Thoracic lesions and Airway Pathology

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Oligohydramnios

Renal
Lung Development

Canalicular

17
28
weeks

Exchanging airways / type I-II cells

Vascular development

Saccular

25
40
weeks

Subdivision & interstitial decrease

Alveolar ducts and structures

Alveolar

30
3 yrs

Alveolarisation/maturation

Microvascularisation

Gestation (wks)

Embryonic

5
8 wks

Lung bud, subsegmental bronchi

Pseudoglandular

7–18 wks

All conducting airways/acinar outlines

Endodermal

5–9 wks

Longitudinal/higher order bronchi

Normal lung growth

Normal

LEFT lung

RIGHT lung

Peralta UOG 2005; 26: 718-724
### Prenatal Diagnosis

Diaphragm
hypoechoic line between lungs – viscera

### Lung and airway lesions

- 2% of detectable malformations - 1/1000 pregnancies
- Types:
  - Airway anomalies
  - Parenchymatous lesions
  - Congenital Cystic Adenomatoid Malformation (CCAM)
  - Bronchopulmonary Sequestration (BPS)
  - Hybrid CCAM-BPS
  - Effusions
  - Congenital Diaphragmatic Hernia (CDH)
- Often regress in utero, but perinatal relevance
  - Space occupying
  - Haemodynamic
  - Obstruction at birth
- 10-50% are associated with other defects and/or chromosomal anomalies: additional studies

### Investigation

<table>
<thead>
<tr>
<th></th>
<th>CCAM</th>
<th>BPS</th>
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</thead>
<tbody>
<tr>
<td>Location</td>
<td>Lobar Above diaphragm</td>
<td>Lower part of the lung Above/under diaphragm</td>
</tr>
<tr>
<td>Blood supply</td>
<td>Pulmonary</td>
<td>Systemic</td>
</tr>
<tr>
<td>Connection to airways</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Textures</td>
<td>Yes/no cystic</td>
<td>In essence not cystic</td>
</tr>
<tr>
<td>Volume</td>
<td>Any</td>
<td>Any</td>
</tr>
</tbody>
</table>
Parenchymatous lesions

- Bronchopulmonary sequestration
  - Systemic arterial supply
  - 80% asymptomatic at birth
  - Point to associated problems (CDH, CCAM)
  - 5% will have pleural effusion
  - Can be ablated in utero: laser, alcohol, ...

- Congenital Cystic Adenomatoid Malformation
  - Relevance is impact on the rest of developing lung
  - Growth falls after 26-29 weeks in 90%
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  - Criteria for therapy: mass effect or hydrops
  - Few data to determine pulmonary hypoplasia in the non-hydropic case
  - Maternal mirror syndrome

In utero management

- Follow up 2 weekly
  - CCAM Volume Ratio (Crombleholme 2002)
  - CVR >1.6: 80% risk for fetal hydrops
  - Fetal hydrops invariably determines poor outcome
  - In previable period in utero treatment, dependent on presentation
  - Few data to determine pulmonary hypoplasia in the non-hydropic case
  - Maternal mirror syndrome

Percutaneous shunting: thorax

- Indications
  - Hydrothorax
  - Macrocystic CCAM (+hydrops)
- Shunt placement
  - Wilson 2004:
    - n=23 shunts; 74% survival
- Alternatives:
  - Repetitive thoracocentesis
  - Pleurodesis
  - Non-cystic: thoracotomy
Effusions

- Overall survival 65%+
  - Experience with shunting largest
  - Alternatives being explored

<table>
<thead>
<tr>
<th>Intervention</th>
<th>GA 1st intervention</th>
<th>Interval to delivery</th>
<th>n</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single T'centesis</td>
<td>31 (28-38)</td>
<td>1</td>
<td>13</td>
<td>7 (54%)</td>
</tr>
<tr>
<td>Multifour T'</td>
<td>31 (30-36)</td>
<td>4</td>
<td>10</td>
<td>12 (67%)</td>
</tr>
<tr>
<td>Shunts</td>
<td>30 (22-36)</td>
<td>5</td>
<td>30</td>
<td>64 (64%)</td>
</tr>
<tr>
<td>TA-shunt</td>
<td>27 (20-34)</td>
<td>7</td>
<td>15</td>
<td>23 (56%)</td>
</tr>
<tr>
<td>Pleurodesis</td>
<td>25 (23-31)</td>
<td>11</td>
<td>5</td>
<td>6 (60%)</td>
</tr>
<tr>
<td>Total</td>
<td>10 (20-30)</td>
<td>9 (9-30)</td>
<td>57</td>
<td>133 (54%)</td>
</tr>
</tbody>
</table>

Deurloo et al, Prenat Diagn 2007

Congenital Diaphragmatic Hernia

- Increasingly being picked up in screening programmes
- Few in utero problems
- Postnatal:
  - Correctable defect
  - Ventilatory insufficiency
  - Pulmonary hypertension
  - Long-term morbidity

Overall outcome:
- Associated: 85% mortality
- Isolated: 30% mortality

Prenatal prediction

- Reduced number of airways
- Reduced and absent vessels
- Abnormal compliance

Liver herniation

Survival: 75% - 93%

Deurloo et al., Prenat Diagn 2007
3. Prenatal prediction

- Extreme
- Severe
- Moderate
- Mild

Survival rate (%):

- < 15
- 15 - 25
- 26 - 35
- 36 - 45

O/E LHR (%):

0 10 20 30 40 50 60 70 80 90 100

3. Prediction of morbidity

- Isolated CDH expectantly managed (n=100)

- Patch o2 (%)
- Oxygen o2 at lhr(%) 
- Gastric intubation
- Tracheostomy
- Sepsis

O/E LHR (%):

0 10 20 30 40 50 60

2 versus 3 dimensional

Cross section at the 4 chamber view
Of ONE lung

volumetric measurement
of two lungs and of liver herniation

From: Jani et al. UOG 2008
MRI volumetry of lung and liver

Liver down
Liver up

Multicenter study prediction on volumetry

Liver up: Survival 50% - volume linear relation to survival
Liver down: Survival 75% - volume is not predictive of outcome

Comparison 2D ultrasound and MRI

Isolated CDH born alive >30 wks, paired observations (n=76)

MRI may be better than 2D US in predicting outcome

Inaccuracies related to the ipsilateral lung volume contribution

Cannie et al, UOG 2008

Comparison of US and MRI

Sensitivity (%)

2D-US: 75, 50, 25
MRI: 100, 75, 50, 25

False positive rate (%)

2D-US: 100, 75, 50, 25
MRI: 0
% liver to thorax ratio (LITR) an independent predictive factor

Fetal intervention stimulating prenatal lung development

FETO procedure
- lung <25% & liver in thorax
- isolated lesion

Balloon in at 28 weeks
Reversal at 34 weeks

Clinical Procedure
- 3.3 mm; loco(regional)
- 8 min
- pancuronium 0.2 mg/kg
- fentanyl 10 µg/kg
- admission: 2 days

Deprest et al, 2005; FETO Consortium 2009
Results Entire FETO Experience (Unedited)

n=210, October 2001 - October 2008.

Gestation at FETO

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<tr>
<th>Median</th>
<th>27 wks</th>
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Analgesia

- General: 8 (4%)
- Epidural: 160 (76%)
- Local: 42 (20%)

Intervention time

| Median | 27 min |

Placenta

- Anterior: 100
- Posterior: 110

Successful FETO

1st attempt: 203 (97%)
2nd FETO: 5%

Results Entire FETO Experience (Unedited)

Gestation at PROM

PROM: 47%

Occurrence of PPROM or delivery < 32 wks (all cases)%
- PPROM & delivery < 32 wks: 9.3%
- Preterm delivery < 32 wks, without PPROM: 3.6%
- Delivery < 32 wks: 12.9%
- PPROM, delivery 32 wks +: 36.8%

• Semantics on Prelabour ROM
  • Iatrogenic
  • Amniorrhaxis: does not mean delivery
    • Is present in 75% cases of preterm delivery
    • Impact dependent on gestational age at delivery (32 wks critical)
Retrieval of balloon

<table>
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<tr>
<th>Method</th>
<th>EXIT</th>
<th>9%</th>
<th>Fetoscopy</th>
<th>46%</th>
<th>Ultrasound puncture</th>
<th>26%</th>
<th>Postnatal</th>
<th>21%</th>
</tr>
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Ultrasonic-guided puncture

Laryngoscopy on EXIT

FETO consortium, n=204, UOG 2009

Survival rates with fetal therapy

- PPROM & delivery
  - Delivery < 32 wks: 15%
  - Survival < 32 wks: 25%
  - Survival > 32 wks: 60%

- Pre-existing lung size determines response
- Maximum increase when O/E LHR = 15-25%

- Early pulmonary morbidity
- Further development: ongoing

FETO does not increase morbidity

- Isolated CDH either expectantly managed (n=100) or FETO (n=37)

- Conventional ventilation
- Enteral feeding
- NICU**
- Oxygen O2 at 28d
- Other variables

Jani et al UOG 2008
www.TOTAL trial.eu

Tracheal Occlusion To Accelerate Lunggrowth

2 multicenter trials in Europe

- ACT FETO (26-30 wks)
  - outcomes: Survival
  - Started: 10/2009

- ACT FETO (30-32 wks)
  - outcomes: Survival w/o BPD
  - Started: 10/2008

Outcome measure: Survival

Survival rate (%)

- extreme
- severe
- moderate
- mild

10/2009

Outcome measure: Survival w/o BPD

Survival rate (%)

 Started: 10/2008
17 inclusions

SEVERE (<25%, liver up or down)
MODERATE (26-35%, any liver & 36-45%, up)

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**Standardized postnatal management**

**Delivery Room**
- No bag mask ventilation
- Immediate intubation
- Peak pressure below 25 cm H2O

**NICU**
- Adapt ventilation to obtain preductal saturation between 85% - 95%
- pH > 7.20, lactate 3 - 5 mmol/L
- Conventional ventilation (CMV) or high frequency oscillation (HFO), maximum peak pressure 25 - 28 cm H2O and mean airway pressure 17 cm H2O
- Targeting blood pressure - normal value for gestational age
- Consider inotropic support

**Pulmonary Hypertension**
- Echocardiography
- Inhaled nitric oxide (iNO)
- First choice in case of non-response
- Chronic phase: phosphodiesterase - inhibitors, endothelin - antagonists, tyrosine kinase inhibitors
- ECMO (if available)
  - Only starting if the patient is able to achieve a preductal saturation > 85%

**Surgical repair**
- Fraction of inspired oxygen (FiO2) below 0.5
- Mean blood pressure normal of gestational age
- Urine output > 2 ml/kg/hour
- No signs of persistent pulmonary hypertension

**Airway anomalies**
- **Congenital High Airway Obstruction**
- **Bronchial stenosis**
- **Ultrasound features**
  - Hyperechogenic lungs, fluid bronchogram
  - No vascular pedicle
  - Letal without EXIT procedure

**Fetoscopic Airway Exploration**
- Tracheo-oesophageal cleft
- Giant neck mass
- Tracheo-oesophageal cleft
- Avoiding any further therapy
- Giant neck mass
- No EXIT
EXIT procedure

OOPS= “Operation On Placental Support”

Maintaining placental circulation

Typical for obstructed airways

Conclusions

• Relevance of thoracic lesions lays in their effect on lung development
  – Parenchymatous lesions: most regress
  – Some cause fetal hydrops: in utero therapy
  – Some cause lethal hypoplasia: in utero therapy
  – Several fetal interventions possible
  – Perinatal management: be prepared
• Airway problems: secure airways at EXIT
• Often associated anomalies or problems

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