Cystic Fibrosis

Introduction

- Inherited multisystem disorder
- Obstruction & Infection of airways
- Dysfunction of epithelial surfaces
- Major cause for CLD & PI

GENETICS

- AR inheritance
- 700 mutations – Chromosome 7
- CFTR-1480 amino acid

  (GI/Panc/Biliary/Sweat glands/ Genitourinary system)
- Most common- Deletion ΔF508

PATHOPHYSIOLOGY

- Failure to clear mucous secretions.
- Paucity of water in mucous secretions.
- An elevated salt content of sweat & other secretions.
- Chronic inflammation limited to respiratory tract.

CFTR Mutation effects

- Greater negative potential difference across the respiratory epithelia.
- Inability to secrete chloride in response to cAMP mediated signals.
- Excessive amounts of sodium are absorbed through respiratory tract.

Classes of CFTR Mutations

- 1. Defective CFTR production due to premature transcription termination signals.
- 2. Defective CFTR processing and trafficking to the apical membrane
- 3. Defective regulation of chloride channel function due to mutations in CFTR phosphorylation
- 4. Defective chloride conductance due to missence mutations in membrane spanning domains of CFTR
- 5. Abnormal splicing of CFTR.

PATHOLOGY

- Eccrine sweat glands & Parotid salivary glands- Not involved.

Lungs

- Bronchiloitis
- Bronchitis
- Goblet cell hyperplasia
- Submucosal gland hypertrophy
- Airway destruction
- Enlargement of bronchial arteries

PATHOLOGY CONT…

Paranasal Sinuses:

- Filled with secretions
- Polyps
- Mucopyocele
- Erosion of bone

Pancreas

- Disruption of acini & replacement with fibrous tissue and fat.
- Calcification

PATHOLOGY CONT…

Intestinal tract:

- Esophageal & duodenal glands distended
- Concretions in appendiceal lumen or cecum.

Focal Biliary Cirrhosis

Uterine cervix

Epididymis/ vas deferens/seminal vesicles

Clinical Manifestations

- Acute or persistent respiratory symptoms
- Failure to thrive
- Abnormal stools
- Meconium ileus/ intestinal obstruction
- Electrolyte, acid-base abnormality
- Rectal prolapse
- Nasal polyps
- Sinus disease
- Hepatobiliary disease

Diagnostic Criteria

Clinical Criteria

Presence of typical clinical features (resp/GI/ GU)

OR

A history of CF in sibling

OR

A positive newborn screening test

PLUS

Laboratory Criteria

Two elevated sweat chloride concentrations

OR

Identification of two CF Mutations

OR

An abnormal nasal potential difference measurement

TREATMENT

- Education & Counseling
- Inhalational Therapy
- Chest Physiotherapy
- Antibiotic Therapy
- Anti-inflammatory Therapy
- Endoscopy & Lavage
- Treatment of pulmonary & intestinal complications
- Nutritional Therapy
- Nasal Polyps

THANKS