for type 1 reaction to occur
- contact with mast cells or basophils with IgG on its surface, on the epithelium will elicit reaction
- the antigen will bind adjacent arms (FAB portion) of IgE molecules. In this way cross link adjacent IgE molecules. This cross linking phenomenon will result in transduction of signals

into the cytoplasm that will cause the release of primary and secondary mediators of inflammation.

- The release of primary mediators is immediate; they comprise of
    - biogenic amines e.g Histamine (causes intense smooth muscle contraction, increased vascular permeability and increased gland secretions in the epithelium)
    - Enzymes e.g neutroproteases and acid hydrolases
    - proteoglycans e.g heparin (anticoagulant) and condroitin sulphate.
- after about 30 min – 2 hrs, release of secondary mediators. Divided into lipid mediators and cytokines
    - lipid mediators – derived from the break down of phospholipids to yield arachidonic acid which is broken down into leukotrienes and prostaglandins
        - Leukotrienes – C4 & D4 - Potent basoactive and spasmogenic agents
            - B4 - Highly chemotactic for neutrophils, eosinophils and monocytes.
        - PGD2 – Causes intense smooth muscle contraction as well as mucus secretion.
        - Platelet activating factor (PAF) – Causes platelet aggregation, release of histamine, smooth muscle contraction, increased vascular permeability and vasodilatation.
            - Also chemotactic for neutrophils and eosinophils.
    - cytokines
        - alpha TNF
        - GM-CSF – more white cell production
        - Macrophage inflammatory proteins.
- the role of eosinophils is important because it produces major basic protein, eosinophil cataioning protein – these are toxic to epithelial cells. They also produce Leukotriene C4 and PAF.

- when it involves a viscera, damage is chronic