Alveolar Capillary Dysplasia With Anorectal Anomaly

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Alveolar capillary dysplasia (ACD) is an uncommon cause of irreversible persistent pulmonary hypertension in full-term newborn. In ACD there is a failure of formation of air - blood barrier in addition to misalignment of pulmonary veins. The etiology of the disease is still not understood. We present a case report of a full-term newborn with ACD associated with anorectal anomaly.

Key words: *Alveolar capillary dysplasia, Anorectal anomaly, Neonate, Persistent pulmonary hypertension.*

Alveolar capillary dysplasia (ACD) is a rare cause of irreversible persistent pulmonary hypertension. Fewer than 50 cases have been described since the first description by Janney, *et al*. [1] in 1981 as a misalignment of pulmonary veins [2,3]. The etiology of disordered alveologenesis is not yet clearly understood. Clinically, there are signs of respiratory failure not responding to therapy. The definitive diagnosis can be established by a lung biopsy [4].

CASE REPORT

A full term 2700 g male infant was born by normal vaginal delivery at the 38 week gestation after uncomplicated pregnancy, with Apgar score 6/9/9. The physical examination detected anorectal atresia and surgical treatment was planned. Preoperative echocardiographic examination did not detect any structural abnormality. Baby did not have tricuspid regurgitation sufficient to generate a measurable signal. There was bidirectional (predominantly left-to-right) shunting at the ductus arteriosus and foramen ovale.The value of right ventricular pre-ejection period / right-ventricular ejection time (PEP/RVET) measured by pulsed doppler at the pulmonary valve was 0.4. The surgery was uneventful but a short time bronchial hyperactivity appeared during induction of anesthesia. After surgery, the infant required mechanical ventilation with FiO_2 0.21-0.3 for 18 hours. On the third postoperative day, the baby was intubated because of dyspnea and impaired oxygenation despite the CPAP treatment. FiO_2 required was 1.0. One day later, there was a progression of severe respiratory failure not responding to any therapy. The *X*-ray examination of the chest did not reveal any pathological changes. Despite resuscitation, mechanical ventilation, and cardiotonic support, the infant died at the age of six days. Autopsy revealed a patent foramen ovale and ductus arteriosus as a result of persistent pulmonary hypertension (PPHN) Edwards stage I –II. Histological examination diagnosed ACD with reduction of capillaries, apposition of pulmonary veins and thickened alveolar-capillary septum (***Fig.* 1**).

DISCUSSION

ACD is a rare lethal condition that has been recognized in recent years as a cause of idiopathic PPHN. The prevalence of ACD is not exactly known [1]. Occasional familiar clustering and documented associations with other non-lethal congenital anomalies, most frequently of genitourinary and gastrointestinal tracts, have been reported [1,2,5]. Chang, *et al*. and coauthors confirmed the deficiency of immunoreactivity of CD 117 hemangioblast precursor cells in lung tissue, which during physiological circumstances produce chemo-reactive substances responsible for vasculogenesis and formation of alveolo-capillary membrane. There is a lack of

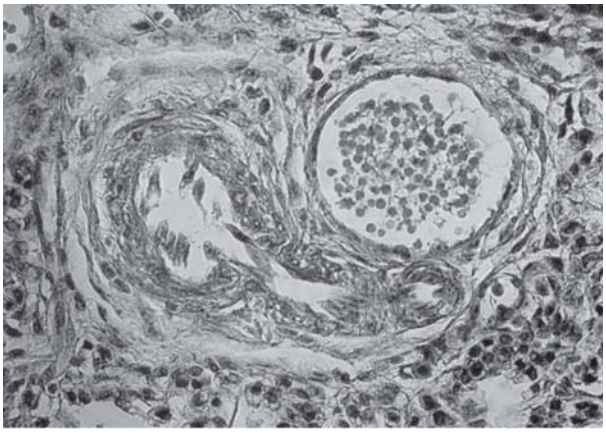

FIG. 1 *Histological signs of alveolar capillary dysplasia with hypertrophy of arterial media and dysplastic vein pass along pulmonary artery sharing common adventitia.*

expression of VEGF isoforms. Principal pathomechanism of the disease is a failure of alveologenesis and formation of blood-gas barrier. Histological analysis reveals misalignment of pulmonary veins, dysplastic capillaries, hypertrophy of pulmonary arteries, lymphangiectasis, and thickened alveolar – capillary septum [7]. In physiological circumstances, pulmonary veins are localized at the periphery of the lobule within interlobular septa. In ACD, they pass along pulmonary arteries, sharing common adventitia in the centre of lung lobule. It is likely that large abnormal capillaries are immature vessels that are arrested at an earlier step of vessels development and have not differentiated into the smaller and more mature size [1, 8]. The dysplastic capillaries may also fail to connect with the pulmonary arteries upstream, which would explain why they are thick-walled in ACD [8].

The pathophysiology of ACD is unclear. It is postulated that reduced number of pulmonary capillaries, hypoxic vasoconstriction and altered vasoreactivity are causes of pulmonary hypertension. The resulting increased right-sided pressure may lead to right to left shunting across patent foramen ovale or ductus arteriosus.

In 50% of cases, pulmonary hypertension progresses within first 24 hours, in other 50% the symptoms develop within several weeks called "the initial honeymoon period". The reason for this period is unknown [9]. This relatively delayed presentation could be ascribed to phenotypical variation of the disease, patchy involvement of lungs or unexpected opening of shunts between pulmonary arteries and veins [6]. Clinical presentation of ACD is nonspecific. There are signs of respiratory failure with developing hypoxemia. *X*-ray examination is frequently without pathological changes. Sometimes bilateral nonspecific infiltrative changes may be present. A variable stage of pulmonary hypertension with right to left shunting and tricuspidal insufficiency can be diagnosed by echocardiographic examination [10].

In our patient, the echocardiography was normal in the preoperative period. Due to a rapid deterioration of clinical condition of the baby there was no time left to repeat the echocardiography.

ACD is a universally lethal disease. All the aggressive therapies including inhaled nitric oxide, mechanical ventilation and ECMO may only reduce transient hypoxemia but do not lead to a long term survival. ACD should be suspected in newborns with respiratory distress that is not responding to the therapy, especially when other congenital anomalies are present. It is recommended to consider early lung biopsy to reduce the number of invasive, expensive and futile procedures that do not improve the likelihood of survival [8].

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