PATHOLOGY OF BRONCHIAL ASTHMA

Bronchial Asthma

Define bronchial asthma.

- Describe types of bronchial asthma.
- Discuss etiopathogenesis of asthma.
- Describe morphological features.

Obstructive and restrictive lung diseases
• Obstructive lung diseases
• (i.e. increased resistance to air flow) include:-
• 1. **Bronchial Asthma**.
• 2. Emphysema.
• 3. Chronic bronchitis.
5. Cystic fibrosis and bronchiolitis.

Why should we care about asthma?

What is Asthma?

• Definition:
• Asthma is a chronic inflammatory disorder of the airways that causes recurrent
spasmodic episodes, due to increased hyperirritability or responsiveness of the bronchial tree to various stimuli.

• This associated with these clinical manifestations:
  • 1. *Wheezing*.
  • 2. *Breathlessness*.
  • 3. *Chest tightness*.
  • 4. *Cough, particularly at night and/or in the early morning*.

It is manifested physiologically by a widespread narrowing of the air passages, which may be relieved spontaneously or as a result of
therapy. Can not cure but can controlled.
Life threatening disease

How long this episodes taking place? (Mild, severe) (Min/hr)
Bronchial asthma risk factors
• 1- Atopy (allergic asthma - largest risk factor - genetic).
2 – Environmental factors (viruses, ...)
occupational exposures, allergens, cold air, dust, smoking, others...).
3- family history.
4-

others.............

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Bronchial asthma
Classifications
Asthma may be
categorized into types
3-
Bronchocstriction triggering
agents - include

(a) Seasonal asthma
(b) Exercise-
induced asthma.

(c) Drug-induced asthma (e.g., aspirin & NSAID).
(d) Occupational asthma

(e) Emotional asthma.
(f) Asthmatic bronchitis in smokers.
4-Recent studies added three subphenotypes of Asthma
, based on Airway inflammation pattern.

Asthma Types

• 1- Atopic asthma (allergic)
sensitization, Extrinsic):

• **Classic example of** type I IgE-mediated hypersensitivity reaction.
  • Usually encountered in patient known case of rhinitis, eczema.
  • Genetic predisposition.

• A positive family history of asthma is common.
• Begins in childhood.

• Triggered by environmental allergens, such as dusts, pollens, roach or animal dander, and certain
types of foods., etc...

- **Diagnosis**: clinical diagnosis is essential

  + ........................................
• (a) Skin test: Using the offending antigen → immediate wheal-and-flare reaction.

• (b) Serum radioallergosorbent tests (called RAST): TO identify the
presence of IgE specific for a panel of allergens.

Asthma Types

2. Non-atopic asthma:
   - Non allergic.

   - Triggered commonly by Respiratory infection due to viruses (e.g., rhinovirus, parainfluenza virus).

   - Family history: less common.
- Skin test: reveals negative reaction.

- Mechanism:

  *It is thought that virus-induced inflammation of the respiratory mucosa → lowers the threshold of the subepithelial vagal receptors to irritants.*

Asthma Types

3- Bronchoconstriction triggering agents

(a) Drug-Induced Asthma.

  - *Aspirin-sensitive asthma* + NSAID occurring with *recurrent rhinitis and nasal polyps.*
- Others examples: adrenergic antagonists, coloring agents.
  Commonly occurs in adult.

**Mechanism:**
Aspirin inhibiting the *cyclooxygenase pathway* of arachidonic acid metabolism without affecting the lipoxygenase route, thus tipping the balance toward *elaboration of the bronchoconstrictor leukotrienes*.

**Asthma Types**

(b) Occupational Asthma.
Caused or worsened by breathing in irritants on the job.

• Triggered/stimulated by:
  • 1) Fumes (epoxy resins, plastics)
  • 2) Metal and dusts (platinum, wood, cotton)
• 3) Chemicals and Gases (formaldehyde, penicillin products, toluene, enzymes).
• 4) Animal substances
• 5) Plants
• - Minute quantities & Repeated exposure.

• - Mechanisms:
  • According to stimulus include:
    • Type I hypersensitivity reactions.
    • Liberation of bronchoconstrictor substances.
    • Hypersensitivity responses of unknown origin.

Bronchial asthma
• 4- Pattern of the Airway inflammation:

• 1) Eosinophilic asthma.

• 2) Neutrophilic asthma.
• 3) Mixed inflammatory asthma.
• 4) Pauci-granulocytic asthma.

• These subgroups may differ in their:
• (a) Etiology.
• (b) Immunopathology.
• (c) Response to treatment.

Asthma Pathogenesis-1

**GENETIC CONSIDERATIONS**
Genetic predisposition
In case of Atopic asthma - type I hypersensitivity

Inheritance of susceptibility genes (postulation) that makes individuals
prone to develop strong $T_H^2$ reactions against environmental antigens (allergens)

Asthma
Pathogenesis-2
1. The airway epithelium and submucosa contain dendritic cells that capture & process antigen \( \text{allergens} \). Initial sensitization \( \rightarrow \) stimulate induction of \( T_{\text{H}2} \) cells.
2. $T_H^2$ cells secrete cytokines e.g. (IL-4, IL-5, IL-13) that promote allergic inflammation and stimulate B cells to produce IgE and other antibodies.
3. Action of Cytokins
(a) IL-4 $\rightarrow$ Production of IgE by B cells.
(b) IL-5 $\rightarrow$ Activates recruited eosinophils.
(c) IL-13 $\rightarrow$ Mucus secretion (bronchial submucosal glands) $\rightarrow$ also Promotes IgE
production by B cells.

Asthma Pathogenesis-3 (Early & Late reaction)
3. IgE coats submucosal mast cells.

4. Repeat exposure triggers the mast cells to release granule contents and produce cytokines and other
mediators $\rightarrow$ induce the **early-phase** (immediate hypersensitivity) reaction and the **late-phase reaction**

Asthma Pathogenesis-4
(Early reaction- Minutes)

- Antigens $\rightarrow$ Th2$^+$ IgE production $\rightarrow$ IgE binding to mast cells leads to Eosp.
recruitment & release of primary mediators =
(Histamine, chemotactic factors, and secondary mediators i.e. leukotriens, prostaglandins, cytokines and neuropeptides). This results in:

- **(A) Bronchospasm** - triggered by direct stimulation of subepithelial vagal (parasympathetic) receptors through both central and local reflexes.

- **(B) Secretion of mucus.**

- **(C) Variable degree of vasodilatation & increase permeability.**

- **(D) Accumulation of leukocytes.**

**Asthma Pathogenesis-5 (Late reaction- Hours)**
- 6- 10 hr later, produces a continued state of airway hyperresponsiveness with eosinophilic and neutrophilic infiltration. (steroid helpful to treat this stage)

**Components:** consists largely of inflammation with recruitment of leukocytes= (Eosinophils, neutrophils, and more T cells).

- Leukocyte recruitment is stimulated by chemokines produced by mast cells, epithelial cells (eotaxin) and T cells, and by other cytokines.

- **Outcome:** persistent bronchospasm, edema, and necrosis of epithelial cells by *The major basic protein of eosinophils.*
Cellular sources of inflammatory mediators & their effects

Morphology of Asthma
Airway remodeling.

• Overall thickening of airway wall.
• Reduction of diameter.
• Basement membrane fibrosis (BM thickening).
• Increases muscle mass (Hypertrophy and/or hyperplasia).
• Increased in size and number of blood vessels.
• Increase number of the submucosal glands.
• Mucus metaplasia of epithelium.
• Increased fibrogenic factors $\rightarrow$ collagen type I,II “scar”
• Irreversible Airflow obstruction.
Bronchial asthma,
microscopic
Curschman’s spirals
Charcot-Leyden crystals
THE END