Congenital Acinar Dysplasia: A Familial Cause of Severe Primary Lung Hypoplasia

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Abstract

Objectives: To report a Saudi family of consanguineous parents who had two daughters with familial congenital acinar dysplasia, who died shortly after birth of respiratory failure.

Case Presentation: A full-term female baby born to a 28-year-old mother via emergency Cesarean section. Antenatally, the mother was diagnosed with preeclampsia and severe oligohydramnios. The baby developed severe respiratory distress immediately after birth and required positive pressure ventilation in the operating room. Echocardiography revealed severe pulmonary hypertension with supra-systemic estimated pulmonary pressure. Despite all management measures, the baby continued to deteriorate with persistent respiratory failure. The diagnosis of CAD was confirmed by open lung biopsy at the age of two months. She passed away at the age of three months due to severe refractory respiratory failure. One year later, her mother delivered another baby girl with CAD who also died of respiratory failure at the age of two months.

Conclusions: CAD is a rare cause of lung hypoplasia. It mainly affects females and its etiology may be through autosomal recessive inheritance. The affected child usually dies of respiratory failure shortly after birth. It should be expected prenatally if there is absence of fetal breathing movements. Fetal monitoring and proper antenatal care may have a role in prevention of CAD.

Key words: Congenital acinar dysplasia, Consanguinity, Primary lung hypoplasia, Respiratory insufficiency.

Introduction

Congenital acinar dysplasia (CAD) is a rare disease with primary lung hypoplasia. Its incidence is unknown and possibly it is under-recognized. It is characterized by developmental arrest of lung growth at the pseudo-glandular embryonic stage(1). Although it runs in the family, there have been no identified genetic mutations. Due to the absence of the respiratory bronchioles, alveolar ducts, and alveoli are absent. Most patients die, early on, from refractory respiratory failure (1&2).

In this report, we present a Saudi family of consanguineous parents who had two daughters with familial CAD. Both daughters died a few months after bith of respiratory failure.

Case presentation

In December 2016, a Saudi 28-year-old mother delivered her first baby via emergency Cesarean section at Khamis Mushayt Maternity and Children Hospital. She had pre-eclampsia and severe oligohydramnios. She was a second-degree relative to her husband. A full-term female infant was born.

Immediately after birth, the baby developed severe respiratory distress and required positive pressure ventilation in the operating room, and received two doses of surfactant due to persistent oxygenation and ventilation issues, in addition to bilateral white-out lung shadows on the x-rays. Echocardiography revealed severe pulmonary hypertension with supra-systemic estimated pulmonary pressure. Broad spectrum antibiotics were started for the possibility of congenital bacterial pneumonia. A chest CT-scan was done and showed bilateral diffuse air-space disease with prominent air bronchograms (Figure 1).

At the age of 65 days, she was referred to King Abdullah Specialist Hospital, in Riyadh, where an open lung biopsy was done, which confirmed the diagnosis of congenital acinar dysplasia (CAD). No other congenital abnormalities were detected.

Despite all management measures, she continued to deteriorate with persistent respiratory failure and diffuse white-out lung zones. At the age of three months, she died due to severe refractory respiratory failure.

In February, 2018, the same mother underwent an emergency Caesarian section at the same hospital, as she had preeclampsia and severe oligohydramnios. She delivered another full-term female baby, which developed severe respiratory distress immediately after birth and was also diagnosed as CAD. The second baby was kept on chronic high-frequency ventilation and died at the age of two months.

The mother was advised to comply to start antenatal care early and fetal monitoring during her future pregnancies. Prevention and early management of oligohydramnios and any pregnancy-associated hypertensive diseases should be considered with pregnancy with fetal monitoring to exclude future occurrence of CAD to her next child.

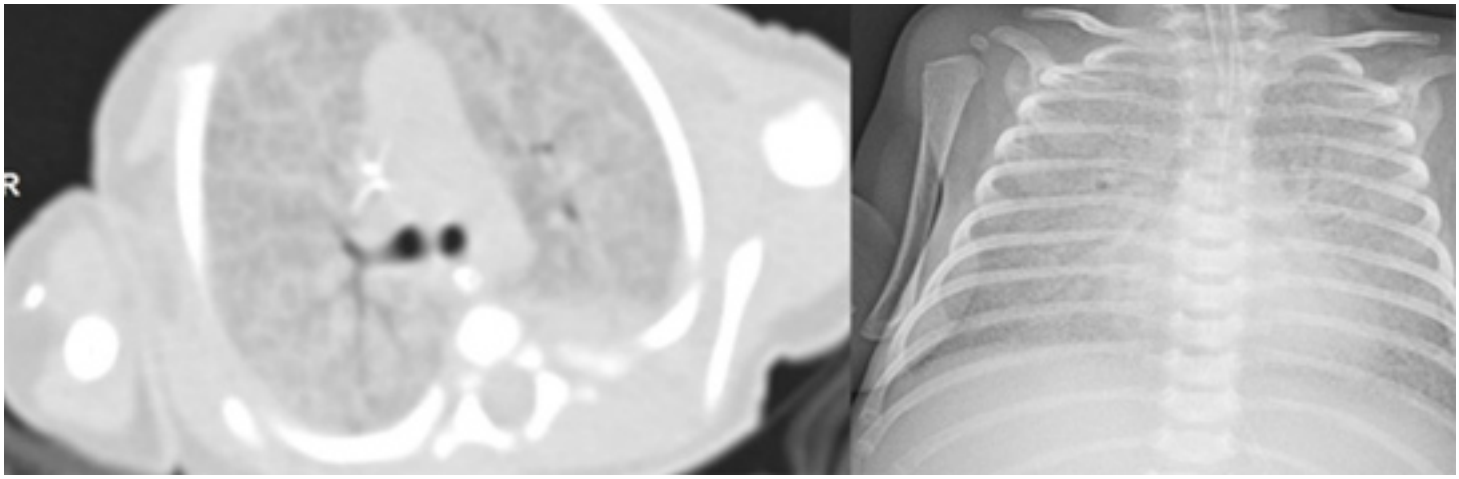

Figure-1: Chest CT-scan and plan x-ray are showing prominent air bronchograms with extensive bilateral air space disease

Discussion

CAD is characterized by the arrest of fetal lung development at the pseudo-glandular stage, and lack of functional gas exchange. It is a diagnosis of exclusion from other diffuse embryologic lung abnormalities with identical clinical presentations (3).

We reported two female babies, who had severe respiratory distress with pulmonary hypertension and died during their infancy due to respiratory insufficiency as a lethal complication of CAD. Their parents were second degree relatives and their mother had preeclampsia and severe oligohydramnios.

The association between oligohydramnios and lung hypoplasia with CAD was explained by Wu et al. (4), who stated that, structurally and biochemically, the fetal lungs may become immature for-gestational-age in mothers with oligohydramnios. Maturation arrest usually affects the peripheral segment of the acinus, which leads to low concentration of lung phospholipids and lack of epithelial tissue development. Kitterman et al. (5) noted that oligohydramnios may limit fetal lung growth and can lead to pulmonary hypoplasia. Severe oligohydramnios can also increase intrathoracic pressure and compression of abdominal contents elevates the diaphragm thus compressing the lungs. The lung fluid escapes through the larynx, thereby significantly decreasing the alveolar distention. Lakshminrusimha and Keszler (6) added that pulmonary hypertension is a prominent feature associated with lung hypoplasia.

DeBoer et al. (7) noted that about 90% of the cases are females and there is a genetic component in the etiology of CAD. Al-Senan et al. (2) stated that, based on the familial finding and since most reported cases were females, X-linked dominant type of inheritance is possible. Nevertheless, Langenstroer et al. (1) argued that, although it is likely that there is an inherited component of this condition, X-linked dominant type of inheritance is unlikely given the early fatality of cases.

However, Moerman et al. (8) reported a family of two daughters who were diagnosed with CAD and suggested an autosomal-recessive mode of inheritance of a gene associated with lung parenchymal development. Therefore, it might be possible to suggest that the two female siblings to consanguineous parents in our report reflect an autosomal recessive inheritance of CAD.

Although there are no definitive prenatal diagnostic tests for CAD (3), the absence of fetal breathing movements is considered the most accurate prenatal predictor of pulmonary hypoplasia, especially in pregnancies complicated by oligohydramnios (9). Moreover, when the radial alveoli count is <4.1 or a lung-to-birth weight ratio of <1.2%, and if the ratio is <0.9%, pulmonary hypoplasia is very likely(10)

To the best of our knowledge, this is the first report of two CAD cases within a Saudi family.

In conclusion, CAD is a rare cause for lung hypoplasia, characterized by developmental arrest of lung growth at the pseudo-glandular embryonic stage. It mainly affects females and its etiology may be through autosomal recessive inheritance. The affected child usually dies of respiratory failure shortly after birth. It should be expected prenatally if there is absence of fetal breathing movements. Fetal monitoring and proper antenatal care may have a role in prevention of CAD.

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