A life-threatening respiratory syncytial virus infection: a previously healthy infant with bilateral spontaneous pneumothorax and acute respiratory distress syndrome

Çağlar Ödek[1], Tanıl Kendirli[1], Ayhan Yaman[1], Bilge Aldemir-Kocabaş[2], Erdal İnce[1]

Divisions of [1]Pediatric Critical Care, and [2]Pediatric Infectious Diseases, Department of Pediatrics, Ankara University Faculty of Medicine, Ankara, Turkey. E-mail: odek@ankara.edu.tr

SUMMARY: Ödek Ç, Kendirli T, Yaman A, Aldemir-Kocabaş B, İnce E.
A life- threatening respiratory syncytial virus infection: a previously healthy infant with bilateral spontaneous pneumothorax and acute respiratory distress syndrome. Turk J Pediatr 2013; 55: 539-542.

Respiratory syncytial virus (RSV) is the leading cause of viral respiratory tract infections in infants and young children. Although the course of RSV infection is usually benign, a small proportion of infants require mechanical ventilation for respiratory failure. We describe an eight-month-old previously healthy female who developed bilateral pneumothorax and acute respiratory distress syndrome (ARDS) secondary to RSV infection. Because of the severe hypoxemia, three doses of surfactant were administered and prone positioning was implemented for nine days. After a prolonged course of mechanical ventilation, she was extubated at day 21 and discharged from the pediatric intensive care unit four days later. We conclude that RSV infections can be severe, and some patients may require mechanical ventilation. Supportive therapies like surfactant replacement therapy and prone positioning can be beneficial in patients with ARDS in whom severe hypoxemia persists despite high levels of positive end-expiratory pressure (PEEP) and plateau pressures.

Key words: respiratory syncytial virus, pneumothorax, acute respiratory distress syndrome, surfactant, prone positioning.

Respiratory syncytial virus (RSV) is the leading cause of viral respiratory tract infections in infants and young children. Most infants are infected during the first year of life[1]. RSV infection usually results in upper respiratory tract illness; however, 20%-30% develop lower respiratory tract disease. Although the course of infection is usually benign, a small proportion of infants require mechanical ventilation for respiratory failure[2]. Prematurity, pre-existing lung disease, congenital heart disease, and immunodeficiencies are certain risk factors for severe disease[3].

Acute respiratory distress syndrome (ARDS) is a severe parenchymal lung injury due to a variety of pulmonary and non-pulmonary causes. It is characterized by hypoxia, diffuse radiographic infiltrates, decreased pulmonary compliance, and pulmonary edema not due to a cardiac cause. In children with ARDS, mortality rates have been reported as high as 40%[4]. Herein, we describe an infant who developed bilateral pneumothorax and ARDS secondary to RSV infection.

Case Report

An eight-month-old previously healthy female was admitted to our pediatric intensive care unit (PICU) with pneumonia and respiratory failure. She was transferred from another hospital where she was first admitted with a two-day history of fever, coughing, wheezing, and respiratory distress. Inhaled salbutamol and intravenous ampicillin-sulbactam were started with the diagnosis of bronchiolitis (Fig. 1a). There was no history of prematurity or respiratory or congenital heart disease. Symptoms rapidly worsened over the next two days, and on hospital day 3 she developed pneumothorax in the right lung. A chest drain was inserted and she was transferred to our PICU. At the time of our PICU admission, the level of consciousness was slightly depressed. Her vital signs were as follows: heart rate,

Fig. 1a. The first chest X-ray upon first admission to the hospital showing bilateral paracardiac infiltrations.

Fig. 1d. Normal chest X-ray taken at the time of PICU discharge.

Fig. 1b. Bilateral pulmonary infiltrates and chest drain on the right side.

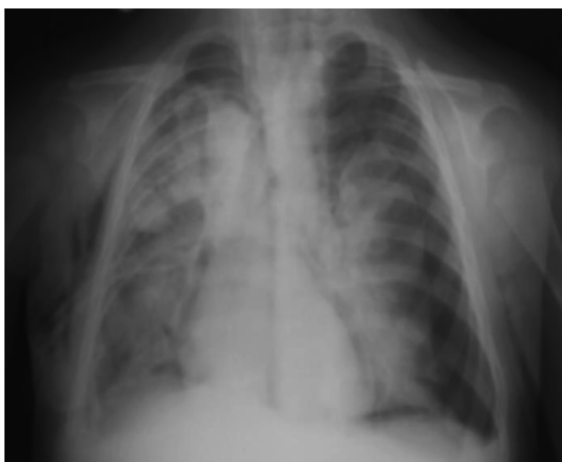**Fig. 2.** Prone positioning of the patient.

Fig. 1c. Chest X-ray at the time of PICU admission showing consolidation and chest drain on the right side and pneumothorax on the left side.

168 beats per minute; respiratory rate, 55 per minute; and pulse oximetry, 85% (oxygen supplementation through non-rebreathing mask). On the physical examination, the infant looked cyanotic and showed severe intercostal, subcostal and suprasternal retractions and nasal flaring. There were bilateral crackles on the chest auscultation. Chest radiograph revealed bilateral infiltrations and chest tube in the right lung (Fig. 1b). Blood gas analysis showed a mild respiratory acidosis and hypoxemia (pH: 7.34, PCO2: 51 mmHg, PO2: 51 mmHg, SaO2: 89.4%, HCO3: 24.9 mEq/L). Complete blood cell count revealed the following measurements: hemoglobin (Hb), 8.3 g/dl; hematocrit, 24.1%; platelet count, 299,000/mm³; and white blood cell (WBC) count, 2600/mm³ (absolute neutrophil count: 1500/mm³). C-reactive protein was 13.1 g/dl. Coagulation parameters

and electrolytes were normal. Pediatric risk of mortality III (PRISM III) and pediatric logistic organ dysfunction (PELOD) scores were 12 and 28, respectively. Her PaO_2/FiO_2 ratio was 56. We defined ARDS using the criteria recommended by the American-European Consensus Conference on ARDS. The patient was intubated and mechanical ventilation was started. Addition of positive end-expiratory pressure (PEEP) up to 12 cm H_2O improved her oxygenation slightly ($PaO_2/FiO_2=98$). As a supportive therapy, 4 ml/kg/body weight surfactant (Survanta, Abbott Laboratories) was administered. Cefoperazone-sulbactam, clarithromycin, teicoplanin, and oseltamivir were started for antibacterial and antiviral coverage. Adequate sedation was provided with midazolam, ketamine, and rocuronium. Three hours after intubation, pneumothorax developed in the left lung (Fig. 1c), and a chest tube was inserted. Twelve hours after PICU admission, hypoxemia worsened ($PaO_2/FiO_2=67.5$) and cardiac arrest developed. Cardiopulmonary resuscitation was performed for two minutes. Epinephrine and dopamine were started. An additional dose of surfactant was administered (4 ml/kg/body weight, Survanta, Abbott Laboratories). RSV was identified from her tracheal aspirate with polymerase chain reaction (PCR) (Seeplex RV15 ACE Detection, Seegene, Korea). PCR was negative for other viruses such as influenza, parainfluenza, human metapneumovirus, and rhinovirus. Tracheal aspirate culture, which was taken at the time of PICU admission, was negative. At PICU day 2, a third dose of surfactant (4 ml/kg/body weight, Survanta, Abbott Laboratories) was administered and prone position (Fig. 2) was implemented for the severe hypoxemia. Prone position was continued for nine days. She showed an improvement with a reduction in oxygen requirement as well as peak inspiratory pressures after three doses of surfactant and implementation of prone positioning. Her oxygen saturation increased to 90-95% from 85-88% and PaO_2/FiO_2 ratio increased to 156. Ventilator pressures were decreased, and on PICU day 21 she was eventually extubated and chest drains were removed (Fig. 1d). She was investigated for cystic fibrosis and immunodeficiencies but the results were negative. On day 25, she was discharged from the PICU.

Discussion

In most cases, the clinical course of RSV infection is uneventful and complications occur infrequently. Secondary air leaks are recognized rare complications of RSV bronchiolitis. Given et al.[5] reported three cases, and another seven cases in total of spontaneous air leaks associated with bronchiolitis were reported previously. Eighty percent (8/10) of these children were previously healthy with no underlying risk factor. RSV was the most common virus reported in children with air leaks[5].

Acute respiratory distress syndrome (ARDS) incidence is estimated from 1% to 5% of children hospitalized in the PICU. Pneumonia, sepsis, aspiration, lung contusion, and toxic gas inhalation are the leading causes of the disease. Endothelial and epithelial injury increases the permeability of the alveolar-capillary barrier, and this leads to influx of protein-rich edema fluid into the air spaces and pulmonary edema. The American-European Consensus Conference on ARDS recommended some criteria for the definition of ARDS[6]. ARDS secondary to RSV infection is rare. Previous studies have shown mortality rates in pediatric patients with ARDS to be in excess of 40%, in contrast to overall low mortality rates of 2-5%[3].

Therapies for ARDS are targeted at decreasing mortality and morbidity and optimizing long-term respiratory function. Minimizing hypoxia and secondary damage to the injured lungs is crucial to prevent other organ dysfunction[7]. Ventilator-induced lung injury plays an important role in the outcome. As a lung-protective ventilation strategy, tidal volumes less than 6-8 ml/kg and inspiratory plateau pressure of less than 25-30 H_2O with permissive hypercarbia and sufficient levels of PEEP are widely used[7]. High-frequency oscillatory ventilation (HFOV) provides early improvement in the PaO_2/FiO_2 ratio, and is associated with higher mean airway pressures and a reduced need for supplemental oxygen in the first 30 days[8]. Previous reports have shown that there are no significant differences in oxygenation failure, ventilation failure, barotrauma, and survival at day 30[6]. We used a lung-protective ventilation strategy in our patient, but HFOV could not be performed because of bilateral pneumothorax.

Prone positioning is a way to recruit atelectatic-dependent zones of the lung and improve

overall oxygenation. It provides an increase in end-expiratory lung volume and a better ventilation-perfusion matching, but studies have shown that it did not improve overall survival. It appears to be safe, and no critical incidents have been reported except facial edema and pressure ulcers[9]. We used prone positioning for nine days in our patient, and observed an improvement in oxygenation. The patient had higher tidal volumes and oxygen saturation with lower ventilator pressures. We did not observe any incidents related with the prone positioning.

The aim of surfactant replacement therapy (SRT) is to reinflate the collapsed areas of the lung, improve compliance, and reduce intrapulmonary shunting. It is a life-saving intervention for the prevention and treatment of RDS in premature infants[4]. Studies have shown that SRT in children with ARDS has significant benefits. It resulted in decreased oxygenation index, decreased mortality, and a higher percentage of response to conventional mechanical ventilation compared to the placebo group[10]. SRT has some risks, including hypotension, hypoxia, and barotrauma[7]. These complications can be life-threatening in critically ill children. Therefore, it must be done by experienced medical staff. Surfactant is expensive but may be cost-effective in ARDS treatment[11]. We used three doses of SRT in our patient and observed an improvement in oxygenation.

In conclusion, we described herein a well-documented case of RSV-induced bilateral spontaneous pneumothorax and ARDS. We performed a lung protective ventilation strategy and used prone positioning and SRT as supportive therapies in our patient. We believe that both SRT and prone positioning were beneficial. Both of these supportive therapies should be used in patients with ARDS in whom severe hypoxemia persists despite high levels of PEEP and plateau pressures.

REFERENCES

1. Piastra M, Caresta E, Tempera A, et al. Sharing features of uncommon respiratory syncytial virus complications in infants. Pediatr Emerg Care 2006; 22: 574-578.

2. Greenough A. Role of ventilation in RSV disease: CPAP, ventilation, HFO, ECMO. Pediatr Respir Rev 2009; 10 (Suppl): 26-28.

3. Hammer J, Numa A, Newth CJ. Acute respiratory distress syndrome caused by respiratory syncytial virus. Pediatr Pulmonol 1997; 23: 176-183.

4. Raghavendran K, Willson D, Notter RH. Surfactant therapy of ALI and ARDS. Crit Care Clin 2011; 27: 525-559.

5. Given K, Schultz A, Douglas TA, Martin AC. Air leaks in children with acute bronchiolitis. J Pediatr Child Health 2008; 44: 604-606.

6. Dauger S, Durand P, Javouey E, Mercier JC. Acute respiratory distress syndrome in children. In: Fuhrman BP, Zimmerman J (eds). Pediatric Critical Care (4th ed). Philadelphia, PA: Elsevier Saunders; 2011: 706-716.

7. Randolph AG. Management of acute lung injury and acute respiratory distress syndrome in children. Crit Care Med 2009; 37: 2448-2454.

8. Arnold JH, Hanson JH, Toro-Figuero LO, Gutierrez J, Berens RJ, Anglin DL. Prospective, randomized comparison of high-frequency oscillatory ventilation and conventional mechanical ventilation in pediatric respiratory failure. Crit Care Med 1994; 22: 1530-1539.

9. Priestly MA, Helfaer MA. Approaches in the management of acute respiratory failure in children. Curr Opin Pediatr 2004; 16: 293-298.

10. Willson DF, Thomas NJ, Markovitz BP, et al. Effect of exogenous surfactant (calfactant) in pediatric acute lung injury: a randomized controlled trial. JAMA 2005; 293: 470-476.

11. Thomas NJ, Hollenbeak CS, Lucking SE, Willson DF. Cost-effectiveness of exogenous surfactant therapy in pediatric patients with acute hypoxemic respiratory failure. Pediatr Crit Care Med 2005; 6: 160-165.