

# Alveolar Capillary Dysplasia Associated with Omphalocele

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## Abstract

Alveolar capillary dysplasia (ACD) is a rare and universally fatal form of persistent pulmonary hypertension of the newborn (PPHN). We report a case of a newborn male baby with a moderate sized omphalocele who developed respiratory distress 10 hours after birth. He deteriorated and succumbed shortly afterwards despite maximal ventilatory support and inhaled nitric oxide. ACD was diagnosed at postmortem examination, and the association of ACD with omphalocele and gut malrotation has not been reported. We suggest including ACD in the differential diagnosis of refractory PPHN in a newborn even with the presence of other risk factors for respiratory failure.

## Key words

Alveolar capillary dysplasia; Omphalocele; Pulmonary hypertension

## Introduction

Alveolar capillary dysplasia (ACD) is a rare and lethal congenital lung disorder characterised by deficient alveolar capillaries and anomalous veins within the bronchoarterial bundles. Affected infants present with severe pulmonary hypertension unresponsive to all current modalities of treatment. There were associated anomalies in half of the reported cases with gastrointestinal, genitourinary, cardiovascular, orthopaedic and respiratory malformations.<sup>1</sup> We report a patient with omphalocele with persistent pulmonary hypertension of the newborn (PPHN), whose atypical clinical course became explainable once the diagnosis of ACD had been established at autopsy. More than 140 cases of ACD have been described since its first

description in 1981 by Janney et al,<sup>2</sup> and there is no survivor to date. An association of ACD with omphalocele and gut malrotation has not been reported in the English literature before.

## Case Report

A male newborn was delivered to a healthy, 33-year-old *para* 2 mother at 38 weeks of gestation. The mother had her first child delivered at term and was healthy. For this pregnancy, fetal omphalocele was diagnosed at 13 weeks of gestation by ultrasound. Serial ultrasound examinations till 33 weeks of gestation showed isolated omphalocele containing intestines only. The pregnancy was otherwise uncomplicated. Elective Caesarean section was performed at 38 weeks, and a baby boy of birth weight 3610 g was born. Apgar scores were 8 and 9 at the first and fifth minutes respectively. Liquor was clear. Examination showed a moderate sized omphalocele. There were no other dysmorphic features. The infant was admitted to our neonatal intensive care unit. Upon admission, there was only mild respiratory distress requiring supplemental oxygen of 25% via nasal cannula to maintain an oxygen saturation above 95%. Blood gas was normal, and chest radiograph showed clear lung fields. Surgical repair was planned on the next day.

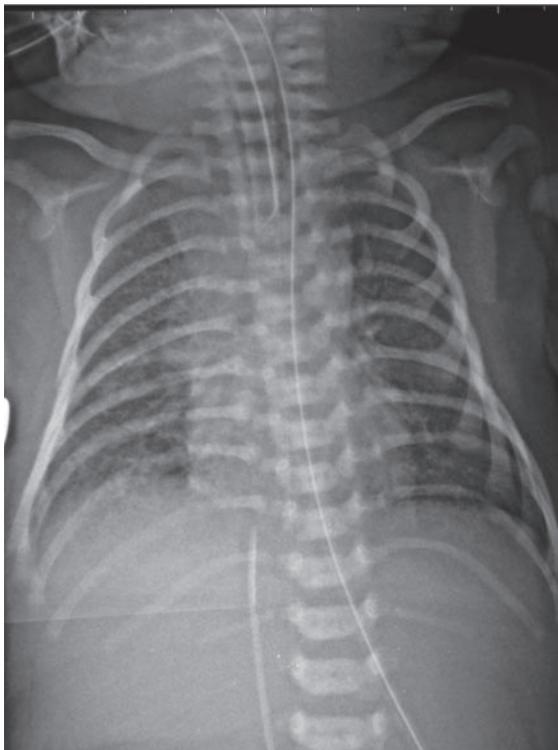
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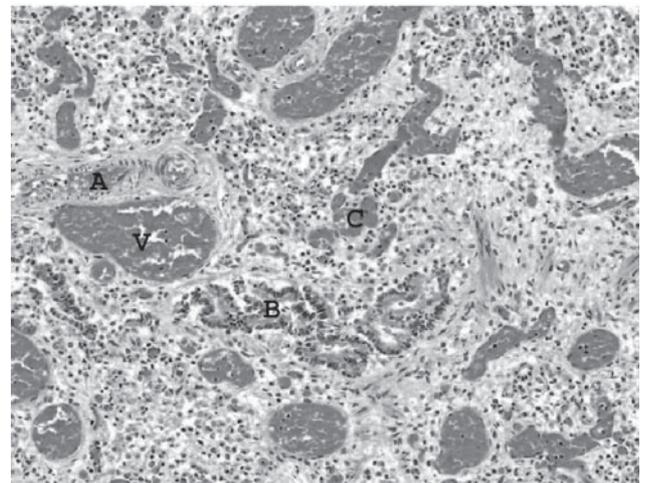
At around 10 hours of life, the infant developed rapid and persistent oxygen desaturation that did not respond to increased oxygen supplement. He was immediately intubated and mechanical ventilation started. Clinical and radiological examination excluded air-leak or pulmonary collapse (Figure 1). There was no setting for sepsis. Inspection of the omphalocele did not show signs of strangulation, and the mass was soft and did not show evidence of tension. Differential oxygenation became apparent, with pre- and post-ductal saturation difference of more than 30%. Two-dimensional echocardiography demonstrated a dilated right atrium and ventricle, right-to-left shunt through a large patent ductus arteriosus and foramen ovale indicating suprasystemic pulmonary blood pressure. There was no other structural heart lesion. A diagnosis of PPHN was made. Therapy with high frequency ventilation, inhaled nitric oxide up to 40 ppm and inotropic support were initiated, which resulted in transient improvement in both pre- and post-ductal oxygen saturations to barely above 90%. The infant deteriorated



**Figure 1** Chest radiograph shows bilateral interstitial lung haziness and reduced lung volumes despite high ventilatory pressures.

again 2 to 3 hours afterwards despite maximal support. Chest radiograph showed bilateral lung haziness with no pneumothorax. In view of refractoriness of the PPHN, treatment with sildenafil, intravenous magnesium sulphate and surfactant replacement therapy were tried without success. The child's condition further deteriorated, with the development of hypotension, profound hypoxemia and hypercapnia.

After discussing with the parents and considering the critical clinical condition and futility of treatment, redirection of goal of therapy to comfort care was adopted and the baby died at around 33 hours of life. An autopsy was performed. There was malrotation and herniation of the distal ileum, caecum, appendix and proximal ascending colon into the omphalocele. There was no evidence of gangrene. The airways contained small amount of yellowish powdery material. The left lung weighed 41 g, the right 48 g. These are about two times heavier than the normal weight of a newborn lung. Grossly, the lung appeared "expanded" but were rubbery and airless. Cut surfaces showed evidence of congestion and some haemorrhagic patches with evidence of early consolidation changes. Histological examination (Figure 2) of the lung parenchyma showed malposition of the pulmonary veins, maldevelopment of the alveolar lobules with small simple rounded air spaces and fewer dilated capillaries in the septal wall. There was increased muscularisation of pulmonary arterioles. These confirmed a diagnosis of congenital ACD.



**Figure 2** Lung tissue histology shows abnormally located veins adjacent to arteries and bronchioles. Dilated capillaries are not in contact with the alveolar epithelium. (A=Arteries, V=Veins, B=Bronchioles, C=Alveolar septa with dilated capillaries)

## Discussion

This is the first case report of an association of ACD with omphalocele and gut malrotation in the English literature. This is the third case being reported in our locality.<sup>2,3</sup> After an apparently uneventful period of 10 hours after delivery with minimal oxygen supplement and respiratory distress, our patient rapidly developed signs of severe PPHN. There was no perinatal risk factor except for the anterior abdominal wall defect. The degree of PPHN despite maximal medical therapy raised the suspicion to an additional congenital pulmonary disease. Postmortem lung biopsy confirmed the diagnosis of ACD.

ACD is an extremely rare developmental abnormality of the lung characterised by PPHN. It was first described by Janney et al in 1981 and is generally considered a fatal condition. The exact incidence of the disease is unclear. More than 140 cases have been described in the English literature,<sup>4</sup> the largest series of 23 cases being reported by Sen et al.<sup>5</sup>

In the vast majority of cases, the patients are full-term infants of appropriate size with normal Apgar scores.<sup>6</sup> The symptoms and time of presentation are related to the extent and distribution of capillary dysplasia and the developmental anomalies of distal airspaces. Patients usually develop symptoms of respiratory distress and cyanosis secondary to severe PPHN within the first 24 hours of life. Rarely presentations as late as 7 weeks and 7 months have been reported.<sup>7,8</sup> Various treatments to reduce pulmonary vascular resistance including inhaled nitric oxide, prostaglandins and cardiorespiratory support with extra-corporeal membrane oxygenation showed only a temporary or no effect, and would not alter the fatal course of this disease.<sup>9,10</sup>

Initial chest radiographs are often reported to be unremarkable as in our case or to show a mild haziness pattern. In one reported series, it showed a 50% pneumothorax rate (either unilateral or bilateral) at the time of initial clinical deterioration.<sup>6</sup> Whether this phenomenon is due to an inherent propensity for pneumothoraces in ACD patients or as a result of aggressive airway management remains unclear.

There are reports of clinical suspicions of the condition by computed tomography thorax<sup>11</sup> and cardiac catheterisation.<sup>12</sup> Definitive diagnosis relies on a detailed pathological examination at autopsy or lung biopsy. The typical histological findings are a remarkable paucity of capillaries localised centrally within thickened alveolar

septa showing a lack of contact with immature alveolar epithelium, and medial thickening of the small pulmonary arteries and muscularisation of the smallest intra-acinar arterioles. Anomalous distended veins accompany the bronchi and pulmonary arteries instead of being in the normal position in the periphery of the lobule may be present, possibly representing bronchial vein tributaries. In some cases, dilated lymphatics can be detected.<sup>13,14</sup> The pathophysiology of PPHN in ACD is unclear. It may include a reduced number of pulmonary capillary vessels and hypoxic pulmonary vasoconstriction caused by an abnormal blood-airspace barrier and altered pulmonary vascular reactivity.

The aetiology of ACD is unknown. There is no sex predilection,<sup>1</sup> and most cases are sporadic. However, the occurrence of ACD in siblings has been reported, suggesting an autosomal recessive inheritance in some cases.<sup>5,15</sup> Rarely, ABCA3 gene mutation (surfactant-related gene) has been reported to be associated with ACD.<sup>16</sup>

A review of published cases of ACD showed that approximately 52% are associated with other congenital anomalies.<sup>1</sup> Of these anomalies, 40% are gastrointestinal, 32% genitourinary, 16% cardiovascular, 8% orthopedic and 4% respiratory. Previously published gastrointestinal abnormalities include malrotation, duodenal atresia, anorectal anomaly, Hirschsprung's disease, absent gallbladder, annular pancreas, pyloric stenosis, oesophageal atresia/tracheo-oesophageal fistula and asplenia.<sup>17</sup> There is also a case of omphalocele and posterior urethral valve associated with ACD.<sup>6</sup> Our case is the first to show an association between omphalocele, gut malrotation and ACD.

A triad consisting of an association of non-lethal congenital malformations, a honeymoon period, and subsequent unremitting hypoxemia, has been proposed to alert neonatal clinicians to ACD.<sup>2</sup> In all children with refractory PPHN who fail conventional therapy, with exclusion of other causes such as meconium aspiration syndrome, fetal asphyxia, surfactant deficiency and polycythemia etc. ACD should be considered and lung biopsy is advocated. Michalsky et al suggested an algorithm for infants with atypical PPHN who are suspected of having ACD.<sup>6</sup> Considering the progression of the disease, with ultimate death in all known infants with ACD, an option could be lung or lung/heart transplantation. If such option is not available, early introduction of compassionate management should be considered, avoiding costly and invasive treatments such as ECMO which can only delay an inevitably fatal outcome.

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