Severe Neonatal *Legionella* Pneumonia: Full Recovery After Extracorporeal Life Support

Andrea Moscatelli, MD\(^a\), Silvia Buratti, MD\(^b\), Elio Castagnola, MD\(^c\), Alessio Mesini, MD\(^d\), Pietro Tuo, MD\(^a\)

**abstract**

*Legionella pneumophila* is responsible for hospital or community-acquired pneumonia. Neonatal legionellosis is associated with rapidly severe clinical course and high mortality rates. We describe a case of hospital-acquired *Legionella* pneumonia in a newborn with undiagnosed tracheoesophageal fistula and acute respiratory failure requiring venovenous extracorporeal membrane oxygenation support before fistula repair. Standardized multiplex polymerase chain reaction assay allowed early diagnosis. Extracorporeal life support associated with appropriate antibiotic therapy, surfactant, and steroid therapy was effective in achieving complete recovery. This is the first report of successful neonatal extracorporeal life support for respiratory failure secondary to *L pneumophila*.

Since the first known outbreak of Legionnaires’ disease in 1976, a significant increase of *Legionella* infections have been documented in recent years, likely due to increased awareness and recognition of the pathogen with rapid diagnostic test availability.\(^1,2\) A few isolated cases or outbreaks of neonatal legionellosis have been reported in the literature, usually presenting with severe pneumonia.\(^3–5\) Venovenous extracorporeal membrane oxygenation (VV-ECMO) support is an established treatment of several respiratory conditions in the neonatal period when conventional treatments fail. Few case series of successful use of ECMO to treat adult patients with acute respiratory syndrome (ARDS) complicating legionellosis have been published.\(^6–8\)

**PATIENT**

The patient was born at 39 weeks gestational age by elective cesarean delivery after an uncomplicated pregnancy in a birth center with a special care nursery. The perinatal period was uneventful. On day of life (DOL) 12, the infant was brought to the emergency department because of fever, rhinitis, cough, and respiratory distress. Chest radiograph showed bilateral basal infiltrates. Blood tests indicated a white blood cell count 16 000/mm\(^3\) with left shift, platelets 460 000/mm\(^3\), low serum sodium (133 mEq/L), and C-reactive protein 16 mg/dL (normal value <0.46). Multiplex polymerase chain reaction (PCR) for virus and bacteria was performed (Seeplex Pneumobacter ACE Detection, Seegene, Seoul, Korea). The patient was admitted with a diagnosis of pneumonia, and empirical intravenous antibiotic therapy was started with ampicillin and a third-generation cephalosporin. After few hours, she was transferred to the NICU/PICU due to deterioration of respiratory status, severe desaturation, and respiratory acidosis. A flexible bronchoscopy was performed for suspicion of tracheoesophageal fistula (TEF), which was confirmed.
in the posterior wall of the trachea, 1.5 cm from the carina (H-type).

In the following days, she presented progressive worsening of the bilateral pulmonary infiltrates, high ventilatory parameters, increasing C-reactive protein (maximum 20 mg/dL), urticaria rash, and signs of septic shock. High-frequency oscillatory ventilation and inhaled nitric oxide were not effective (oxygenation index 65); hemodynamic support with epinephrine was started. On DOL 16, VV-ECMO was commenced with resting settings on high-frequency oscillatory ventilation. Ultrafiltration was required for oligoanuria and severe fluid overload. Hemodynamic status improved on VV-ECMO. On ECMO day 1, screening for viral and bacterial respiratory pathogens became available and was positive for Legionella pneumophila, confirmed on 2 samples of bronchoalveolar lavage by real-time PCR. Serogroup was not analyzed. Antibiotic therapy with ampicillin, rifampin, and azithromycin was administered for 21 days. Methylprednisolone pulses, surfactant administration with flexible bronchoscopy, surfactant lavages, and respiratory physiotherapy were implemented. Improvement of pulmonary infiltrates was observed in the following days. After 10 days, ECMO support was discontinued (DOL 26), and the patient was stable on conventional ventilation. Chest computed tomography on DOL 30 demonstrated diffuse ground glass infiltrates and consolidations with bilateral cystic lesions of various sizes, the main one in the right inferior lobe, 20 × 30 × 20 mm in size (Fig 1). Surgical repair of TEF by right cervical approach was performed 5 weeks after ECMO discontinuation to allow adequate resolution of the cervical hematoma due to surgical cannulation and repair of the internal jugular vein. Postoperative course was complicated by bilateral vocal cord paralysis requiring tracheostomy at 4 months of age. At 1 year of age, chest compute tomography showed resolution of the cystic lesions with mild ground glass appearance in the right inferior lobe and bilateral linear fibrotic lesions in the posterior aspects of the lower lobes (Fig 1). Follow-up has been uneventful, and the patient is asymptomatic with normal neurodevelopmental outcome at 2 years of life. Environmental cultures performed in the birth center after the diagnosis of Legionella infection in our patient demonstrated colonization of the water distribution system with Legionella pneumophila. No other cases were identified.

**FIGURE 1**
Nonenhanced chest computed tomography scan. A, After discontinuation of VV-ECMO. B, At 1 year of age showing complete resolution of consolidations and cystic lesions; residual ground-glass appearance and fibrosis.

**DISCUSSION**

Legionella pneumophila is a Gram-negative bacillus responsible for hospital or community-acquired pneumonia. Legionella is considered a rare cause of pneumonia in immunocompetent children, and in a review of 76 pediatric cases, 38% were under 1 year of age.5 The incubation period ranges between 2 and 7 days.9 Legionella is acquired through inhalation of contaminated aerosolized water from cooling towers, humidifiers, respiratory therapy equipment, and potable water systems. As in our case, a positive environmental link has been identified in 88% of pediatric cases of hospital-acquired Legionella.5 A large outbreak of Legionella infection in term neonates in Cyprus occurred in 2008 due to contamination of a cold mist humidifier.4 Hospital and domestic birthing pools have also been reported as source of severe or fatal infections in the neonatal period.3,5,10

Clinical presentation, radiologic features and natural course of Legionella pneumonia in children are not specific and often similar to other forms of pneumonia.5 Clinical presentation may range from mild symptoms to a fulminating course complicated by multiple organ failure. Immunosuppression, neoplasms, immunodeficiency, organ transplantation, and underlying pulmonary disease are recognized risk factors in the adult and pediatric population, where neonatal age and prematurity are additional risk factors for severe disease.1,5 Mortality rates of severe Legionella pneumonia are high, 30% to 33% in adult ICUs,11,12 23% to 41% in the pediatric age, and 55% in neonatal cases.5

Urine antigen testing, culture from respiratory tract secretions or pleural fluid, and antibody titers could be used for diagnosis, although DNA amplification by PCR warrants high specificity and rapid response if standardized assays are available.13

Intravenous azithromycin is the current treatment of choice for L pneumophila in the pediatric patients.1,14 Combination therapy with rifampin is recommended in severe cases, although no evident additional benefits have been demonstrated.1,15 It has been noted that mortality rates are significantly lower in children treated with timely and appropriate antibiotic therapy (23% vs 70%).5 Empirical therapies for community-acquired pneumonia or neonatal sepsis are not efficacious in Legionella infection. In cases in which pneumonia is not responsive to β lactamase therapy, Legionella should be suspected and specific diagnostic tests should performed.
Lung injury and severe respiratory failure in the reported case were likely secondary to 2 coincident factors: *Legionella* infection and inhalation due to undiagnosed TEF. ECLS is an effective treatment of acute respiratory failure due to several etiologies when conventional ventilatory support fails. Series and single cases of ECLS for severe *Legionella* pneumonia in adult patients have been reported, but, to our knowledge, only 1 case of ECMO support for neonatal *Legionella* infection is reported in the literature with no mention of outcome. Query of the Extracorporeal Life Support Organization registry (1990–2014) identified 2 neonatal cases (9 and 17 days of life) and 2 infants with *Legionella* pneumonia supported with venovenous or venoarterial ECMO with no survivors. In the most recent retrospective study of 12 adult patients with *Legionella* pneumonia treated with VV-ECMO, 75% of patients were successfully weaned off ECLS, with 67% survival to discharge, compared with 25% survival in a previous study of 8 confirmed cases. Our patient was successfully weaned off ECLS after a 10 day-course of VV-ECMO without significant complications.

The role of surfactant replacement therapy in ARDS is controversial. Experimental and clinical evidence demonstrated surfactant dysfunction with qualitative and qualitative abnormalities of both phospholipids and proteins. It has been proven that *Legionella* species secrete phospholipase A, which may act as a powerful agent in the mediation of pathogenicity due to destruction of lung surfactant and epithelial cells. Exogenous surfactant therapy during ECMO and surfactant lavage to remove thick respiratory secretions seemed to be an effective therapeutic strategy. Recent reviews and meta-analysis suggest that the use of low-dose corticosteroids is associated with improved mortality and morbidity outcomes and that they may play an effective role as adjunctive therapy for ARDS in adults. Low-dose methylprednisolone in our patient was not associated with adverse effects.

Recognition of *Legionella* species as a potential cause of neonatal and pediatric pneumonia is essential because clinical course may rapidly become severe and life threatening. Standardized multiplex PCR assays represent an important diagnostic tool to rapidly identify unrecognized pathogens. Early diagnosis, appropriate antibiotic therapy, and ECLS associated with adjunctive therapies such as surfactant and steroids were effective in achieving an excellent outcome.

**ACKNOWLEDGMENTS**

We gratefully acknowledge the contribution of Dr Elisabetta Lampugnani for critically reviewing the manuscript.

**ABBREVIATIONS**

ARDS: acute respiratory disease syndrome
DOL: day of life
ECLS: extracorporeal life support
PCR: polymerase chain reaction
TEF: tracheoesophageal fistula
VV-ECMO: venovenous extracorporeal membrane oxygenation

**REFERENCES**


Severe Neonatal Legionella Pneumonia: Full Recovery After Extracorporeal Life Support
Andrea Moscatelli, Silvia Buratti, Elio Castagnola, Alessio Mesini and Pietro Tuo
Pediatrics 2015;136:e1043
DOI: 10.1542/peds.2014-3291 originally published online September 21, 2015;
Severe Neonatal *Legionella* Pneumonia: Full Recovery After Extracorporeal Life Support

Andrea Moscatelli, Silvia Buratti, Elio Castagnola, Alessio Mesini and Pietro Tuo

*Pediatrics* 2015;136;e1043

DOI: 10.1542/peds.2014-3291 originally published online September 21, 2015;

The online version of this article, along with updated information and services, is located on the World Wide Web at:

http://pediatrics.aappublications.org/content/136/4/e1043