Paediatric Lung Lesions
14.45h – 15.30h
Cystic lung lesions and pneumothorax

R 2878/16

Specimen: Thoracic Specimen

Medical history/ Clinical informations:
Boy, 3,5 yrs;
status post DILV (Double Inlet Left Ventricle)
TGA (transposition of great arteries), subarortic
stenosis (→ s.p. DKS (Damus-Kaye-Stansel-
Operation) and Glenn-operation in Russia)
Acute: cyst between RPA (=right pulmonary
artery) and RPV (=right pulmonary vein)

Macroscopy
Square specimen of 3.3 x 3.3 x 3.2 cm,
lacerated on one side.

Microscopy
Cyst
lining: ciliated pseudostratified columnar
epithelium

wall: cartilage, seromucous glands,
fibromuscular tissue

Bronchiogenic cyst

= congenital malformation of the
respiratory tract;
diagnosed mainly in children,
rarely in adults

Diagnosis:
Bronchogenic cyst
Bronchogenic Cyst: Aetiology:
- anomalous budding of the foregut during embryological development
  ⇒ part of the spectrum of bronchopulmonary foregut malformations

Localisation:
- any point of the tracheobronchial tree
  - rarely (case reports):
    - cervical,
    - intrapleural,
    - cutaneous,
    - esophageal,
    - cardiac and
    - subdiaphragmatic retroperitoneum

Bronchogenic Cyst: Pathology

Macroscopy:
- unilocular cyst, filled with thick, clear fluid
- no communication with the tracheobronchial tree

Histology:
- cyst lining: respiratory epithelium, occasional foci of squamous metaplasia;
- cyst wall: resembles wall of larger airways: smooth muscle, bronchial glands, and cartilage plates = most reliable diagnostic criterion

Infected cyst: chronic and/or acute inflammation (acute and/or chronic inflammatory cells);
may result in denuded epithelium with subsequent squamous metaplasia

Differential diagnosis
- Pericardial cyst: lined by mesothelial cells
- CPAM: bronchogenic cysts very seldom contain lung tissue
- Thyroglossal Cyst: 25% of thyroglossal duct cystes are found below hyoid bone and in ektopic thyroid, no cartilage
- Foregut cyst: lined by stratified squamous or columnar epithelium with double muscular layer
- Abscess: would be connected with bronchial tree
- Cystic teratoma: multiloculated; may contain 3 germline derivatives

Fall 8

Gross specimen: Partial right-sided lung resection

Medical history/ Clinical informations:
Girl, term-born, 9 d. Lung malformation?
Microscopy
- Irregular bronchiolar-like structures
- Lining by ciliated epithelium
- No mucous cells
- Thin fibro-muscular layer
- Air-filled spaces
- No cartilage

Diagnosis:
CPAM (Congenital pulmonary airway malformation) Typ II
former: CCAM (congenital cystic adenomatoid malformation)

CPAM (Congenital pulmonary airway malformation)
Hamartomatous lung lesion characterised by cystic and adenomatous
- tracheal,
- bronchial,
- bronchiolar or
- acinar structured tissue
-> abnormal pulmonary branching morphogenesis

Stocker: 5 categories based on the proposed site of defect in the tracheobronchial tree

Pathogenesis
Hypothesis explaining the different types of CPAMs resp their origine from
- different levels of the tracheobronchial tree and
- at different stages of lung development,
possibly influenced by in utero airway obstruction / atresia:
occlusions of (major) airways at the CPAM margin can be found in most cases
Tip from experience:
dissection parallel to brochial hilus (from resection margin) and consecutive dissection of the proximal and distal airways
Pathogenesis of CPAM

1. ↑ expression of HOX B5 gene (= member of the homeobox family, located on chromosome 17)
- implicated in the process of imbalanced apoptosis/proliferation
- encoded protein: sequence-specific transcription factor involved in lung and gut development.

Increased expression: associated with occurrence of bronchopulmonary sequestration (BPS) and CPAM

2. GDNF (= glial cell derived neurotrophic factor): may mediate proliferation-/apoptosis-dysbalance in part
- growth factor widely expressed in developing organs with epithelial-mesenchymal interaction
- has been described in epithelial and endothelial cells from normal fetal lungs and epithelial cells from CPAMs, but not in normal lung tissue from older infants and children.

Additional informations for CPAM type 2
- When streaks of differentiated skeletal muscles: *rhabdomyomatous dysgenesis*: special subgroup of type II or a distinct further lesion?
- Hybrid forms with features of CPAM type 2 and extralobar pulmonary sequestrations
- In up to 60%: other congenital anomalies, e.g. esophageal atresia with tracheoesophageal fistula, bilateral renal agenesis, renal dysgenesis, intestinal atresia, other pulmonary malformations, resp. diaphragmatic, cardiac, central nervous system, and bony anomalies.
- Association with other congenital malformations suggests that insults resulting in type 2 CPAMs occur during the third week of gestation

Additional informations

Type 0
- "acinair dysplasia" (Rutledge and Jensen, Hum Pathol 1986)
- Associated with cardiovascular anomalies and dermal hypoplasia
- Involved entire lung ⇒ extremely impaired gas exchange ⇒ death at birth
Additional informations to type IV:

Most important differential diagnosis: cystic pleuropulmonary blastoma

For diagnosis of blastoma areas extensive sampling is necessary

CPAM Type IV cyst have alveolar cell lining: surfactant-staining: positive

CPAM should not be diagnosed when there are signs of acute or chronic inflammation or scarring

⇒ One should be very careful when diagnosing a CPAM in older children or adults

Prenatally:

intrauterine sonographic diagnosis (variable presentation)

Large CPAMs and mediastinal shift

→ obstruction of the lower V. cava + heart compression

→ augmented central venous pressure → fetal hydrops

Gilbert-Barness: „It is important to remember that ‘fetal’ CPAM cannot - in most circumstances – be classified using Stocker 0-4 criteria and that attempts to do so will not be rewarding“

Specimen: pulmonary tissue from the left side

Medical history/ Clinical informations:
Boy, 7 d; status post intrauterine pigtail-catheter. „lung malformation“?

Fall 9

Macroscopy:

Nearly pyramid-shaped lung tissue, 17 g, max. 4,4 x 3,0 x 3,3.

Cut surface: fine pored parenchyma.

Diagnosis:

Extralobar Sequestration with pleural granulation tissue (status post pigtail catheter)

Further information after diagnosis: intraoperative ligation of an artery originating from the aorta.
Bronchopulmonary sequestration

= nonfunctioning mass of lung tissue with an abormal arterial blood supply from the systemic blood circulation and without communication with the tracheobronchial system

### 4 subtypes

- **Intralobar sequestration (ILS)**
- **Extralobar sequestration (ELS)**
- **Hybrid BPS / CPAM-lesions**
- **Bronchopulmonary-foregut malformation (BPFM)**

### EPIDEMIOLOGY

- in about 1 in 10,000 to 35,000 live births
- **ILS** : Male = females
- **ELS** = **male** predominance (antenatally reports: ratio of male/female: 3:1
- bronchopulmonary-foregut malformation (BPFM): **female** predominance.

Subtypes (2)

- **Hybrid BPS / CPAM lesions** : BPS (typically ILS) occurs in combination with a CPAM (have been reported in up to 50 % of cases of BPS). Show:
  - histological features of CPAM
  - a blood supply from a systemic artery

- **Bronchopulmonary-foregut malformation (BPFM)**
  = rare variant, in which the sequestered lung tissue (either ILS or ELS) is connected to the gastrointestinal tract

**Attention**: Sometimes the term BPFM is used to include all foregut malformations
**Pathogenesis**

most widely accepted embryologic theory: development early in the pseudoglandular stage of lung development (5 to 17 weeks of gestation), prior to separation of the aortic and pulmonary circulations

⇒ explains the wide spectrum of pathology observed, including

- connections to the systemic circulation,
- the presence of separate visceral pleura in ELS
- lack thereof in ILS
- the occurrence of hybrid lesions with features of BPS + CPAM
- the occasional associations with bronchogenic cysts
- the occasional connections to the foregut,
- associated anomalies (e.g. congenital diaphragmatic hernia)

**Hypothesis for ELS:**

abortive buds of the foregut / developing tracheobronchial tree resp a portion of the developing lung is mechanically separated from the rest of the lung by

- compression from vascular structures
- traction by aberrant systemic vessels
- inadequate pulmonary blood flow.

**HOX B5 Gen:** ↑ expression of these gene was found in sequestrations

**Pathogenesis**

hypothosis for ELS:

In up to 50% ELS presents partially or completely as CPAM

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**ILS:**

• Formerly: acquired rather than a developmental lesion; occlusion of a bronchial branch by aspirated material or inflamed debris.

⇒ pneumonia distal to the obstruction

⇒ O2-supply for this lung tissue: by systemic blood flow from pleural granulation tissue → "new" systemic arterial supply persists after involution of pneumonia

Basis of this hypothesis:

- the late presentations of ILS in historical series
- observations that systemic arterial collaterals (resembling BPS) occasionally develop in the setting of pulmonary inflammatory processes

**ELS** vs **ILS**

<table>
<thead>
<tr>
<th>Age at diagnosis</th>
<th>ELS</th>
<th>ILS</th>
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</thead>
<tbody>
<tr>
<td>ca. 60% &lt; 1 y</td>
<td>50% &gt; 20 y; children: rarely</td>
<td></td>
</tr>
<tr>
<td>M : F</td>
<td>3:1 bzw. 4:1</td>
<td>M ≥ F</td>
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<tr>
<td>Venous draining</td>
<td>Mainly systemic (&gt;80%); in about 20%: partially or complete by pulmonary veins</td>
<td>95% pulmonary 5% partially or totally by V. hemiazygos, azygos or lower or upper V. cava</td>
</tr>
<tr>
<td>Diaphragmal defect</td>
<td>often</td>
<td>seldom</td>
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**Specimen:** Partial lung resectate

**Medical history/ Clinical informations:**

Boy, 36 d, born at in 33. week of pregnancy postnatally O₂ demand ↑ ↑ → assisted respiration (CPAP), followed by intubation and fractionated application of Curosurf® ⇒ rapid improvement and extubation

X-ray at day 7 (due to apnoe-bradykardia-syndrome): bulla in left upper lobe
**macroscopy:**

Cyst wall: 4.2 x 3.5 cm, max 0.3 cm thick

Inner side: shiny; septae indicated
outside: small seam of lung parenchyma

**Diagnosis:**
Subpleural lung cyst with lining by pneumocytes and old bleeding (wall + lung tissue)

**Pneumatocele**

**Pneumatocele**

= acquired, thin walled air filled intrapulmonary cystic lesion

**causes:**

I: **Inflammation** (most frequent, 66%):
   Staph. aureus-pneumonia;
   inflammation → necrosis + liquefaction of the lung parenchyma → permeation of air → subpleural dissection → thin walled cyst

II. traumatic: after thoracic trauma
   external force + rapid decompression → augmented negative intrathoracal pressure („bursting lesion“ of the lung)

**Postpneumonic pneumatocoele:**

valvular obstruction: air gets into the lung, but can not leak out of the lung segment due to missing pores of Kohn (pores in alveolar septae between adjacent alveoli)

⇒ cysts

Explains why postpneumonic pneumatoceles are comparatively rare in adults

**restitutio ad integrum:** m ainline within 4-6 weeks – in some cases during 1 year

⇒ Reluctance towards operative procedures is justified

In this case a pneumonic genesis could be excluded

Hypothesis:

- PEEP-therapy (positive endexpiratory pressure = positive airway pressure at end of expiration)
  ↓
- Barotrauma-like laceration of alveolar walls

Isolated finding

⇒ focal lowering of the alveolar resistance by surfactant-dispensation
Specimen:
Left upper lobe

Medical history/ Clinical informations:
Boy 24d, born at term
According to parents: since birth intermittend „conspicious“ breathing;
After week 1: increasing sucking weakness
At day 22: emergency hospitalisation in hospital near home; diagnosis: pneumothorax → transfer to university clinic

Macroscopy:
Upper left lung lobe, max. 11 x 8 x 3 cm
On incision not collapsing lung tissue
Cut surface: pale grey, segmented by septae. Alveolar structure visible

Diagnosis
Congenital lobar emphysema (CLE)
= congenital lobar overinflation
Infantile lobar emphysema

Congenital lobar emphysema
Hyperinflation: results from a variety of
disruptions on bronchopulmonary
development due to abnormal
interaction between embryonic
endodermal and mesodermal lung
components, leading to altered
number of airways of alveolar or
alveolar size („Hyperplasia“)
Up to no: in about 50% nor causative
agent known
Identifiable cause: extrinsic or intrinsic
obstruction
⇒ globe valve –mechanism („trapped
air“)
Or bronchial atresia

Causes of extrinsic/extraluminal obstruction:
1) Vascular malformations/anomalies (pulmonar artery sling; abnormal
pulmonary venous return, right sided ductus arteriosus Botalli with right
aortic arch,
2) Intrathoracic tissue (bronchogenic cyst, teratoma, esophageal duplication)

Causes of intrinsic/intraluminal obstruction:
1) Stenosis/ atresia of a bronchus or abnormal origin of a bronchus (from
trachea or bronchus lobaris superior dexter)
2) defects in the bronchial wall (ontogenetic defect → deficient bronchial
cartilage → airway collapses during expiration)
3) meconium or mucus plug, granulation tissue (endotracheal suction) or
mucosal fold (with partial obstruction), foreign bodies

Intraluminal: more often than external
Not definitively identified cause: up to 50%
## Site

<table>
<thead>
<tr>
<th>1. Left upper lobe</th>
<th>40 – 50%</th>
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<tbody>
<tr>
<td>2. Right middle lobe</td>
<td>25 – 35%</td>
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<tr>
<td>3. Right lower lobe</td>
<td>20%</td>
</tr>
<tr>
<td>4. Multiple lobes</td>
<td>up to 18%</td>
</tr>
<tr>
<td>5. Bilaterale</td>
<td>Rarity</td>
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Prenatal ultrasound diagnosis ⇒ diagnosis is known at birth

## Histology

Wide varity:

Simple, uniformly enlarged distal airways and airspaces

Polyalveolar form

## Boys > girls (1.8:1 to 3:1)

## Polyalveolare Form des ILE

- size and number of the conducting airways are normal
- But: enlarged/dilated alveoli, that are increased in number

⇒ Radial alveolar count (RAC): 2- to 3-fold

\[
RAC = \text{radial alveolar count: drawing of perpendicular line from pleura to terminal bronchiolus and counting of all alveolar septae, crossed by this line}
\]

Born at term: 4.4 ± 0.9

## Symptoms:

- Progressive respiratory distress up to cyanosis over weeks to months,
- Rarely: recurrent respiratory infection up to pneumonia
- Sucking weakness with failure to thrive or vomiting

Intensity of symptoms are related to:

- Size of the affected lung lobe
- Compression of the surrounding lung tissue
- Extent of the mediastinal shift

Time of presentation:

- 25 - 33% of all cases. At birth
- 50% till first month
- Nearly all till 6 months
- Rare cases asymptomatic over years

## Therapy:

- Neonate with respiratory distress: resection of the lobe (minimal invasive thoracoscopy)
- Babies/toddlers/older children without/with minimal symptoms: Conservative management
- Resection date: controversially issue

## ILE: localised bronchial obstruction

emphysema due to generalised bronchial defect
Williams Campbell Syndrom
1960 first description by Williams und Campbell
- defective, progressively quantitatively and qualitatively diminishing bronchial cartilage (missing and/or reduced and/or soft) at the sub-segmental level

Histology:
bronchiektasis, thin-walled
panacinary emphysema

Clinic: starts in childhood

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R 253/16

Specimen:
Left upper lung (apex)

Medical history/ Clinical informations:
Male, 16 yrs, cyst with short stalk on lung apex

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Macroscopy:
Whitish, cystic sac of 4.2 x 2.2 x 2 cm,
ruptured over 2x1.5 cm
Inner face: smooth, shiny

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Bulla type I (according to Reid)
- Greatly overinflamed sac, with a narrow neck (not in this specimen)
- Typical for localised (distal acinar) emphysema
- Most common localisation: extreme apex of either or both lungs.
- Common cause of spontaneous pneumothorax in young adults
- Can progress to a sizable area of pulmonary destruction,
- Bulla: often used to describe such lesion, when > 1 cm;

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Bullae
- Type I - small amount of lung involved, greatly overinflated, resulting in an empty sac with a narrow neck.
- Type II: shallow layer of lung with a broad neck and at least some lung remnants
- Type III - large amount of lung parenchyma often extending back to the hilum and with lung tissue remnants evenly distributed through the bulla

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„Apical pleural Fibrosis“
- Pleura: reactive tissue
- Signs of pleural reaction: increased vascularity, inflammation, mild fibrosis, fibrous thickening,
- In most cases of moderate to severe centrilobular emphysema:
  - relatively nonspecific form of fibrosis, but: fibrous tissue often has a more granular or less organized appearance than well-formed collagenous fibrosis
  - Blebs and bullae as result of emphysema in the apical portion of the upper lobes show nonspecific types of pleural reactions, with mesothelial hypertrophy and hyperplasia, submesothelial fibrosis and varying degrees of inflammation („fibroinflammatory-type tissue“).