Pulmonary Hypoplasia in Congenital Defects

Joshua E. Petrikin, MD
Assistant Professor Pediatrics
June 28th, 2013

I have no financial conflicts of interest to disclose

Case 1
- 39 wk infant with born via SVD
- Develops tachypnea and grunting in the DR
- Bag mask CPAP given
- Clinical situation quickly deteriorates with poor oxygenation and perfusion
- Abdomen is scaphoid
- Pt intubated and stat CXR obtained
Case 1 continued

- NG Placed
- BG on CMV 6.9/118/33/-15
- FiO2 up to 1.0
- PIP 30, Peep 6, Rate 55
- Bolus of fluid given
- BG 7.08/110/29/-15

Case 1 continued

- Switched to HFOV
- MAP 16, Hz 10, Amp 35
- Still poor oxygenation and ventilation
- HFOV settings increased over time to MAP 25, Hz 6, Amp 55
Case 1 continued

- Was on 100% O2 with MAP of 26 and pAo2 of 35
- OI = 74 (!)
- What now?
Case 1 continued
- 23 day ECMO course marked by repeated failure to tolerate weaning
- Surgery on ECMO at day 20
- Bleeding and silo placed on day 21
- Ongoing blood loss and coagulopathy until off on day 23
- Death hours after removal from ECMO pump

Case 2
- 39 wk infant with born via SVD
- Develops tachypnea and grunting in the DR
- Bag mask CPAP given
- Respiratory distress continues
- Intubated and Stat CXR
Case 2 continued

- Minor vent settings with acceptable BG
- 7.25/49/87/-6 on 30% O2
- Pt weaned off ventilator on DoL 3 but continued resp distress
- Surgery on DoL 5
- Extubated on POD2

What’s the difference?

- Both cases with congenital malformations impacting the lungs
- Each malformation compressing adjacent lung
- Both infants required Mechanical Ventilation
  - One minor and the other maximal
- One died and the other discharged on RA to home
Critical Difference

- Unaffected lung normal vs hypoplasia
- Hypoplasia seen in:
  - CDH
  - Prune belly
  - Mid-trimester PPROM
  - Renal Agenesis
  - Premature Ductus Arteriosus closure
  - Idiopathic

Objectives

- Describe normal pulmonary development
- Describe pathophysiology of pulmonary hypoplasia
- Discuss management issues
- Identify long term sequelae

Normal Development

- Stages of Lung Development
  - Wk 4-7: embryonic stage
    - Lungs start to fill pleural cavities, primitive bronchi form
  - Wk 8-16: pseudoglandular period/stage
    - Organ looks like a gland, lined with columnar cells
    - Lung arteries form and follow the airways
Normal Development

- Wk 17-24: canalicular stage
  - Respiratory bronchioles form, columnar cells -> ciliated cuboidal
  - Blood vessel formation continues with capillary ingrowth
- Wk 24 to birth: terminal sac stage
  - Alveoli buds form and differentiate into Type I and Type II epithelia
  - Surfactant is produced (measured by Lethicin: Sphingomyelin ratio – 2:1 is good)

Normal Development

- Birth to 8 yrs of age: postnatal or alveolar period
  - 30 million alveoli increase to 300 million in the mature lung
  - Septation: growing alveoli are subdivided by septa such that the average size of an alveolus remains constant.
Normal Mature Lungs

- ~ 2,400 kilometers (1,500 mi) of airways
- ~ 300 to 500 million alveoli
- Total surface area 70 square meters (750 sq ft)

Surface Area

Normal Development

- Seems to Require
  - Normal thoracic cavity
  - Fetal breathing movements
  - Fetal lung liquid at positive pressure
  - Normal amniotic fluid volume
Abnormal Development

- Space occupying lesions in the chest
  - congenital diaphragmatic hernia
  - congenital cystic adenomatoid malformation
  - pleural effusions
- Malformed chest wall resulting in a small thoracic cavity
  - Kyphoscoliosis
  - Skeletal dysplasias

Abnormal Development

- Oligohydramnios
  - Bilateral renal agenesis or cystic dysplasia
  - Urinary outflow obstruction
  - Prolonged premature rupture of the membranes
- Neuromuscular disorders which prevent normal fetal breathing movements.

Hypoplasia with CDH

- Fewer airways
- Fewer blood vessels
- Fewer alveoli
- Hypermuscular peripheral pulmonary arteries
Hypoplastic Lung

Normal Development

Pulmonary Hypoplasia

- Fixed increased vascular resistance
- Persistent Pulmonary Hypertension (PPHN)
- Decreased Surface area for gas exchange
- Hypoxemia and Metabolic acidosis
CDH and Hypoplastic Lungs

- CDH most well researched cause
- May be different animal than other causes
- More muscular arteries?
- Less response to pulmonary vasodilators?
- Perhaps Hypoplastic lungs are the primary defect?

Management of Hypoplastic Lungs (via CDH)

- CDH EURO Consortium Protocol
- Initial Management
  - Avoid High Airway Pressures
  - Establish adequate Pre-ductal arterial saturation
  - Target sats 85% - 95%
  - Intubate Immediately
  - Minimize acidosis and hypoxemia

Management of CDH Initial Steps

- Avoid bag mask ventilation
- Low Peak Pressures (<25 cm H2O)
- Start at 100% O2 and wean down as able
- Place NG and obtain vascular access
Management: Initial Steps

- BP Support
  - PVR remains elevated
  - Increase BP to minimize R->L shunting is sats < 80-85%
  - Bolus NS once or twice
  - Inotropes/vasopresors
- Sedation and Analgesia
  - May lower BP
  - Paralysis(?)

Management: Initial Steps

- Surfactant
  - Makes sense
  - May increase ECMO and mortality
  - Avoid in CDH (some data)
- All advice is level D
  - Expert Opinion, Case series, extrapolation

Management: In the NICU

- Preductal Sat Target: 85-95%
- Postductal Sat: > 70%
- PaCO2 Target: 45-60
- pH > 7.2 and Lactate < 5 mmol/l
- UOP > 1ml/kg/hr
**Management In the NICU**
- Conventional Ventilation
  - PIP ≤ 25, PEEP 4-5, R 45-60
- HFOV
  - If PIP > 28 on CMV
  - Studies lacking
  - Typically used as rescue
  - MAP for adequate expansion
  - Freq CXR with vent changes
- All advice level D

**Management: NICU**
- Monitor Hemodynamics
  - HR – normal range
  - Cap Refill < 3 sec
  - UOP > 1 ml/kg/hr
  - Lactate < 3 mmol/l
  - If signs of hypovolemia, can give NS 10-20 ml/kg up to 3 times

**Management: Hemodynamic**
- Inotropic therapy
- Hydrocortisone
- Poor perfusion: Vasopressor
- Evidence Level: D
Management: PHTN

- CDH
  - Decreased arterial structures
  - Adventitial and medial wall thickening
  - Increased smooth muscle cells in all pulmonary arteries
  - Abnormal intra-acinar arterioles
  - Shunting R→L leading to hypoxemia

Management: PHTN

- ECHO can confirm
- If Preductal Sats < 85 and poor organ perfusion; optimize BP
- Dopamine, Dobutamine, Epinephrine, Norepinephrine
- Pulmonary vasodilators
  - iNO: improves PaO2 and decreases ECMO
    - Less useful in PHTN with CDH

Management: PHTN

- iNO: Evidence of Shunting, OI>20, or saturation differential > 10%
- Prostins: If suprasystemic PA pressure
- Sildenafil: Needs more study
  - Use only in chronic phase
**Endogenous Nitric Oxide (NO) Effects**

- L-arginine → NOS → L-citrulline
- NO → sGC → cGMP
- cGMP → PDE → 5'GMP
- 5'GMP → Jc Calcium → Vasodilation

### INO Therapy

**Indications**
- PPHN or hypoxemic respiratory failure
- OI ≥ 15, reversible pulmonary disorder
- ECHO - no evidence of CHD
- Dosage: > 20ppm no additional benefit (optimal lung inflation & adequate CO)
- Treatment Failure: OI > 25 transfer, OI > 40 ECMO
- Discontinuation: OI < 10, 2-6 days of INO
- Contraindications:
  - (No benefit in CDH)

### Management: ECMO

- Role in CDH is unclear
- Potential reversibility is key
- Preductal sats < 85%
- Postductal sats < 70%
- pH < 7.15 and/or Lactate ≥ 5 mmol/l
- PIP > 28 or MAP > 17
- Hypotension resistant to fluid and inotropes with UOP < 0.5 ml/kg/hr
- Trial of therapy
- Evidence Level D
CDH Management: Surgery
- Immediate after birth had higher mortality
- Ideal timing unknown
- Await maximal drop in PVR
- Surgery on ECMO leads to bleeding
- Surgery after ECMO can exacerbate PHTN

CDH Management: Surgery
- Data indicate repair after ECMO has better outcomes
- Large defect may need a patch
- If replaced contents prohibit wound closure, may need silo

Management: Sedation and Analgesia
- Sedate and monitor using scoring system (NPASS)
- Avoid paralysis
- Sedation may decrease BP and decrease sats
Management- PPHN

<table>
<thead>
<tr>
<th>Proven therapy</th>
<th>Unproven therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperventilation</td>
<td>X</td>
</tr>
<tr>
<td>Gentle ventilation</td>
<td>X</td>
</tr>
<tr>
<td>Alkali infusion</td>
<td>X</td>
</tr>
<tr>
<td>IV Vasodilators</td>
<td>X</td>
</tr>
<tr>
<td>HFV</td>
<td>X</td>
</tr>
<tr>
<td>Surfactant*</td>
<td>X</td>
</tr>
<tr>
<td>ECMO</td>
<td>X</td>
</tr>
</tbody>
</table>

Therapeutic options for PPHN are varied with wide range of variations in their use.

PROGNOSIS & FOLLOW-UP

- NINOS: INO not associated with an increase in neurodevelopmental, behavioral or medical abnormalities at 2 yrs of age
- Conservative Management without induced alkalosis & paralysis: no hearing loss and good outcome (Marron et al)

Mortality varies by diagnosis
- With all available therapies MR < 20-25%
- MAS survival close to 100%
- CDH- survival variable

Morbidities linked to severity of clinical course, diagnosis and complications
- At risk for neuro-developmental abnormalities
- Hearing Loss: high risk of late onset sensorineural hearing loss
- Pulmonary recovery typically excellent if MAS
- High risk for late pulmonary hypertension if CDH
CDH Outcomes
- Highest morbidity
  - Patch repair
  - ECMO
- Chronic Lung Disease
- Reactive Airway Infections
- Persistent Pulmonary Hypertension
- Degree of Pulmonary underdevelopment and severity of iatrogenic injury

CDH Outcomes
- 16% - 50% of survivors req supplemental O2
  - Many with diuretic and bronchodilators
- 25% Obstructive airway disease
- 50% with asthma
- 4% req tracheostomy
- Lung function may improve over time (slowly)

CDH Outcomes
- Chronic pulmonary hypertension
  - Overall mortality attributable 50%
- Sildenafil used with caution in chronic therapy
  - One study with concern about increased death
CDH Outcomes

- GER
  - 23% req fundoplication
  - Worse with Patch repair
  - ECMO
  - Intrathoracic liver
- Oral Aversion
- Failure to Thrive

CDH Outcomes

- Nearly universal MRI abnormalities
- Those not treated with ECMO
  - 54% working at grade level at 8-12 years
- Emotional and behavioral problems

CDH Outcomes

- ECMO
  - 19% with severe neurodevelopmental problems
  - 25% free of significant impairment
  - 60% with SN Hearing loss
  - Progressive
CDH Outcome
- Reherniation 5-80%
- Intestinal Malrotation 100%
- Chest wall deformities
  - Asymmetry 48%
  - Pectus 18%
  - Significant Scoliosis 27%
  - Worse with larger defect

Recap
- Pulmonary Hypoplasia multifactorial
  - CDH, Idiopathic, Oligohydramnios, PPROM, other
  - Treatment is lung protection while maintaining organ oxygenation and pH
  - ECMO if reversible
- Outcomes depend of etiology
  - More acidotic, hypoxic, hypotensive the worse the outcome

Thank You
- Questions?