ALVEOLAR CAPILLARY DYSPLASIA WITH MISALIGNMENT OF THE PULMONARY VEINS (ACD/MPV) AND PULMONARY INTERSTITIAL GLYCOGENOSIS (PIG): A FATAL OUTCOME IN A TERM INFANT

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Alveolar capillary dysplasia with misalignment of the pulmonary veins (ACD/MPV) and pulmonary interstitial glycogenosis (PIG): A fatal outcome in a term infant

Introduction

ACD/MPV is a rare disorder and characterized by respiratory distress syndrome with cyanosis caused by a persistent pulmonary hypertension of the newborn (PPHN). PIG is a rare, usually non-lethal form of interstitial lung disease in newborns. It is characterized by an accumulation of glycogen in interstitial cells. The combination of ACD/MPV and PIG is extremely rare and often leads to severe respiratory problems in the newborn.

Case

- Term infant, 39 3/7 weeks of gestation, with unremarkable pregnancy checks
- Caesarean section due to pathological doppler in the late pregnancy
- Admission to neonatology due to hypoglycemia and primary respiratory distress syndrome required oxygen and noninvasive ventilation with a maximum oxygen requirement up to FiO2 of 0.6
- Due to progressive impairment of oxygenation, ventilation and echocardiographic suggestion of an anomalous pulmonary venous return a tansfer to the Children's University Hospital Zurich was made
- Thoracic CT scan: evidence of a pneumopathy and pronounced PHT component
- Respiratory decompensation and persistent oxygenation disorder → intubation, inhalative nitric oxide, catecholamines and installation of a veno-arterial extracorporeal membrane oxygenation (VA-ECMO)
- Lung biopsy: ACD/MPV, additional PIG
- Unsuccessful ECMO weaning → Redirection of care was initiated and the boy passed away on DOL 20
- Genetic: Detection of a pathogenic FOXF1 variant

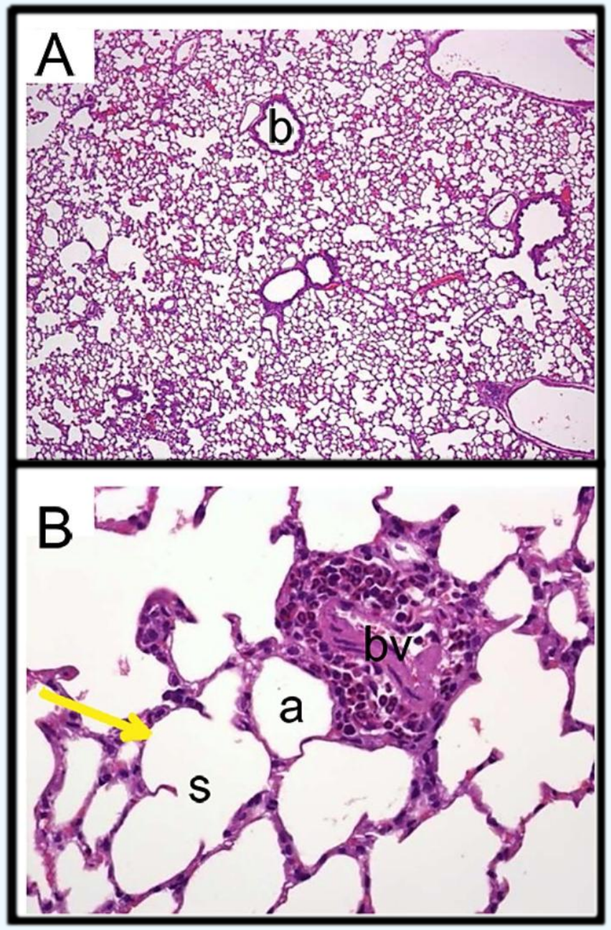

Figure 1: Lung histology of non pathological naive rat lung (after HE)
(A) Naive rat lung showing a normal architecture (100x magnification), (b) indicates normal bronchioles.
(B) Naive rat lung with alveolar sacs (s), expanded and non-filled alveoli (a), thin septa (arrow), and blood vessels (bv), (400x magnification).

Campos-Martorell, Mireia; Hernández-Guillamón, Mar; Rosell, Anna; Gomis, Javier; Salat, David; García-Bonilla, Lidia; et al. (2015). Representative images of lung histology after HE stain.. PLOS ONE. Figure. https://doi.org/10.1371/journal.pone.0099169.g004.

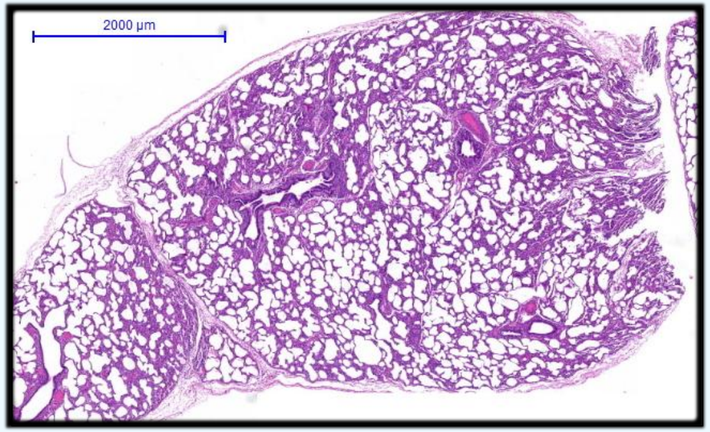

Figure 2: Lung histology of the reported case
Lung tissue with enlarged, rounded, simplified airspaces and patchy widening of alveolar septa (HE, overview).

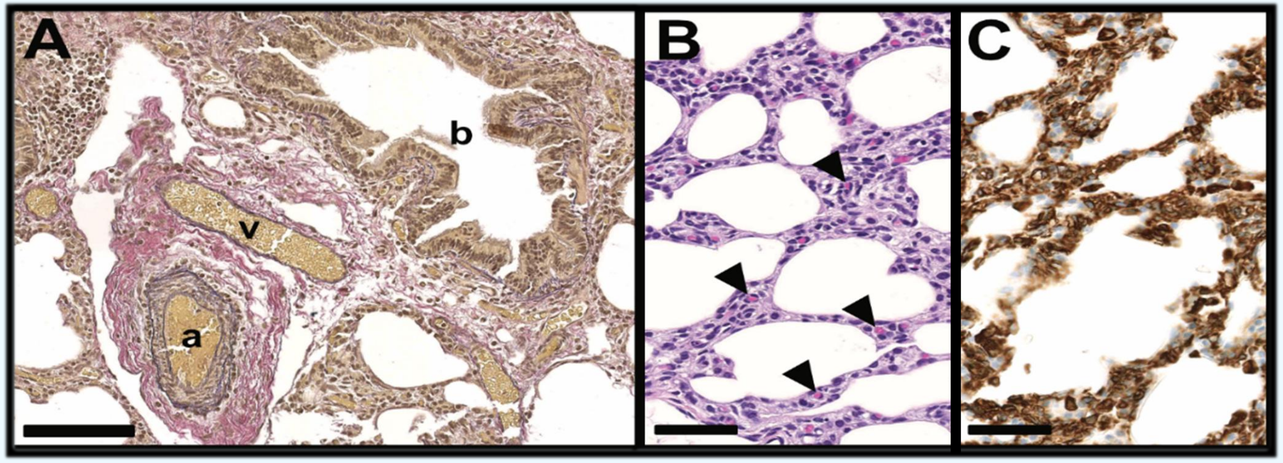

Figure 3: Lung histology of the reported case
(A) Misalignment of the pulmonary vein (v), which is directly adjacent to the pulmonary artery (a) and the bronchiole (b) (*EVG, scale bar = 100 µm*).
(B) Thickened alveolar septa with reduced number of alveolar capillaries (arrowheads) located centrally in the interstitium and not in the alveolar lining (histological feature of ACD/MPV) (*HE, scale bar = 50 µm*).
(C) Immature interstitial cells with immunopositivity for vimentin (histological feature of PIG) (*scale bar = 50 µm*).

Discussion

ACD/MPV (incidence approx. 1:100.000) especially in combination with PIG (incidence approx. <1:1 000.000) is a rare disorder and characterized by respiratory distress syndrome with cyanosis caused by a PPHN.
Usually, term infants with normal birth weights are affected within the first 24 hours of life. The mortality of ACD/MPV is almost 100%. It results from structural defects of the alveolar-capillary unit, usually leads to severe respiratory insufficiency and is diagnosed post-mortem. It is often associated with mutation in the FOXF1 gene encoding a transcription factor that plays a central role in the embryonic development of the pulmonary mesenchyme. Gold standard is currently the histological examination of the lungs. There are no curative therapeutic approaches except for an extremely rare lung transplantation. Treatment is mainly supportive, focusing on oxygenation, ventilation and nutrition. More than 80% of the affected patients also have additional malformations involving the heart, gastrointestinal, genitourinary and musculoskeletal systems.

Conclusion

- Consider pneumopathy syndromes in cases of neonatal early, severe pulmonary hypertension that does not respond to iNO, surfactant or ventilation in term infants.

- Main differential diagnosis of ACD/MPV and PIG are congenital lung malformations (such as CPAM, pulmonary sequestration), congenital heart defects (e.g. TGA, hypoplastic left heart syndrome), surfactant deficiency syndrome (e.g. mutations in SP-B, SP-c, ABCA3), metabolic or neuromuscular diseases (e.g. myopathies, central hypoventilation).

- A multidisciplinary consultation with neonatologists, pulmonologists, radiologists and pathologists is essential for early diagnosis, optimal care and parent`s counseling.

Authors & Affiliation

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