6 cases of pediatric pulmonary diseases

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Case #5

- Six month old, female infant
- 24 weeks gestation
- In NICU
- Intubated or nasal canula
- Fever, endotracheal secretions *Staph. aureus*
Bronchopulmonary dysplasia

- Northway et al, 1967
- Nash et al, 1967
- Acute respiratory distress
- Regeneration
- Transition
- Chronic disease (> 1 month)
In the ‘90s

- Improved ventilation
- Surfactant therapy
- Better management of infections and complications
- ↓ HMD, ↓ BPD
Chronic Lung Disease of Prematurity (CLDP)
- Infections
- Fluid overload
- Circulatory abnormalities
- Patent ductus arteriosus
- Surfactant abnormalities
- Nutritional deficiencies
- Genetic factors

Pathogenesis of BPD
- Damage → Repair → Fibroproliferative changes (TGF-β, NO, VEGF)
- Arrested development, disrupted morphology, architecture and vasculature

BPD now:
- > 1,200 g, > 30 weeks - no lung disease
- <1,000 g - 30% incidence of BPD
- Some with no initial RDS
- Increasing oxygen requirement
- Severe lung disease - Chronic lung disease (CLD) of prematurity

Husain et al, 1998
Pathogenesis of BPD

- Coordination of growth between airways and vessels
- Failure of pulmonary vascular growth during saccular or alveolar stages
- Decreased septation
- Pulmonary hypoplasia

NICHD/NHLBI/ORD workshop
Jobi et al, 2001

- Nomenclature - BPD
- Definition
- Pathogenesis
- Prevention
- Future research directions

Case #6

- 36 week gestation
- Anydramnios
- Apgars of 5 and 5 at 1 and 10 min.
- Bilateral renal agenesis
- Potter’s syndrome
Pulmonary hypoplasia

- Defective or incomplete development
- Number and size of alveoli
- Growth factors
  - Space
  - Motion
  - Fluid

Pulmonary hypoplasia - causes

- Decreased intrathoracic space
  - Congenital diaphragmatic hernia
  - Polycystic kidney disease
  - Severe polyhydramnios
  - Skeletal malformations
  - Intrathoracic mass

- Decreased fetal respiratory movements
  - Anencephaly
  - Neuromuscular disorders
- Oligohydramnios
  - Renal agenesis/dysplasia
  - Amniotic fluid leak
- Unknown mechanism
  - Trisomies 13, 18, 21
  - Sporadic or familial cases
In-utero interventions
- Repair of CDH
- Replacement of amniotic fluid
- Resection of urethral valves

Pulmonary hypoplasia
- 10% of all neonatal autopsies
- 30% of deaths <1 week of age
- 50% of congenital malformations
- Criteria for diagnosis

Pulmonary hypoplasia
- Page and Stocker: 77 of 756 cases, lung weight:body weight
- 0.012 if = or > 28 weeks gestation
- 0.015 if < 28 weeks gestation
- 17.4 ÷ 2730 gm = 0.006
- Hemorrhage, infection, HMD
Radial alveolar count

- Gestation (weeks)  
  - 24  
  - 30  
  - 35  
  - 40  
- RAC  
  - 2  
  - 3  
  - 4  
  - 5

Radial alveolar count

- Autolysis  
- Infection  
- Hemorrhage  
- Formalin inflation

Pulmonary hypoplasia

- Tissue maturity  
- Lung volume  
- Size  
- Lung to body weight ratio  
- Radial alveolar count

Case 8a

- 28 weeks gestation, 840 gm male  
- Apgars of 0 and 1 at 1 and 5 min.  
- Intubated, oxygen  
- Cyanosis, Rx dopamine  
- Patent ductus arteriosus, grade IV cerebral hemorrhage, sepsis  
- Died at 11 days of age
Congenital pulmonary lymphangiectasia (CPL)

- Rare, usually fatal
- Dilated lymphatics within interlobular septa and pleura
- Obstructive cardiac malformations (>60%)
- Generalized lymphangiectasis
- Isolated pulmonary lesion
**Congenital pulmonary lymphangiectasia**
- Male predominance (2.5:1)
- 5-10% are stillborn
- Cyanosis, respiratory distress
- Fluid abnormalities (chylothorax, pleural effusion, fetal hydrops, polyhydramnios)
- Both lungs

**Congenital pulmonary lymphangiectasia**
- Lungs bulky, firm, non-compressible
- Cut section: fluid filled dilated lymphatics
- Microscopic: dilated, increased lymphatics around bronchovascular bundles, interlobular septa and pleura
  - myxoid to dense connective tissue
  - EMH

**Congenital pulmonary lymphangiectasia**
- Differential diagnosis
- Congenital lobar emphysema
- Interstitial pulmonary emphysema
  - Location
  - Lining (CD31, CD34, D2-40)
  - Associated malformations
  - History
  - Live births only

**Case #9**
- 6 year old male, cough with rust colored sputum
- Bilateral patchy pulmonary infiltrates
- Progressive disease with frank hemoptysis
- Developed pneumonia, Rx
- Died in 6 weeks
Pulmonary hemosiderosis
- Infection
- Blood dyscrasias
- Chronic heart failure
- Pulmonary hypertension
- Neoplasia

Pulmonary hemosiderosis
- Primary (idiopathic)
- Secondary (immunologically mediated renal or vascular diseases)

Idiopathic pulmonary hemosiderosis
- Anemia, hypoxemia (85%), dyspnea and hemoptysis (65%)
- 3-6 years (4 months to young adults)
- Changing shadows
- Interstitial lung disease
- Hemoptyis, iron deficiency anemia and diffuse parenchymal infiltrates

Idiopathic pulmonary hemosiderosis
- Eosinophilia in 12-15%
- Normal renal function
- No autoantibodies
- Celiac disease
- Immunosuppressive therapy (86% five-year survival)
- Recurrence after lung transplantation

Idiopathic pulmonary hemosiderosis
- BAL
- Biopsy
- Autopsy
  - Macrophages
  - Iron in connective tissue, elastic fibers
  - Fibrosis, reactive changes
  - Mast cells
  - Negative IF
Case #10

- 4 month old male
- 27 weeks gestation, 1100 gm
- BPD, hydrocephalus, V-P shunt
- Staphylococcal ventriculitis
- 48 hours of cough, secretions, and rapid breathing
- Nasopharyngeal swab -ve

Autopsy findings

- External measurements normal for corrected age of 42 weeks gestation
- Lungs: 150 gm (normal 53 ± 10 gm)
- Enlarged tracheobronchial lymph nodes
- Aqueductal stenosis, hydrocephalus, V-P shunt intact, complications of ventriculitis
Respiratory syncytial virus (RSV) pneumonia

- Infants and young children
- Cold → bronchiolitis/pneumonia in half the patients 6 wk to 6 month old
- 40-90% of bronchiolitis/pneumonia due to RSV
- 1% hospitalization
- 1% mortality (3000-4000 deaths/year)

RSV pneumonia

- Predisposing conditions
  - Congenital heart disease
  - BPD
  - Immunosuppression
- Replicates in respiratory mucosa
- Rare extrapulmonary disease
- Pathogenesis
RSV pneumonia

- Bronchiolitis
  - epithelial necrosis
  - mucus and debris
  - lymphocytes
  - epithelial regeneration with polypoid epithelial protrusions and squamous metaplasia

- Pneumonia
  - extensive plugging
  - inflammation
  - necrosis
  - hyaline membranes
  - giant cell pneumonia

RSV pneumonia

- Inclusions: cytoplasmic
- Small eosinophilic globules
- Bronchial or bronchiolar epithelial cells
- With or without a halo
- Best seen in giant cells

Differential diagnosis of RSV

- Human metapneumovirus
- Measles: intranuclear inclusions
- Parainfluenza: rare, but same as RSV
- Adenovirus: intranuclear (central or smudge cell), with enlarged nucleus and cytoplasm (DD: CMV)
- Culture, EM, IHC

Human metapneumovirus (hMPV)

- A paramyxovirus, first isolated 2001
- Lower respiratory tract disease in very young and elderly
- Wheezing, croup, pneumonia
- 20% of all previously virus-negative cases

IFA for hMPV using recombinant baculovirus-expressing hMPV F protein (Bac-F IFA)
Differential diagnosis of RSV

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AFIP 1950-1996
198 CASES

Benign 72
- Inflammatory myofibroblastic tumors 60
- Chondromatous hamartoma 3
- Granular cell myoblastoma 3
- Leiomyoma 3
- Bronchial chondroma 1
- Teratoma 2

PRIMARY PULMONARY TUMORS IN CHILDHOOD

Inflammatory Myofibroblastic Tumor
- Plasma Cell Granuloma
- Inflammatory Pseudotumor

Malignant 127
- Carcinoid tumor 37
- Carcinoma of salivary gland type 13
- Bronchogenic carcinoma 31
- Sarcoma 32
- Malignant fibrous histiocytoma 1
- Pleuropulmonary blastoma 11
- Pulmonary blastoma (adult type) 2

PRIMARY PULMONARY TUMORS IN CHILDHOOD

Benign
- Inflammatory myofibroblastic
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- Bronchial chondroma
- Teratoma

PRIMARY PULMONARY TUMORS IN CHILDHOOD

Inflammatory Myofibroblastic Tumor 42
- M:F 20:22
- Age < 1 year 1
- 1-4 4
- 5-9 7
- 10-14 11
- 15-20 19
**MYOFIBROBLASTIC TUMOR**

- Inflammatory Pseudotumor
- Most common tumor of the lung
- Symptoms
  - Fever 22%
  - Cough 20%
  - Pain 11%
  - Pneumonia 9%
  - Hemoptysis 9%
  - Asymptomatic 30%

**INFLAMMATORY MYOFIBROBLASTIC TUMORS**

- Histologic Types - 32 cases in children
- Organizing pneumonia 16
- Fibrous histiocytoma 44
- Lymphoplasmocytic 40

Conran, Stocker - in press
IMT - immunohistochemistry

- Vimentin 99%
- Smooth muscle actin 92%
- Muscle-specific actin 92%
- ALK-1 75%
- Desmin 69%
- Cytokeratin 36%
- KP-1 24%
- CD30 6%

INFLAMMATORY MYOFIBROBLASTIC TUMOR

- EBV detected in 41% of lymph node, hepatic and splenic tumors
- HHV8 in pulmonary IMTS
  - Different spectrum of viral genes than KS or Castleman’s disease

INFLAMMATORY MYOFIBROBLASTIC TUMOR

- Outcome
- Surgical resection with recurrence in 14%
- May extend into hilum or mediastinum to obstruct trachea or esophagus and cause death
- Rare report of “metastasis”

PRIMARY PULMONARY TUMORS IN CHILDHOOD

- Hamartomas
  - Chondroma of bronchus
  - Chondromatous hamartoma
  - Lymphangiomatosis
  - Fibroleiomyomatous hamartoma
  - Lipomatous hamartoma
  - Fibroma
  - Leiomyoma
HAMARTOMAS

- Carney’s Triad
- Pulmonary chondroma
- Gastric stromal tumors
- Extra-adrenal paraganglioma
- Primarily in females 10-25 years

Size and location of lesion determines symptoms
- Endobronchial - small, firm, round to oval masses may obstruct entire lobe
- Peripheral - small to large, 3 to 20 cm masses of soft to firm, grey tone to yellow-brown tissue
- Treatment: resection, large lesions in infants may prove fatal