

Alveolar Capillary Dysplasia with Misalignment of Pulmonary Veins: An Autopsy Case Report

CLINICAL HISTORY

This is the case of a 13-day-old female infant delivered at 34 2/7 weeks to a 38-year-old G1P0 mother with spontaneous rupture of membranes, via cesarean section on 2/26. Prenatally, the infant was diagnosed with an omphalocele and a 17q12 duplication encompassing the HNF1B gene; the karyotype was normal female.

At birth, the Apgar scores were 8 and 8 at 1 and 5 minutes respectively; her weight was 2620 grams. Continuous positive airway pressure was started at 4 hours of life due to cyanosis, increased work of breathing, and poor tracing on pulse oximetry. She experienced pulmonary failure and coded on 2/27 with desaturations in the low 60s with shunting, requiring extra corporeal membrane oxygenation (ECMO) cannulation; decannulation was performed on 3/7. On 3/8 she was diagnosed with pulmonary hypertension via echocardiogram and was consented to receive treprostinil (Remodulin) therapy on 3/9; she received prostaglandin and dopamine infusions as adjunctive therapies. Despite prostaglandin therapy a closed PDA was identified on echocardiogram on 3/10.

Over the course of the hospital stay, she received multiple units of fresh frozen plasma, platelets, and red blood cells. Overall, she had multiple desaturation events with several ventilator methods tried without success. On 3/11 the family decided to withdraw care and the infant was pronounced deceased at 16:14. The family requested a limited autopsy (in vitro exploration and removal of lungs only) that was performed on 3/12.

GROSS AUTOPSY FINDINGS

The external exam reveals multiple signs of therapeutic intervention and a firm, brown umbilical stump measuring 8.5 cm in length and 1.5 cm in diameter at its insertion to the abdominal wall.

The left lung weighs 61 g and shows an incomplete fissure while the right lung weighs 69 g and appears to be unilobular. There are 2 cc of bilateral serous pleural effusions.

The peritoneal cavity contains 6 cc of hemorrhagic fluid. A portion of mesentery is noted entering the umbilicus and extending up the midline to the liver.

Attached to the mesentery are loops of large and small bowel. The right colon and appendix are located in the left upper quadrant. The remainder of the colon is present in the left half of the abdomen. The large bowel appears to loop and enter/exit the retroperitoneum multiple times. The small bowel is present in the right half of the abdomen.



Figure 1. Heavy (consistent with 44+ weeks) and abnormally lobulated lungs. Unilobular right lung (a) and bilobed left lung with incomplete fissure (b).

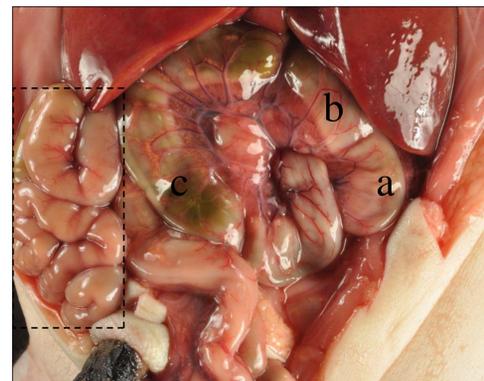


Figure 2. Intestinal malrotation. Cecum (a), ascending colon (b), descending colon (c), and small bowel (dashed box).

MICROSCOPIC FINDINGS

The lung parenchyma is premature for 34-36 weeks gestation and is more consistent with the beginning of the sacular stage of pulmonary development. The alveoli are simplified with thickened septa containing centralized capillaries. The bronchovascular sheath contains thickened muscular arteries, bronchioles and veins/venules. Venous structures are absent from the intralobular septa.

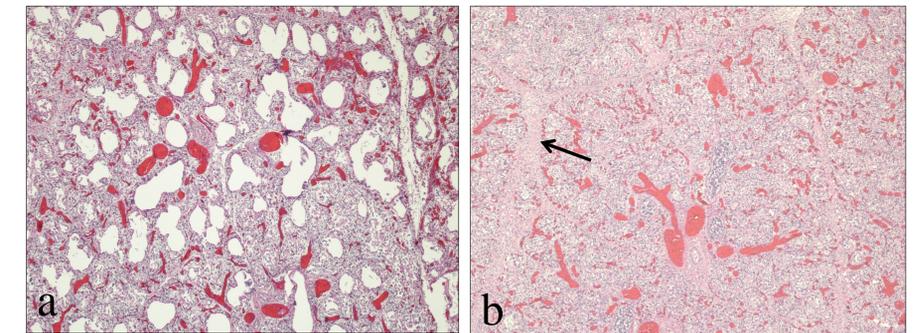


Figure 3. Abnormal lung parenchyma shows decreased number of air spaces with thickened intra-alveolar septa (a), and lack of venous structures within the intralobular septa (b, arrow)

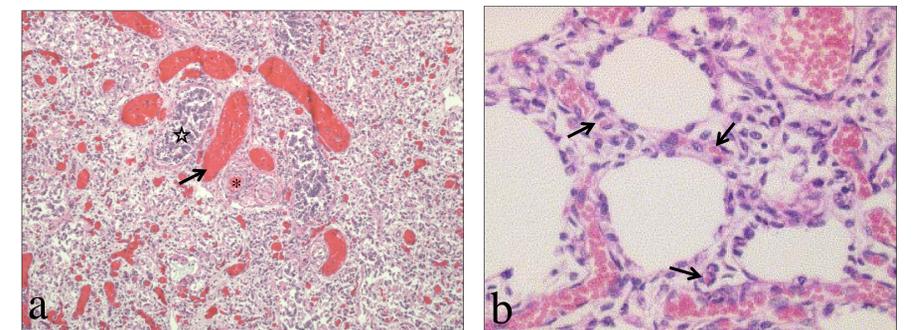


Figure 4. Abnormal placement of veins/venules (a, arrow) within the bronchovascular sheath alongside thickened muscular arteries (a, asterisk) and bronchioles (a, star). Thickened intra-alveolar septa with centralized capillaries (b, arrows).

FINAL AUTOPSY DIAGNOSIS AND DISCUSSION

The features of persistent pulmonary hypertension, veins/venules in the bronchovascular sheath, simplified alveoli, thickened septa with centralized capillaries, and the presence of thickened muscular arteries, are consistent with alveolar capillary dysplasia (ACD) with misalignment of the pulmonary veins. This is a very rare, primary developmental lung disorder with a mortality rate that approaches 100%. Between 60-80% of patients with ACD have extra-pulmonary manifestations including, intestinal malrotation, congenital heart defects, and TE fistulas. Most cases are deemed to be sporadic, however, a familial predisposition has been linked to deletions of the FOX transcription factor gene cluster (FOXF1, FOXC2, FOXL1) and point mutations of the FOXF1 gene. A diagnosis of ACD should be considered in any newborn presenting with hypoxemia and idiopathic pulmonary hypertension.