Pseudomonas aeruginosa pleural empyema in a preterm infant

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Pleural empyema is defined as the pyogenic infection of the pleural space with purulent effusion. Although it is frequently seen in children and therapy protocols have been developed for it, there are only a few reports about pleural empyema in newborn infants. To our knowledge, just one preterm infant has been reported in the literature. In this article, we report an male infant born at 29 weeks of gestation who had pleural empyema on the 53rd day of life. Multidrug-resistant *Pseudomonas aeruginosa* (*P. aeruginosa*) was isolated from his pleural fluid culture. We suggest that this is the first preterm infant with P. aeruginosa empyema.

Key words: Pseudomonas aeruginosa, pleural empyema, preterm infant, nosocomial infection.

Pleural empyema is known as the pyogenic infection of the pleural space with purulent effusion. Empyema is frequently seen in children and standard therapy approaches have been developed for it. However, it is a very rare entity in newborn infants, with only some 20 case reports in the literature[1-4]. It is also a very unusual condition in preterm infants, with only one case report in the literature who was reported as having *Serratia marcescens* pneumonia, empyema and pneumatocele[2].

It has been suggested that insufficient immune response of the newborn in the early days of life can not localize the infection to the pleura, and furthermore, that the capacity of the pleura to produce exudate is limited. Due to these factors, the incidence of empyema in newborn infants has been considered to be very low[1].

Staphylococcus aureus, Escherichia coli, hemolytic group B Streptococcus, hemolytic group A Streptococcus, Klebsiella spp. and Serratia spp. are the most common causative agents that are isolated[3,5,6]. To our knowledge, *Pseudomonas aeruginosa* (*P. aeruginosa*) has not been isolated in any pleural empyema. Therefore, we suggest that this is the first case report of a preterm infant who developed *P. aeruginosa* empyema during hospitalization.

Case Report

A male infant was born by cesarean section at 29 weeks' gestation to a 23-year-old primigravida mother with Apgar 3-6 at the 1st and 5th minutes, respectively. His mother was routinely followed-up during pregnancy and she was hospitalized due to severe preeclampsia the last week before birth. The birth weight was 1170 g (10-50th centile), birth length was 37 cm (10-50th centile) and head circumference was 26.2 cm (10-50th centile). Physical examination revealed respiratory distress and tachypnea (64 breaths/min), cyanosis, intercostal and subcostal retractions, and prematurity findings. He was intubated due to respiratory distress after birth and given two doses of surfactant because there was reticular granular pattern with air bronchograms on his postero-anterior chest X-ray. His first cranial ultrasonography was performed at 24 hours of life and showed bilateral grade III intraventricular hemorrhage. He was given ampicillin and gentamicin therapies for sepsis. He developed necrotizing enterocolitis on the 3rd day of life. He could not be extubated until the 28th day of life and his chest X-ray was evaluated as chronic lung disease. Therefore, a five-day weaning course of dexamethasone and diuretic medication was

given. His first ophthalmological examination for retinopathy of prematurity (ROP) was found as normal. On the 43rd day of life, while he was followed as intubated, his respiratory distress increased and his physical examination revealed decreased audible breath sounds on the middle and inferior parts of the right lung. Pleural effusion and pneumatocele were determined in his chest X-ray (Fig. 1). His

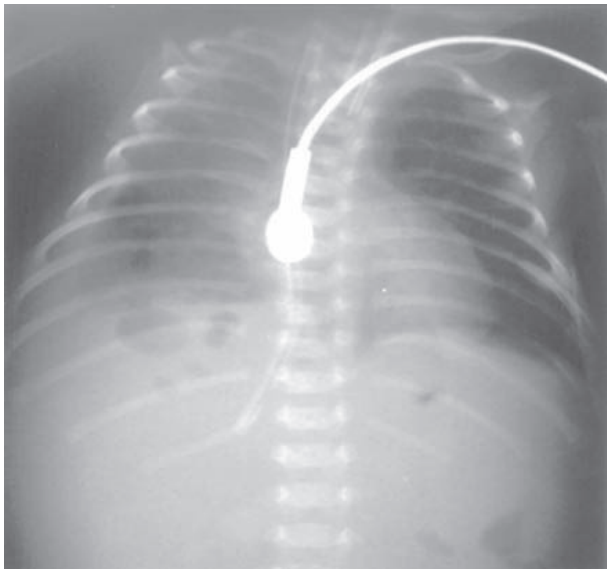

Fig. 1. Postero-anterior chest X-ray of the patient showing pleural effusion and pneumatocele in the right lung.

thorax ultrasonography revealed septated consolidation areas in which the maximum thickness reached 1 cm in the inferior lobe of the right lung. Thoracentesis was performed with the guide of ultrasonography, 3 ml purulent pleural fluid was removed, and a thoracotomy tube was placed at the same time. There were many polymorphonuclear leukocytes in the Giemsa-stained smears of this fluid and there were coccobacilli and rare Gram-positive cocci in the Gram-stained smears. In the biochemical analysis of pleural fluid, density was 1005, pH was 8, lactate dehydrogenase (LDH) was high at 1590 UI/L (serum LDH was 270 IU/L), protein was also high at 4.8 g/dl, glucose was too low to be measured, and Rivalta reaction was found to be positive. His complete blood count showed marked leukocytosis with leukocytes of 22400/mm^3 and peripheral blood smear revealed 6% rod neutrophils, 64% neutrophils, 22% lymphocytes, and 8% monocytes with 20% of toxic granulation. His C-reactive protein was found to be higher than 15 mg/dl (normal <0.5 mg/dl). Multidrug-resistant *P. aeruginosa* was isolated from the pleural fluid culture and he was treated with meropenem (100 mg/kg/day) and amikacin (22.5 mg/kg/day). It was sensitive only to amikacin. Drainage from the thorax tube persisted for 21 days and *P. aeruginosa* was isolated in four other pleural fluid and tracheal suction cultures. No organism was isolated from blood and cerebrospinal fluid cultures. After his respirations and his chest X-ray improved and no drainage was seen from the thoracic tube, it was removed and chest X-ray showed improvement (Fig. 2). His immunological studies were found to be normal. Cystic fibrosis mutation analysis was found to be normal. Computerized thorax tomography performed after his stabilization revealed diffuse fibrotic and atelectatic changes in both lungs and volume loss in the left lung (Fig. 3). His discharge from the hospital was planned once adequate feeding and weight gain were achieved, but another sepsis episode occurred on the 190th day of hospitalization. He was again intubated due to pneumonia and respiratory insufficiency. He was given antibiotic medication, but did not respond to this therapy and died during this sepsis episode. No organism was isolated from his tracheal suction, blood, urine or cerebrospinal fluid cultures.

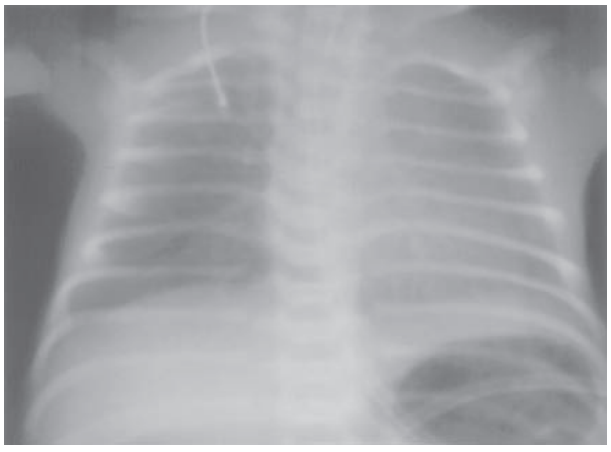

Fig. 2. Postero-anterior chest X-ray showing improvement after the removal of the thoracic tube.

Discussion

Although pleural empyema is seen frequently in children, it is very uncommon in neonates. The most common causative agents in pleural empyema in children are *S. aureus*, *E. coli*,

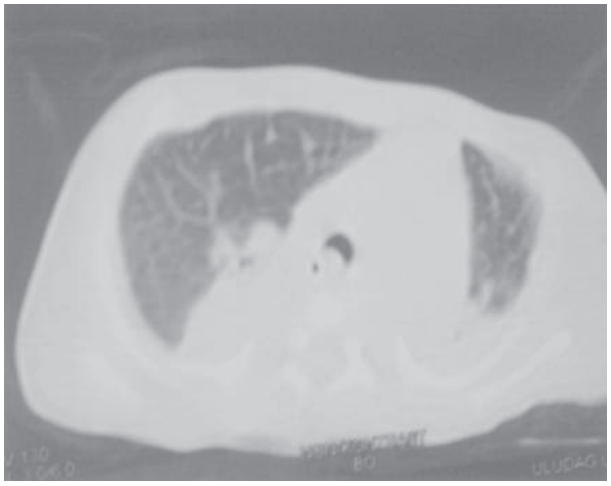

Fig. 3. Computerized thorax tomography showing diffuse fibrotic and atelectatic changes in both lungs and volume loss in the left lung.

hemolytic group B Streptococcus, hemolytic group A Streptococcus, Klebsiella spp. and Serratia spp. Therefore, Gram-positive agents are more suspicious than Gram-negative bacteria in the pleural empyema of neonates[3,5-9]. Pleural empyema due to Gram-negative agents as *E. coli, Klebsiella pneumoniae*, *Enterobacter cloacae* and *S. marcescens* has been reported in literature[2,10-13]. However, we could not find a neonatal empyema report in newborns associated with P. aeruginosa. Although Pseudomonas spp. have been defined as a causative factor in nosocomial pneumonia and sepsis in both neonates, children and adults who are immunocompromised, no empyema case associated with this agent has been described previously.

P. aeruginosa is a motile, aerobic, Gram-negative bacillus with the ability to survive in harsh environments. Although it is an opportunistic bacteria that rarely causes severe infection in normal hosts, it can be an important pathogen causing hospital-acquired infections and severe infections in individuals such as preterm infants who have underlying serious disease[14,15].

Attachment to the appropriate host cell, colonization, local invasion, production of virulence factors, and dissemination with systemic manifestations determine the pathogenecity of any microbe. Protein structures such as pili and fimbriae on the surface of Pseudomonas are necessary for attachment to the epithelial surfaces. After the colonization of the epithelium, some of the organisms produce a biofilm containing a mucoid polysaccharide called alginate. Strains that produce biofilms might be less susceptible to antimicrobial action and this may have a role in the pathogenesis of pulmonary disease caused by this organism. Virulence is associated with the production of multiple proteases and these may lead to the disruption of epithelial tight-junctions. This distribution probably contributes to the attachment process. *P. aeruginosa* also produce cytotoxin and heat labile and heat stable hemolysins, which inhibit polymorphonuclear lymphocyte function and degrade host lipids, respectively. Many of these products may have a role in the dissemination to other organs except local invasion. Furthermore, exotoxin A and exoenzyme S are the novel products of Pseudomonas and they are responsible for the development of sepsis syndrome of this bacteria[14,15].

P. aeruginosa has an outer bilipid layer, a periplasmic space and an inner bacterial membrane, and this complex structure causes resistance to natural defensins and antimicrobial agents. *P. aeruginosa* produce beta lactamases and plasmid-associated beta lactamases. These plasmid-associated elements are usually coexpressed with other resistance mechanisms, including aminoglycoside modifying enzymes, which render the organism multidrug-resistant[15].

The frequency of nosocomial infections in neonatal intensive care units has increased in the last years due to the improved survival rates of low birth weight premature infants[14-17]. These nosocomial pathogens are usually multidrug-resistant organisms such as *P. aeruginosa*, Enterobacter spp. and Klebsiella spp. *P. aeruginosa* has been recognized as a neonatal pathogen for almost 50 years. Because of the factors such as very low birth weight (VLBW) infants having a more fragile skin barrier, an immature immune system, prolonged use of invasive devices, and colonization with hospital flora, neonates and especially VLBW infants have an increased risk for nosocomial infections. The sinks, water baths, respiratory equipment, hand solutions, antiseptics, and neonatal incubators are the most common reservoirs of *P. aeruginosa*[16-18].

In neonates, pneumonia and bloodstream infections are the most common nosocomial infections. It had been reported that *P. aeruginosa* was an infrequent pathogen for nosocomial pneumonia and bloodstream infections, but its mortality rate was found to be high[16-18]. Leigh et

al.[19] stated that *P. aeruginosa* infections had a 50% mortality rate among infants whose birth weight was less than 1500 g. They described feeding intolerance, prolonged parenteral nutrition, longer duration of intravenous antibiotics, and necrotizing enterocolites as risk factors. They also found that mortality was inversely associated with age at diagnosis, and these results showed the importance of this pathogen in neonates. In addition, in a more recent study, the mortality of a *P. aeruginosa* outbreak in a neonatal intensive care unit was reported as 35%[17].

Bilikova et al.[20] reported ventilatory support and therapy with corticosteroids as the most important predictors of *P. aeruginosa* infections in a study including 246 infants, 34 of whom had infections due to *P. aeruginosa*. Our case had ventilatory support and was also given corticosteroid therapy for chronic lung disease. These factors may contribute to the development of *P. aeruginosa* empyema.

In conclusion, *P. aeruginosa* may lead to empyema in VLBW infants who have risk factors such as ventilatory support, therapy with corticosteroids and an immature immune system.

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