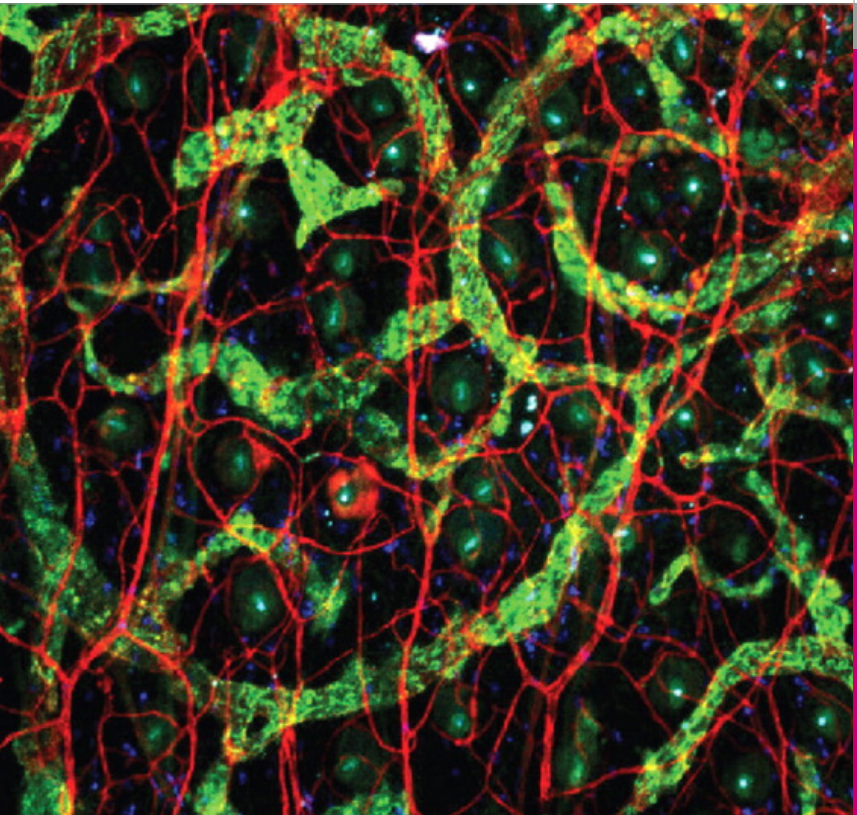
SWISS SOCIETY OF NEONATOLOGY

Apgar 7/5/5 – what can go wrong so fast?



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Title figure:
Proximity of mast cells (blue) to blood (red, CD31) and lymphatic (green, LYVE-1) vessels in the mouse skin (Source: www.boodjournal.org)

This male infant was born at home at 40 4/7 weeks of gestation to a G5/P3 mother (i.e., planned home delivery). Pregnancy, including serologies and a morphological ultrasound examination at 22 weeks, had been normal. As customary for home deliveries, two midwives were present at birth. During labor, the cardiotocogram was always normal and after rupture of membranes clear amniotic fluid was noted. The infant's birth weight was 3830 g (P 50 – 90).

Immediately after birth, the boy cried vigorously and was placed on the mother's chest. Shortly thereafter, the cry became weaker despite stimulation by the midwife. At 4 minutes of life, he was noted to become increasingly dyspneic, cyanotic and the heart rate decreased to less than 100 beats per minute. The infant's condition failed to improve after suctioning, stimulation and oxygen admininstation. Apgar scores assigned by the midwive were 7, 5, and 5 at 1, 5 and 10 minutes, respectively. At 10 minutes of life, an ambulance was called.

When the ambulance team arrived at about 17 minutes of life, the baby was found to be pale, gasping, bradycardic, and bag mask ventilation was started. A pediatrician arrived at around 30 minutes of life; an umbilical venous catheter (UVC) was placed and the infant was intubated. Despite high inspiratory pressures, there was poor chest rise and the infant continued to be profoundly hypoxemic (SpO_2 60 % at

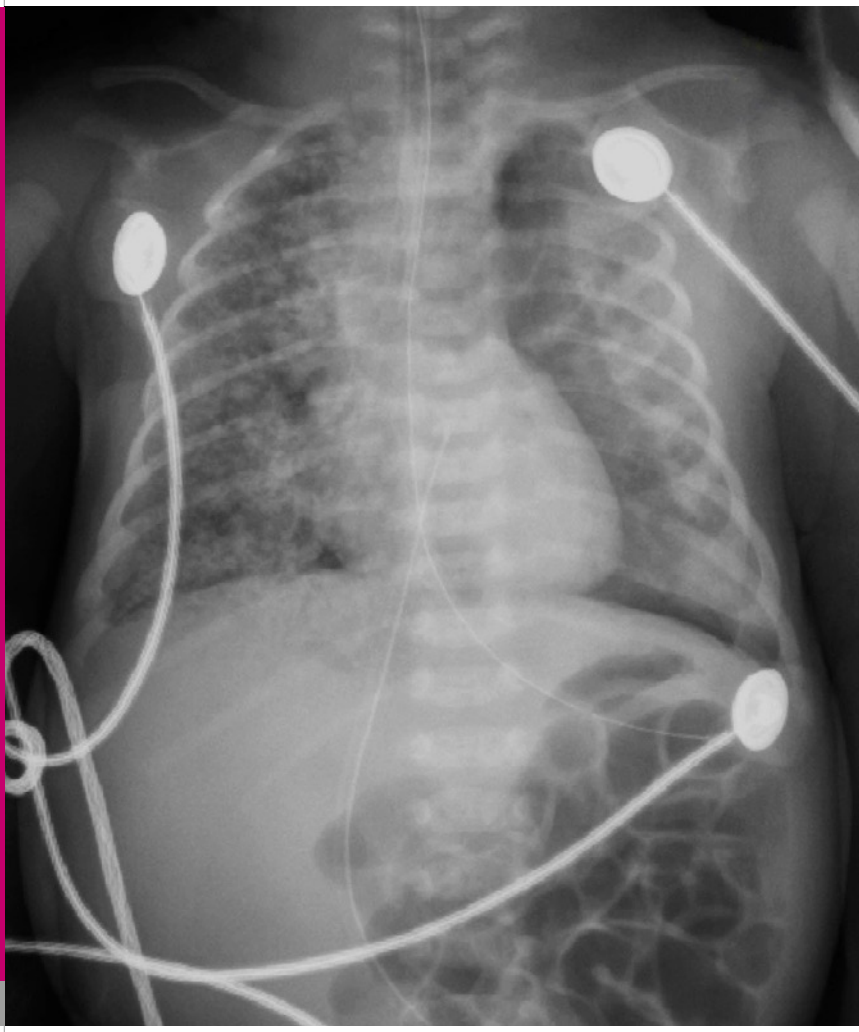

Fig. 1

Chest X-ray at the age of 1.5 hours: diffuse reticulonodular pattern on the right side, a left-sided pneumothorax, right main stem intubation, the tip of the UVC projecting over the right atrium.

an FiO_2 of 1.0). Heart rate remained at 100 beats per minute and blood pressure was normal with a mean of 57 mmHg. Normal saline (10 ml/kg) was given twice and 10% dextrose was started. At 50 minutes of life, the baby arrived at the closest regional hospital and a level III neonatal transport team took over.

At 60 min of life, the baby's SpO_2 was 35%, he continued to be difficult to ventilate and his temperature was 33.5°C. A first venous blood gas sample showed severe mixed acidosis with a pH 6.72, a pCO_2 14.7 kPa, a base excess -19.7 mmol/l and a lactate concentration of 16 mmol/l. A chest X-ray revealed a left-sided pneumothorax, right main stem intubation, intracardiac position of the UVC, as well as hyperinflated lungs with a diffuse reticulo-nodular pattern (Fig. 1).

The position of the endotracheal tube was corrected, and the pneumothorax was drained. The infant's heart rate increased to more than 100 beats per minute after one dose of intravenous epinephrine. At this point, it was decided to attempt transfer to the level III neonatology unit. Transport by helicopter took around 15 minutes, and the baby arrived in the NICU at 2.5 hours of age.

Thirty minutes later, the baby was put on high frequency oscillatory ventilation (HFOV; Sensor Medics®). Despite increasing ventilator settings (MAP from 15 to 22 mbar, amplitude up to 60 mbar) there

was no improvement in oxygenation or ventilation. At this point, another chest X-ray showed correct position of the endotracheal tube, proper position of the left-sided chest tube, a small right-sided medial pneumothorax and projection of the tip of the UVC over the right atrium (Fig. 2).

Echocardiography documented normal anatomy, but poor biventricular function. Inhaled nitric oxide (iNO) and inotropic support were initiated, but the baby's condition did not improve. At 4 hours of life, an arterial blood gas sample showed a pH of 6.53, a pCO_2 15.7 kPa, a base excess -27 mmol/l and a lactate concentration of 29 mmol/l. In presence of persisting bradycardia, refractory hypoxemia and hypercarbia with resulting profound mixed acidosis, and after discussion with the parents, life-sustaining therapies were felt to be futile and were discontinued. The boy died in the arms of his parents shortly thereafter.

Autopsy findings were consistent with a diagnosis of congenital pulmonary lymphangiectasia (CPL): macroscopically, cysts spreading throughout the entire lung parenchyma were recognized (Fig. 3, 4); these could be identified as enlarged lymphatic vessels on microscopic examination using a specific stain to identify lymphatic endothelial cells (Fig. 5).

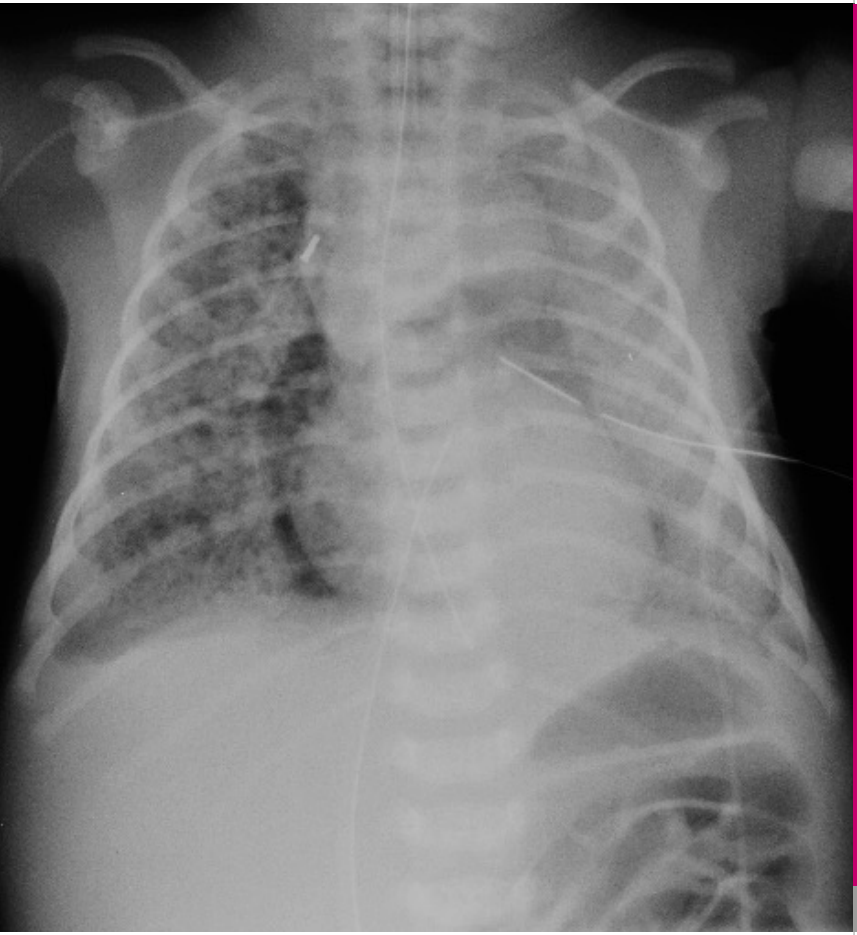

Fig. 2

Chest X-ray at the age of 5 hours after arriving at the level III NICU: left-sided pleural drain, right-sided medial pneumothorax (venous cannula used for drainage still in situ), tip of the UVC projecting over the right atrium, correct position of the endotracheal tube.

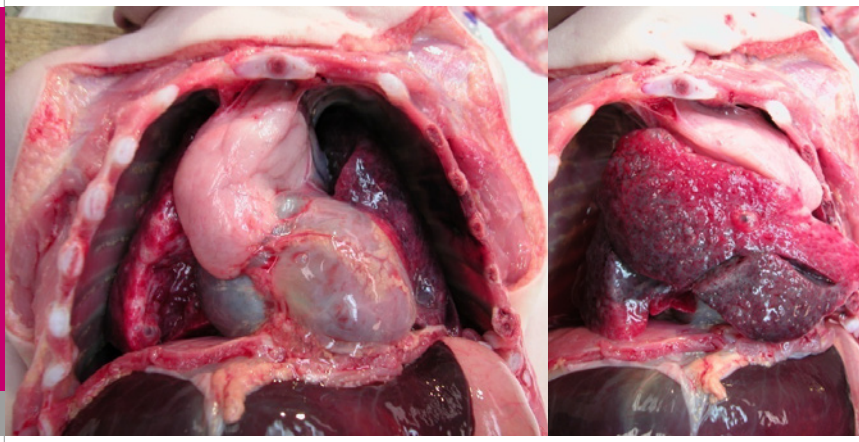

Fig. 3

Macroscopic autopsy findings: multiple bilateral subpleural cysts.

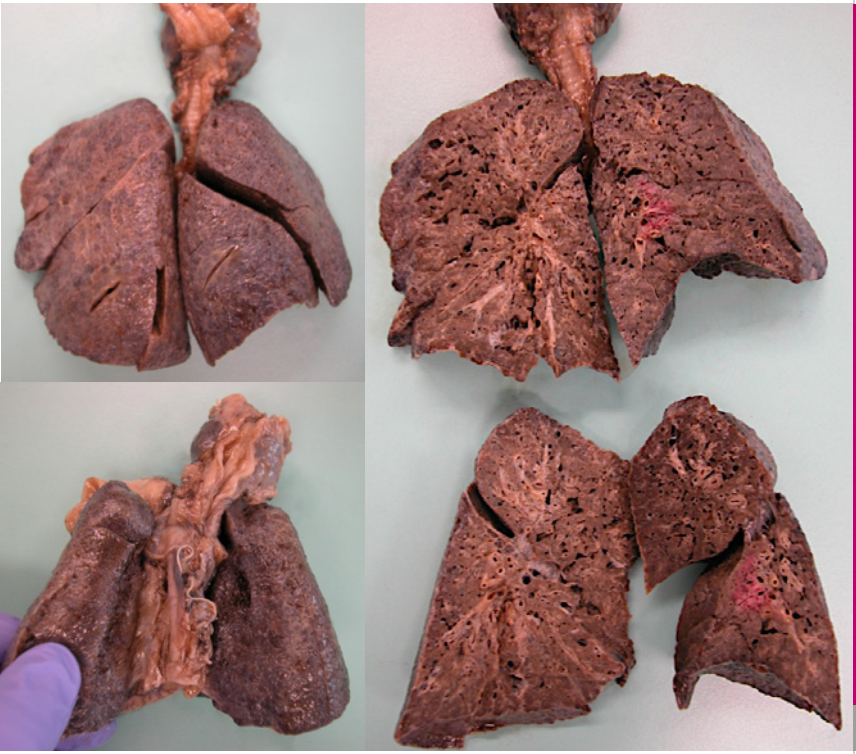

Fig. 4

Macroscopic autopsy findings: multiple cysts of different sizes are recognizable throughout the lung parenchyma (right lung: 44.2 g, left lung: 41.6 g).

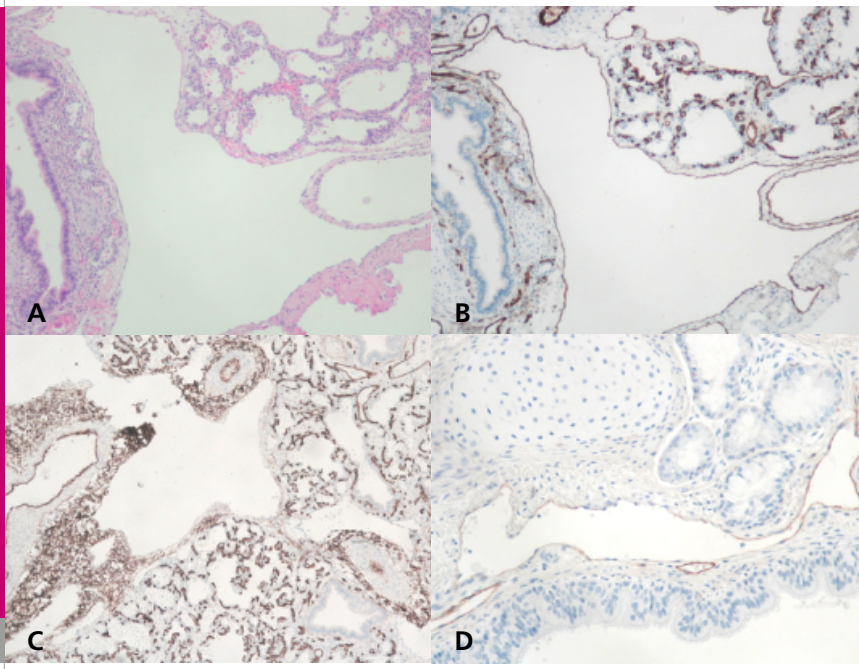

Fig. 5

Microscopic autopsy findings: enlarged subpleural, interlobular, perivascular and peribronchial lymphatic vessels (A: HE stain; B: CD31 stain: marker of endothelial cells; C: CD34 stain: marker of blood vessel endothelial cells; D: D2-40 stain: marker of lymphatic endothelial cells, differentiating lymphatic from other endothelial cells).

CPL is a rare lung malformation characterized by dilatation of the pulmonary lymphatic vessels. There are two pulmonary lymphatic sets, a superficial one, which drains the subpleural space and a deep one, which runs within the interlobular septa and along the bronchovascular bundles. Both drain to the hilum and then from the bronchiomediastinal lymph trunks into the large systemic lymphatic vessels (e.g., the thoracic duct) or directly into the brachiocephalic veins (1). Hypotheses of CPL pathogenesis include persistence of large lymphatic fetal channels (normal regression usually occurring from 9 to 16 weeks of gestation) or mechanical obstruction of lymphatic channels (2).

In 1970, Noonan et al. suggested the following classification (3): 1) CPL in the context of generalized lymphangiectasia; 2) CPL secondary to pulmonary venous hypertension or obstruction associated with cardiovascular anomalies; 3) CPL as a primary developmental defect of pulmonary lymphatic vessels.

The precise incidence of CPL is unknown. However, in autopsy studies of babies who were stillborn or died in the first hours of life, CPL was found in 0.5 – 1% (1, 4). Males are more commonly affected than females, and familial forms and correlations with genetic syndromes (i.e., Noonan, Down or Fryns syndrome) have been described (5). Given the negative family history, absence of congenital heart disease and the histological findings, our case corresponds to CPL Noonan group 3.

The major differential diagnoses of CPL are pulmonary interstitial emphysema (PIE) and diffuse pulmonary lymphangiomatosis (DPL) (6, 7). PIE is an accumulation of air in the interstitial space and usually appears secondary to volu-/barotrauma. DPL is a developmental abnormality with an increased number of complex anastomosing lymphatics. It is characterized by multiple lymphangiomas with diffuse proliferation and increase of the numbers of lymphatic vessels; in contrast, in CPL, the number of lymphatics is not increased.

The diagnosis of CPL may be suspected based on the clinical presentation, as well as the presence of interstitial reticulo-nodular markings and hyperinflation on chest X-ray. Pleural effusions can also occur; in fact, some patients may have a prenatal history of polyhydramnios, non-immune hydrops and bilateral pleural effusions. On CT scan, diffuse thickening of the interstitium and the interlobular septa can be observed. However, clinical signs and symptoms, as well as radiological findings are non-specific (1), and diagnosis can only be made by histological examination (7).

In liveborn infants, CPL may present immediately after birth - as in our patient - with severe respiratory distress, tachypnea and cyanosis; the mortality rate of such cases of CPL has historically been reported to be close to 100% (4). More recently, survival has been reported for babies with CPL when hydrops and/

or pleural effusion were known antenatally and an agressive treatment was adopted, including in utero drainage of pleural effusions and amnioreduction, as well as aggressive postnatal intensive care (7 – 9). In contrast, patients with CPL who become symptomatic after weeks or months with persistent tachypnea, cough and wheezing appear to have a significantly better prognosis (4, 8, 11).

In conclusion, we report a newborn infant who presented with acute respiratory distress due to CPL. Despite maximum intensive care, the infant died 4 hours after birth. When presenting in the neonatal period, CPL severely compromises neonatal adaptation and is usually fatal.

REFERENCES

1. Esther CR Jr, Barker PM. Pulmonary lymphangiectasia: diagnosis and clinical course. Pediatr Pulmonol 2004;38:308 – 813 *(Abstract)*

2. Xiao ZY, Tao Y, Tang XY, Chen GJ, Guo L. Congenital pulmonary lymphangiectasis. World J Pediatr 2009;5:68 – 70 *(Abstract)*

3. Noonan JA, Walters LR, Reeves JT. Congenital pulmonary lymphangiectasis. Am J Dis Child 1970;120:314 – 319 (no abstract available)

4. Bouchard S, Di Lorenzo M, Youssef S, Simard P, Lapierre JP. Pulmonary lymphangiectasia revisited. J Pediatr Surg 2000;35:796 – 800 *(Abstract)*

5. Scott-Emuakpor AB, Warren ST, Kapur S, Quiachon EB, Higgins JV. Familial occurrence of congenital pulmonary lymphangiectasis. Genetic implications. Am J Dis Child 1981;135:532 – 534 *(Abstract)*

6. Yamada S, Hisaoka M, Hamada T, Araki S, Shiraishi M. Congenital pulmonary lymphangiectasis: report of an autopsy case masquerading as pulmonary interstitial emphysema. Pathol Res Pract 2010;206:522 – 526 *(Abstract)*

7. Yamada S, Hisaoka M, Hamada T, Araki S, Shiraishi M. Congenital pulmonary lymphangiectasis: report of an autopsy case masquerading as pulmonary interstitial emphysema. Pathol Res Pract 2010;206:522 – 526 *(Abstract)*

8. Laje P, Wilson RD, Guttenberg M, Liechty KW. Survival in primary congenital pulmonary lymphangiectasia with hydrops fetalis. Fetal Diagn Ther 2008;24:225 – 229 *(Abstract)*

9. Mettauer N, Agrawal S, Pierce C, Ashworth M, Petros A. Outcome of children with pulmonary lymphangiectasis. Pediatr Pulmonol 2009;44:351 – 357 *(Abstract)*

10. Bellini C, Mazzella M, Arioni C, Campisi C, Taddei G, Tomà P, Boccardo F, Hennekam RC, Serra G. Hennekam syndrome presenting as nonimmune hydrops fetalis, congenital chylothorax, and congenital pulmonary lymphangiectasia. Am J Med Genet A 2003;120A:92 – 96 *(Abstract)*

11. Barker PM, Esther CR Jr, Fordham LA, Maygarden SJ, Funkhouser WK. Primary pulmonary lymphangiectasia in infancy and childhood. Eur Resp J 2004;24:413 – 419 *(Abstract)*

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