CASE 4.3
Respiratory Distress Syndrome and Bronchopulmonary Dysplasia | Level 3

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1. What is the subjective and objective evidence for the diagnosis of BPD in this patient?

SUBJECTIVE FINDINGS: Increased work of breathing, tachypnea, retractions, pulmonary decompensation despite use of albuterol, edema, and difficulty weaning ventilator settings, including supplemental oxygen

OBJECTIVE FINDINGS: History of RDS requiring treatment with surfactant, chest radiograph showing diffuse haziness throughout, hypoinflation on RLL, rule out cardiac etiology given ECHO is normal, inability to wean from ventilator, respiratory rate (35 breaths per minute, above ventilator set rate in SIMV mode); on physical exam, course rhonchi noted, diffuse rales and wheeze on auscultation, edematous in appearance

2. Describe the risk factors for, clinical presentation of, and recommended treatment for neonatal RDS.

Risk for RDS is dependent on gestational age and birth weight as necessary amount of surfactant for normal lung function occurs at approximately 36 weeks gestation. As such, the risk for RDS is increased for neonates born less than 36 weeks gestation, but it is highest for those born less than 30 weeks gestation. Surfactant serves to lower surface tension in the alveoli, thereby helping to keep them open for air exchange and prevention of alveolar collapse. Surfactant is crucial at around 36 weeks gestational age in the saccular phase of lung development. Inadequate surfactant can result in atelectasis and impaired gas exchange and ultimately RDS. The administration of antenatal corticosteroids encourages the maturation of surfactant production in the fetus. This patient was born at an extremely low birth weight of 800 g at 26 weeks gestation, and his mother did not receive antenatal corticosteroids, which placed him at risk for RDS.

Neonates with RDS present with respiratory distress, including tachypnea, intercostal retractions, grunting, and cyanosis. The onset of symptoms is usually soon after delivery (e.g., a few hours after birth). Laboratory findings may include hypoxemia, hypercapnia, and mixed acidosis on blood gas measurements. The neonate will also likely have increased oxygen requirements and may require mechanical ventilation to maintain respiratory function. On chest radiograph, diffuse reticular-granular opacification with defined large airways may be noted. Given the overlap of signs and symptoms with other conditions,

such as neonatal sepsis, a differential diagnosis is done by considering the onset of symptoms, clinical presentation, and objective findings such as the chest radiograph.

Given the etiology of RDS is centered on the lack of surfactant, recommended treatment for RDS is the administration of exogenous surfactant via the endotracheal tube. The administration of surfactant replaces the deficiency due to prematurity. Clinical trials have demonstrated the efficacy of surfactant resulting in reduced risk of acute pulmonary injury (pneumothorax, interstitial emphysema), development of chronic lung disease, and mortality. Early administration (within 2 hours of birth) has been shown to improve these outcomes versus delayed administration. Patients who may benefit most from surfactant therapy with regard to mortality are those born less than 30 weeks gestational age or less than 1,250 g. Surfactant is available as both synthetic and natural in origin. Administration of surfactant can be considered prophylactic in nature, which is given within 30 minutes of birth, and rescue, which is administered once the diagnosis of RDS is established. Early rescue is defined as administration within 2 hours of birth; delayed rescue is after 2 hours following birth. One dose is given initially and then, depending on the specific surfactant, doses may be repeated up to four total doses. Patients who require mechanical ventilation for respiratory support with oxygen requirements exceeding FiO_2 30% may benefit from repeat dosing. Administration of repeat doses is dictated by symptoms (e.g., tachypnea, retractions) persisting during the observation period after the first dose, which is typically the dosing interval of the specific agent. The number of repeated doses is dependent on selected agent, ranging from two to four doses.

Beractant (4 mL/kg/dose) and calfactant (3 mL/kg/dose) are bovine derived, both with potential for up to four repeated doses, at 6 and 12 hours between doses, respectively. The newly approved synthetic surfactant, lucinactant, dosed at 5.8 mL/kg/dose for up to three doses separated by at least 6 hours, contains a peptide to mimic human surfactant protein B and has no animal-derived components. This patient received poractant alfa, which is porcine derived, dosed at 2.5 mL/kg initially followed by 1.25 mL/kg for two subsequent doses at birth, doses separated by 12 hours. Selection of surfactant product is dependent on institution formulary (i.e., usually institutions select one agent), which is based on available, limited comparative efficacy data and cost. Patients receiving surfactant should be continuously monitored for lung volume and compliance as evidenced by persistence of symptoms of respiratory distress (tachypnea, poor oxygenation, increased work of breathing), and requirement for respiratory support (e.g., mechanical ventilation).

3. Discuss approaches in the prevention of BPD in premature neonates.

BPD is a long-term complication of RDS and is also called *chronic lung disease of infancy*. BPD can arise from any acute lung disorder that results in respiratory failure and need for long-term mechanical ventilation (e.g., a month) for respiratory support. Clinicians now view BPD differently due to advances in perinatal care and neonatal respiratory therapy. The "new BPD" is now clinically milder and is characterized by reduced alveolar development secondary to prematurity, still involving airway injury with inflammation and fibrosis. BPD was more severe in nature due to lung injury from older mechanical ventilation methods, which resulted in more aggressive therapy. Additionally, the manifestation of disease was longer in duration. Instead of being considered a disorder primarily due to lung injury due to respiratory support from mechanical ventilation, BPD is a developmental disorder ultimately due to prematurity. Aside from preventing BPD through prevention of RDS by the administration of surfactant, other pharmacotherapy has been studied.

Vitamin A is an antioxidant needed for tissue differentiation and cell growth. Premature neonates, especially those born with extremely low birth weight, are deficient in vitamin A. Studies have shown reductions in BPD and mortality in premature neonates with a birth weight less than 1,000 g, when vitamin A 5,000 units was administered 3 times a week for 4 weeks. This patient received vitamin A as a measure to prevent BPD development.