

## Case Reports

### Congenital Acinar Dysplasia (CAD): Case Report of an Extremely Rare Cause of Pulmonary Hypoplasia

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#### Introduction

The primary function of lung is to accomplish exchange of oxygen & carbon dioxide to accommodate the need of aerobic cellular respiration. To accomplish this a large thin alveolar capillary membrane is required.<sup>1</sup> Lung development takes place in 5 (five) phases like 1. Embryonic phase 2. Pseudoglandular phase 3. Canalicular phase 4. Saccular phase and 5. Alveolar phase.<sup>1</sup>

Congenital Acinar Dysplasia (CAD), an extremely rare form of pulmonary hypoplasia, is a lethal condition characterized by arrest of lung morphogenesis at the end of Pseudoglandular phase leading to non development of acinar structure distal to terminal bronchiole resulting in absence of gas exchange between lungs and its circulation. Treatment of this condition is limited to supportive care. We are going to describe a case of lethal pulmonary hypoplasia caused by CAD.

#### Case Report

A 2.44 kg female baby at 36 weeks gestation was delivered by elective repeat lower segment cesarean section, the product of a consanguineous marriage. Mother was a 30 yrs old Saudi woman G<sub>4</sub>P<sub>3</sub>A<sub>0</sub>L<sub>2</sub> with a history significant for a previous neonatal demise despite aggressive respiratory support including surfactant replacement therapy. Maternal medical and labor history were unremarkable. The infant was non vigorous at birth with a nuchal cord noted, and required positive pressure ventilation. APGAR score was 6 & 8 at 1 & 5 minutes respectively. Cord blood gas was P<sup>H</sup> 7.27, PCO<sub>2</sub> 41.6, BE -7, HCO<sub>3</sub> 17.2. Initial physical examination demonstrated an appropriate gestational age infant with no distress, and was admitted to the well baby nursery.

At 3 hours of age, the infant was noted to be tachypneic and required oxygen prompting admission to NICU. Capillary blood gas from baby showed P<sup>H</sup> 7.29, PCO<sub>2</sub> 37.3, BE -7.6, HCO<sub>3</sub> 17.7. CXR showed bilateral haziness.

The infant was intubated for progressive hypoxemic respiratory failure and responded to one dose of surfactant, leading to extubation within 24 hours. The respiratory status deteriorated within 48 hours with CXR (Fig. 1) demonstrating bilateral opacities leading to reintubation and mechanical ventilation with additional surfactant administration with partial and



Fig.-1: CXR of Congenital Acinar Dysplasia

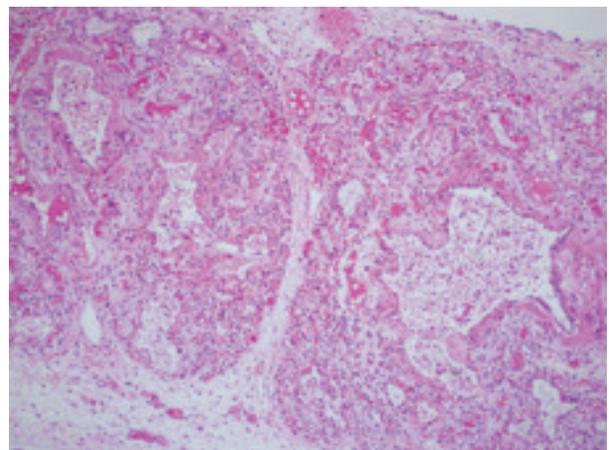


Fig.-2. Histopathological picture of Congenital Acinar Dysplasia

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transient responses to each dose. A sepsis work up was performed and broad spectrum antibiotics were initiated. Echocardiogram showed moderate size PDA with no evidence of PPHN.

She was subsequently switched to high frequency oscillatory ventilator on day of life 12 for worsening respiratory failure and required bilateral chest tube placement following the development of

pneumomediastinum, pneumopericardium, pneumothorax, and subcutaneous emphysema over the neck and upper chest.

She died following an acute respiratory arrest on the following day unresponsive to resuscitation.

Bilateral lung biopsy which was taken after the death of the baby showed features consistent with CAD. (Fig. 2&3)



مستشفى الملك فيصل التخصصي  
ومركز الأبحاث  
King Faisal Specialist Hospital  
and Research Center  
KFSHRC\_REF

Referral MRN: KFSH MRN:90228772  
Requisition #: Accession #:SP-12-006669  
Patient Name: Saeed, Eida Salem  
Sex: Female Age: 3 months DOB: 25-May-12  
Referring Client: KFSHRC Reference Lab  
Client Address: P.O. Box 3354 MBC#10  
Phone #: (Tel): (966-1) 442-4230 City: Riyadh 11211  
Results To:

**Surgical Pathology Report**

Case Number: SP-12-006669 Collected Date/Time: 09-Jul-12 12:00:00  
Responsible Pathologist: Al-Dayel, Fouad Hassan Received Date/Time: 09-Jul-12 12:59:00

**Patient History**

Referral from Abha General Hospital-Assir Region, MRN 86721. A 4-day-old female baby delivered by CS, looks near term (37 weeks gestation), observed to have tachypnea and distress three hours after delivery. Family history of one baby who died one year back after six days of life, full term with possibility of surfactant protein B deficiency.

**Specimen Submitted**

1. RIGHT LUNG BIOPSY
2. LEFT LUNG BIOPSY

**Gross Description**

1. The specimen is received in formalin labeled biopsy of right lung. It consists of two fragmented pieces of wedge like pale tan soft tissue measuring 1 x 1 x 0.3 cm and 1.3 x 1 x 0.3 cm. Bisected and entirely submitted in one cassette.
2. The specimen is received in formalin labeled biopsy of left lung. It consists of two fragmented pieces of pale tan wedge like soft tissue measuring 0.5 x 0.4 x 0.3 cm and 1.1 x 0.8 x 0.4 cm. Bisected and entirely submitted in one cassette.

Date/Time: 10/07/2012 06:21

**Diagnosis**

- 1. RIGHT LUNG BIOPSY:**  
MORPHOLOGY IS CONSISTENT WITH ACINAR DYSPLASIA.
- 2. LEFT LUNG BIOPSY:**  
MORPHOLOGY IS CONSISTENT WITH ACINAR DYSPLASIA.

Al-Dayel, Fouad Hassan, Consultant  
(Electronically signed by)  
Verified: 08-AUG-2012 15:17  
FMQ

Dr. Mizan  
Specialist NICU  
Code No. 154 & P. 157

Fig.3: Histopathology report of Congenital Acinar Dysplasia

## Discussion

Congenital Acinar Dysplasia (CAD) is a lethal developmental disorder of the lung and a rare cause of primary pulmonary hypoplasia. Lung development begins early in human gestation (by day 25) and extends well into childhood. The primary goal of lung development is to create a large gas exchange area with a thin air-blood barrier. This is achieved by branching of the airways to form the conducting and proximal respiratory airways and by septation to subdivide the airspaces into alveoli. Development of lung takes place in 5 (five) stages, these are 1. Embryonic phase 2. Pseudoglandular phase 3. Canalicular phase 4. Saccular phase and 5. Alveolar phase.<sup>1,2</sup> The timing of these stages is not always fixed and considerable overlap may occur between stages.<sup>1</sup>

Embryonic phase begins with the development of lung bud on the ventral surface of the foregut just caudal to the laryngotracheal sulcus at 25 days of gestation and extends upto 7 weeks of gestation. The lung bud continues to grow by dividing in a dichotomous fashion giving rise to the conducting airways and five primordial lung lobes (two on the left and three on the right). The pseudoglandular phase extends from 7 to 16 weeks of gestation, resulting in completion of all 16 divisions of bronchi responsible for gas conduction. The canalicular phase extending from 16 to 28 weeks is responsible for transformation of pre-viable lung to the potentially viable lung that can exchange gas. Three major events take place during this stage are – a. appearance of acinus, b. epithelial differentiation with the development of potential air-blood barrier, and c. beginning of surfactant synthesis with type II cells.<sup>2</sup> *Acinus* is the gas exchange unit of the lung and encompasses a respiratory bronchiole and all of its associated alveolar ducts and alveoli. A terminal bronchiole with all of its associated acinar structures constitutes a *lobule*.<sup>1</sup>

The saccular stage encompasses the period of lung development from 28 weeks to term. The terminal sac or saccule is the distal airway structure that is elongating, branching and widening until alveolarization is completed, which is initiated from the terminal saccules by the appearance of septae in association with capillaries, elastin fibres, and collagen fibres.<sup>2</sup>

Alveoli begin to appear at about 32 weeks of gestation, most alveolar development occurs postterm. At the time of birth a term infant has 30% of adult number of alveoli.

The lung grows postnatally mainly by an increase in alveolar number, and by 4 years of age the adult number of alveoli a total of between 200 million and 600 million is formed. The subsequent increase of lung volume and surface area is due to increase in alveolar size.<sup>1-3</sup>

Factors which may delay or interfere with alveolarization are mechanical ventilation, antenatal and postnatal glucocorticoids, proinflammatory mediators, hyperoxia or hypoxia and poor nutrition. Whereas Vitamin A (retinoids) and thyroxine stimulate alveolarization.<sup>2</sup>

Pulmonary hypoplasia can result from primary defects in lung morphogenesis as well as from neurologic diseases associated with decreased fetal breathing movements, derangements of chest wall that restrict fetal breathing movements, renal disorders that compromise amniotic fluid volume and thereby restrict fetal breathing, or space occupying masses that restrict lung growth. Earlier the interference more severe is the pulmonary hypoplasia.<sup>1</sup>

In CAD lung development is arrested at the end of Pseudoglandular stage (16 week of gestation). As a result lung is developed upto the level of terminal bronchiole. No structure develops beyond this level. So baby will be delivered with hypoplastic lung with the absence of gas exchanging unit 'acinus', leading to ventilation failure and death.

Diagnosis of pulmonary hypoplasia can be made by (1) Lung to birth weight ratio of  $\leq 0.9\%$ , and (2) RAC (Radial alveoli count)  $\leq 4.1$ , which is defined as the number of alveoli cut by a line from the respiratory bronchiolar epithelium to the nearest connective tissue septum.<sup>6</sup>

The incidence of congenital pulmonary hypoplasia is 1 in 1000 live birth; this includes both primary and secondary pulmonary hypoplasia.<sup>4</sup> But the incidence of pulmonary hypoplasia due to CAD is unknown and seems to be under recognized, because of diagnostic difficulty. From 1986 to 2004 only seven cases have been reported with a definitive diagnosis of CAD. Of those, six were female, and the longest survivor lived for 2 months.<sup>5</sup> Of note our case is also a female baby. The etiology of CAD is not well understood. A genetic component seems likely, but a definite pattern is not apparent from the small number of documented cases.<sup>5</sup> From the cases reported so far it appears that females are more affected than males (9:1). So far 3 (three) male babies were reported to have this

form of pulmonary hypoplasia, one of them delivered in Alhada hospital Taif, K S A.<sup>8</sup> It also appears that acinar dysplasia has a tendency to recur in families in 40% of cases, suggesting an autosomal recessive pattern of inheritance. There is a case report of identical twins with acinar dysplasia.<sup>7</sup> CAD is diagnosed by exclusion of all other causes of pulmonary hypoplasia and a summation of clinical, imaging and histopathological findings such as in our case. Without autopsy this condition can be missed very easily because it can't be differentiated clinically from congenital alveolar dysplasia and alveolar capillary dysplasia. In both of these two conditions development of lung is arrested at the canalicular stage. In congenital alveolar dysplasia there is extreme retardation in alveolar development and in alveolar capillary dysplasia there is capillary misalignment and medial muscular thickening of the small pulmonary arterioles.<sup>5</sup> Congenital acinar dysplasia should also be differentiated from surfactant protein B deficiency (SP-B deficiency) and type-3 cystic adenomatoid malformation (CAM). Lamellar bodies are absent in infants with surfactant protein B deficiency. The presence of dysplastic lung tissue on histopathology and the presence of lamellar bodies in electron microscopy support the diagnosis of CAD and excludes the diagnosis of SP-B deficiency.<sup>8</sup> Congenital cystic adenomatoid malformation is due to an overgrowth of terminal bronchioles with cysts of various sizes and no development of normal alveoli. Cartilage is absent in type 3 CAM and it is a localized lesion and it compresses adjacent unaffected lung tissue while CAD causes generalized lung hypoplasia.<sup>8,9</sup>

### Conclusion

In conclusion hypoxemic respiratory failure in a newborn baby represents a diagnostic and therapeutic challenge. Rare causes of pulmonary hypoplasia including CAD should be considered in the neonate with respiratory failure not responsive to maximum medical therapy. An autopsy is essential to the diagnosis of these causes of hypoxemic respiratory failure.

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