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Exogenous Pulmonary Surfactant Replacement Therapy in a Neonate with Pulmonary Hypoplasia Accompanying Congenital Diaphragmatic Hernia

- A Case Report -

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Pulmonary hypoplasia(PH) commonly occurs in association with oligohydramnios and other congenital anomalies, especially congenital diaphragmatic hernia(CDH). Pulmonary hypoplasia is an important factor, as persistent pulmonary hypertension, in the prognosis of CDH. In some reports, there is a decrement of pulmonary surfactant in PH accompanying CDH. Recently, there are some reports that exogenous pulmonary surfactant therapy is effective in experimental animal model and neonatal respiratory distress with PH. We report a case of a 5 day-old male neonate, who had shown dyspnea and diagnosed as left pulmonary hypoplasia accompanying CDH. The CDH was surgically treated and the ipsilateral PH, with intratracheal administration of exogenous pulmonary surfactant postoperatively. After exogenous pulmonary surfactant application, the left lung volume was increased on chest roentgenogram and lung perfusion scan findings, and there was an improvement in oxygenation and clinical manifestations. We suggest that postoperative exogenous pulmonary surfactant replacement therapy is effective in the case of PH and further trials are needed to clarify the optimal dose and timing of supplementation of surfactant for treatment of infants with PH accompanying CDH.

Key Words : *Exogenous pulmonary surfactant therapy, Pulmonary hypoplasia, Congenital diaphragmatic hernia, Lung development*

INTRODUCTION

Pulmonary hypoplasia (PH) may be either unilateral or bilateral, and is commonly associated with congenital anomalies, especially congenital diaphragmatic hernia (CDH). It may be seen as an isolated entity (so called primary pulmonary hypoplasia) or be secondary to lesions restricting lung growth. Unilateral pulmonary hypoplasia results from the presence of bowel within the thorax mechanically restricting growth by CDH (Fanaroff and Martin, 1987). In most cases, there is a reduction in the number of bronchial generations, suggesting an effect at 10 and 14 weeks gestations, as in CDH. (Chernick and Kendig,1990).

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The effects of PH on the lungs include respiratory distress and pulmonary hypertension. The specific treatment, i.e., high frequency ventilation, and extra corporeal membrane oxygenation (ECMO) were recommended in severe cases of PH with CDH after surgical repair in order to relieve these findings.

Recent studies have reported that hypoplastic lung has a structural and biochemical immaturity inducing pulmonary surfactant deficiency, and that administration of exogenous pulmonary surfactant may provide therapeutic benefits in animal models and neonatal respiratory distress with PH.

We present a first case report of PH accompanying CDH, which was successfully treated with exogenous pulmonary surfactant in Korea.

CASE REPORT

A five day-old male neonate was transferred from an other hospital to Kyung-Hee University Hospital for management of tachy-dyspnea and poor feeding developed on the 3rd day of life. He was well 3 days prior to admission, before he showed poor feeding and insidiously ongoing tachy-dyspnea. His gestational period was 40 weeks, birth weight of 3,800 gm and deliverd via vagina spontaneously at a private obstetric clinic. He had neither a specific birth history such as neonatal asphyxia, oligohydramnios, polyhydramnios, and prolonged rupture of amniotic membrane except slightly weak initial crying and activity.

His body temperature was 37℃, pulse rate 160 /min, respiration rate 112/min. On physical examination, he was acyanotic but very lethargic. There were asymmetric chest expansion (left > right), severe subcostal retraction, and decreased breathing sound of left lung field on auscultation. The abdomen showed scaphoid appearance without bowel sound and movement. The white blood cell count was 7,700/mm^3, hemoglobin 9.0g/dl, hematocrit 25.9%, platelet 178,000/mm^3. On arterial blood gas analysis (ABGA), pH was 7.28, PCO_2 49.5 mmHg, PO_2 60.6mmHg, HCO_3 22.4mmol/L, base excess (B.E) -4.5, and SO_2 89%, a/APO_2 0.69. On initial chest roentgenogram, the left lung field was fully filled with intestines and the stomach without normal pulmonary radiolucency, and the heart and the mediastinum were displaced to the right side (Fig.1). On suspicion of CDH, an emergency operation was performed. The liver, the stomach, the transverse colon, small bowels, and the spleen were found in the left thoracic cage, and the ipsilateral lung was 4x5cm sized, hypoplastic and collapsed. On the 1st day of postoperation, the ABGA was 7.31- 43.3 mmHg - 113.6mmHg - 0.49 - 0.03 (PH - PCO_2 - PO_2 - a/APO_2 - ventilatory index in order) on controlled mechanical ventilation (CMV) state (FiO_2 0.4, respiration rate 40/min, PIP/PEEP 20/3mmHg) with conventional ventilator (Bear cub Co.,U.S.A.), the chest roentgenographic findings showed pleural effusion and still small, hypoplastic and collapsed left lung without the change in the size (Fig. 2). There was no evidence of persistent pulmonary hypertension.

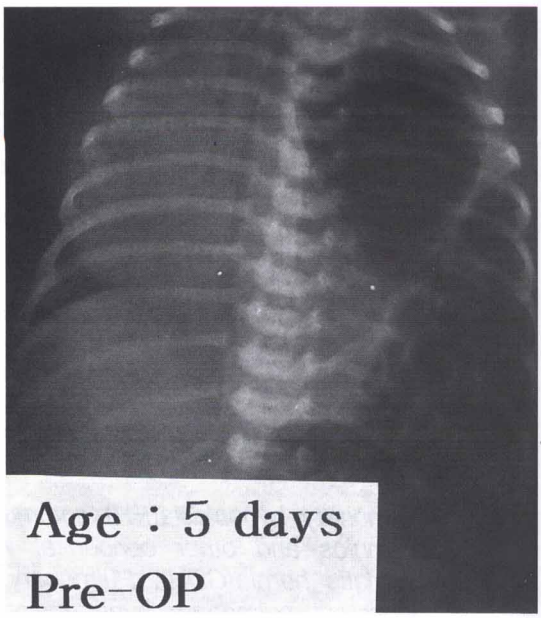

Fig. 1. The chest roentgenogram obtained on admission showed that the left lung field filled with gaseous shadows of the intestines and the stomach, the heart and mediastinum were displaced to the right side.

To expand the collapsed left lung, exogenous pulmonary surfactant, 60mg of the Surfacten® (Surfactant-TA, Tokyo Tanabe Co, Japan) was introduced into the left lung selectively via the trachea and left main bronchus on the 1st and the 2nd day of postoperation respectively on CMV state. The chest roentgenographic findings obtained 12hrs and 30hrs after administration of surfactant showed a much expanded left lung and nearly corrected the right side displacement of heart and mediastinum (Fig. 3).

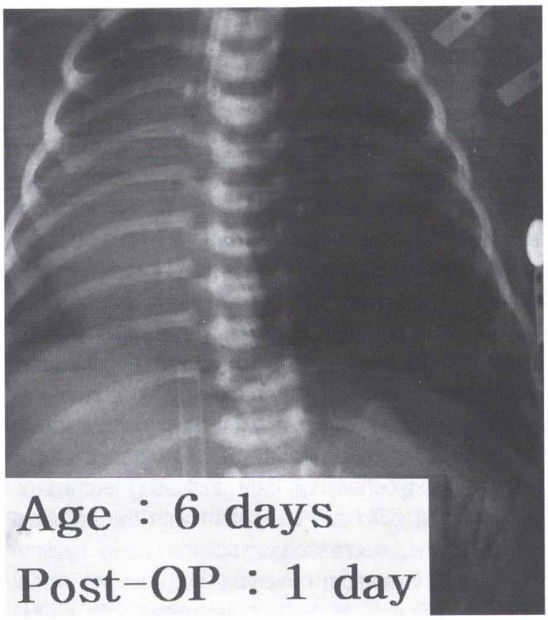

Fig. 2. The chest roentgenogram obtained immediately after operation showed pleural effusion and small, hypolastic and collapsed left lung.

The ABGA checked 12hrs after surfactant therapy was 7.31 - 43.3mmHg - 113.6mmHg - 21.8mmol/L - (-3.9) - 97.8% - 0.91 - 0.014 on CMV state (FiO_2 0.25, respiration rate 30/min, PIP/PEEP 20/3 mmHg). On the 3rd day of post-surfactant therapy, there was a sudden occurrence of left tension pneumothorax and a chest-tube was inserted. On the 10th day of post-surfactant therapy, the chest tube was removed and there was slight pneumonic infiltration and pleural effusion in left lung field on chest roentgenogram. On the 14th day of post-surfactant therapy, a lung perfusion scan was performed. Both lungs were of the same volume, showed radioisotope uptake as seen in the chest roentgenogram (Fig. 4). On the 16th day of post-surfactant therapy, the neonate was discharged with much expanded left lung, improved pneumonia and pleural effusion with not only normal respiration but also good feeding, activity, and weight gain (Fig. 5).

DISCUSSION

PH is an important complication of CDH and frequently causes severe respiratory failure resulting

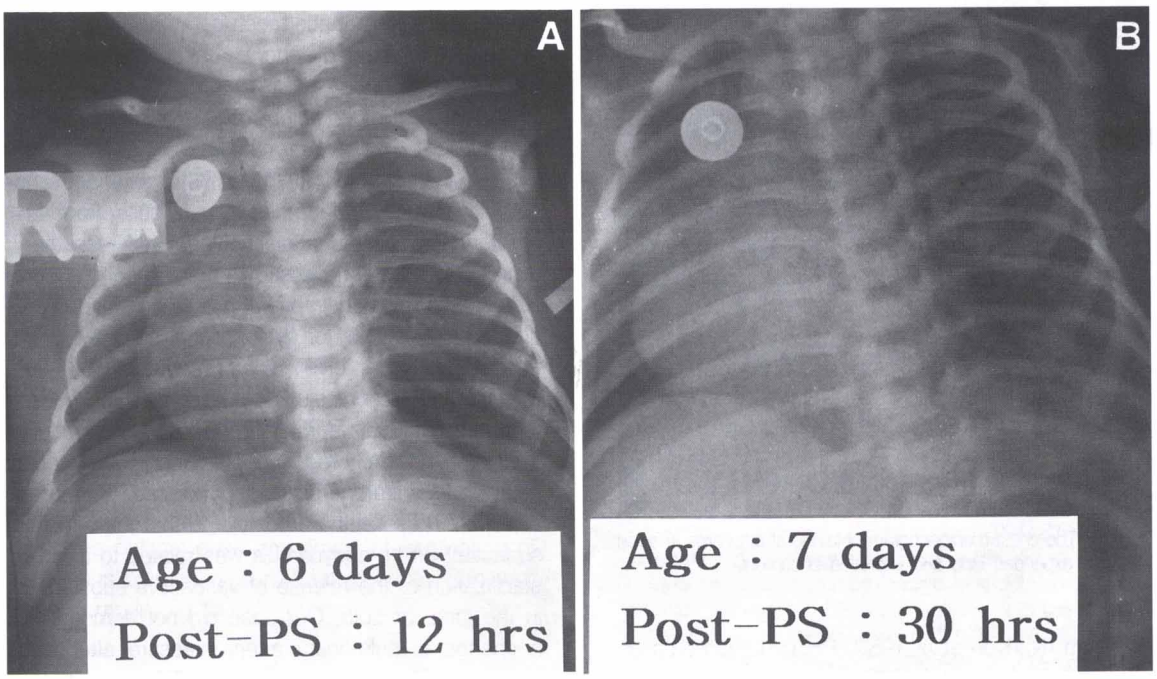

Fig. 3. The chest roentgenogram obtained at 12 hrs (A) and 30 hrs (B) after surfactant administration respectively showed a much expanded left lung and nearly corrected displacement of the heart and mediastinum.

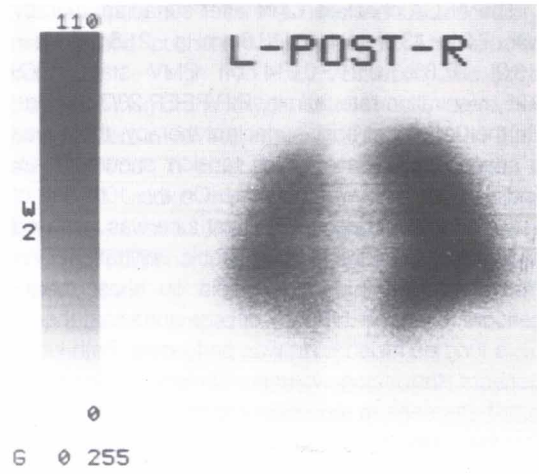

Fig. 4. The lung perfusion scan obtained on the 14th day of post-surfactant therapy showed that there were the same volume of both lungs showing radioisotope uptake as seen in the chest roentgenogram.

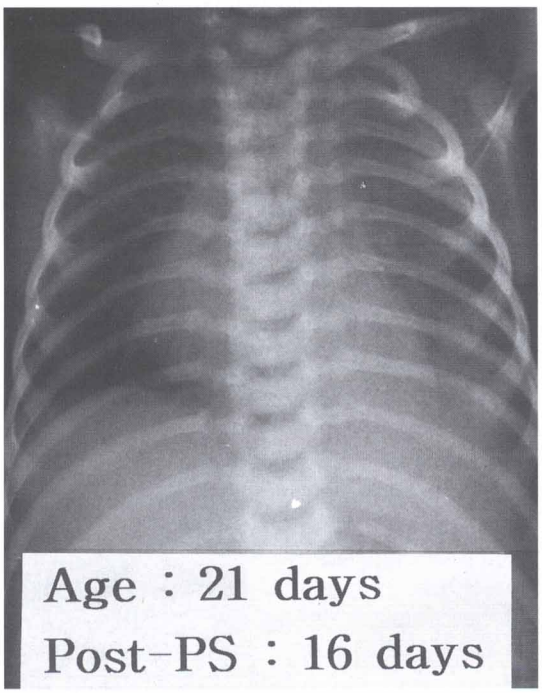

Fig. 5. The chest roentgenogram obtained at discharge showed a much expanded lung and improved pneumonia.

in death (Nguyen et al.,1983). PH usually occurs on the ipsilateral side of CDH. However, the contralateral lung is often more or less hypoplastic. A number of studies demonstrate the retardation of bronchiolar branching, abnormal development of bronchiolar cartilage and reduced total number of alveoli in the ipsilateral lung of CDH (Kitagawa et al., 1971 ; Itoh and Itoh,1988). Wigglesworth et al. (1981) reported that the hypolastic ipsilateral lung in two cases of CDH had an immature structure with low phospholipid concentration, whereas the contralateral lung was structurally and biochemically more mature. The results of postmortem biochemical studies have shown that lower phospholipid content and lecithin/sphingomyelin ratios and absent amniotic fluid phosphatidylglycerol, as in premature, surfactant-deficient infants with respiratory distress syndrome (Berk and Grundy, 1982 ; Hisanga et al., 1984). The biochemical data indicating surfactant deficiency in CDH are consistent with the reduced lung volumes, decreased compliance, and hyaline membrane formation observed both in the lamb CDH model and in human neonates with CDH. There is increasing evidence suggesting that the surfactant system in CDH is associated with quantitative and qualitative phopholipid deficiency, a reduction in surfactant associated proteins, each contributing to a dysfunctional surfactant system in a newborn with CDH (Wilcox et al.,1995). We think that it is clear that the neonate with PH accompanying CDH has deficiency in pulmonary surfactant system.

Surfactant is a complex mixture of phospholipids and surfactant proteins, synthesized by alveolar type II cells, that absorbs at the air/liquid interface and acts to reduce surface tension. Results from laboratory and clinical studies of neonatal respiratory distress syndrome have shown that exogenous surfactant therapy can improve pulmonary function in surfactant deficiency or dysfunctional state (Fujiwara et al.,1980 ; Notter et al.,1985 ; Fujiwara et al.,1990 ; Bae,1994). A recent study by Kappa et al. showed that the artificial surfactant, Exosurf (Burroughs Wellcome, U.S.A.), reduced pulmonary artery pressure in respiratory distress syndrome (Kappa et al.,1992). These authors postulated that the effect of surfactant on hemodynamics was related to alveolar stabilization or the release of vasoactive substances in the lung, or both. Our case did not demonstrate a change in pulmonary artery pressure after surfactant application. In the views of these authors, surfactant may be beneficial in preventing persistent

pulmonary hypertension, which is one of important prognostic factors in CDH.

Studies by Glick and Bos et al. showed that exogenous surfactant therapy, which has proven to be successful in respiratory distress syndrome, may be beneficial in pulmonary hypoplasia accompanying CDH (Bos et al.,1991; Glick et al.,1992). Scheffers et al.(1994) reported that exogenous surfactant therapy had short-term effect on CDH in rats. Bos et al. (1991) reported that in some newborn infants with CDH, surfactant therapy might induce a transient but important improvement of oxygenation and this improvement might lead, especially when used as a prophylactic measure, to a reduction of barotrauma to the hypoplastic lung and a reduction of risk factors for persistent pulmonary hypertension as well as to the possibility of gaining time to introduce other treatments such as ECMO. In our case, ipsilateral tension pneumothorax occurred after surfactant application. We think that the pneumothorax may be due to an inappropriate control of artificial ventilator.

We tried the treatment with exogenous pulmonary surfactant to a newborn with PH accompanying CDH postsurgically with half of the usual dosage of surfactant treated respiratory distress syndrome. Nakayama et al.(1991) reported that preoperative administration of surfactant to newborn infants with CDH might have possible benefit in survival rate. However, a study reported that doses of surfactant might be more useful if administerd later in the clinical course, preferably in the postoperative period (Lotze et al.,1994).

Our conclusion in this case report is that in newborn infants with PH accompanying CDH, exogenous pulmonary surfactant replacement therapy may cause increase in lung compliance resulting in increased lung volume and marked improvement of oxygenation. Although the use of surfactant for infants with CDH has been shown to result in transient improvement in oxygenation, there are no available controlled trials using surfactant in this population. We think that further trials are needed to clarify the optimal dose and timing of application of exogenous pulmonary surfactant to a newborn with PH accompanying CDH.

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