Fulminant *Mycoplasma* Infection Requiring ECMO in a Previously Healthy Child: Case Report and Review

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Abstract

Keywords

- *Mycoplasma pneumoniae*
- extracorporeal membrane oxygenation
- acute respiratory distress syndrome

Mycoplasma pneumoniae is a common cause of pneumonia and rarely requires hospitalization. We present a case of a 12-year-old girl who developed acute respiratory distress syndrome requiring extracorporeal membrane oxygenation (ECMO). Eight cases of *Mycoplasma* infection requiring ECMO reported to the Extracorporeal Life Support Organization and 16 cases reported in the literature are summarized with 72.7% survival cumulatively.

Introduction

Mycoplasma pneumoniae is a common cause of pneumonia in children and adolescents that is typically easily treated in the outpatient setting.¹ Occasionally, more severe disease occurs and requires inpatient treatment, ventilatory support, and rarely, extracorporeal membrane oxygenation (ECMO). We present a case of a previously healthy 12-year-old girl who developed acute respiratory distress syndrome (ARDS), respiratory failure, and cardiac arrest requiring ECMO support. Eight cases of *Mycoplasma* infection requiring ECMO have been reported to the Extracorporeal Life Support Organization (ELSO) registry as well as 15 cases reported in the literature that are summarized here.

Case Report

A previously healthy 12-year-old girl presented to clinic with a 2-week history of mild cough and a 2-day history of a sore throat, pain underneath her tongue that developed into a clear blister-like lesion, and unilateral facial swelling. Antihistamines given at home did not improve her symptoms. She was taken to her primary care physician (PCP) where she had a white blood

cell (WBC) count of $14 \times 10^9/L$ and was prescribed amoxicillin that she was unable to tolerate due to emesis. She returned to the PCP the following day, received intramuscular ceftriaxone, and was noted to have an increased WBC count of $23 \times 10^9/L$. The following day, she was seen in the emergency room (ER) due to worsening cough, facial swelling, and fever where she was noted to be hypoxic with a chest X-ray demonstrating bilateral infiltrates. She was admitted and started on levofloxacin but due to continued clinical deterioration, was broadened to piperacillin–tazobactam, azithromycin, voriconazole, and vancomycin within 2 days of admission to the outside hospital (OSH). She was found to be positive for *Mycoplasma* immunoglobulin (Ig)M and IgG, and azithromycin was changed to doxycycline. She was transferred to the pediatric intensive care unit for respiratory decompensation and was intubated but continued to have worsening hypoxia requiring escalation to high-frequency oscillatory ventilation. She was also started on norepinephrine and epinephrine due to hypotension. Due to ongoing hypoxia, she was cannulated to venovenous (VV) ECMO. During cannulation, she had pulseless electrical activity (PEA) cardiac arrest and received C-reactive protein, epinephrine, and bicarbonate. Her ionized calcium level was noted to be

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very low at 0.54 mmol/L prior to PEA arrest with postarrest value of 1.57 mmol/L after replacement. The etiology of hypocalcemia was unclear. She had two additional PEA arrests and due to cardiac dysfunction was converted to venoarterial (VA) ECMO and transferred to a university hospital for further management. Though an echocardiogram earlier in her clinical course showed normal cardiac function, her echocardiogram after transfer showed minimal cardiac contractility. Therefore, milrinone was started. The following day, echocardiogram showed significant improvement with ejection fraction calculated at 48%. Epinephrine and norepinephrine were weaned off over 24 hours and milrinone in 48 hours. Due to obstruction of distal flow to the right femoral artery from ECMO arterial cannula despite placement of reperfusion cannula, she developed compartment syndrome in her right leg requiring fasciotomies. She was transitioned to VV ECMO on day 2 of admission to the university hospital and was decannulated after receiving 9 days of ECMO.

She also developed renal failure with acute tubular necrosis. She received 5 days of continuous renal replacement therapy (CRRT) and due to persistent uremia, received peritoneal dialysis (PD) after CRRT was discontinued. She required 9 days of PD with subsequent normalization of renal function. She also developed an intraparenchymal hematoma in the left parietal lobe while on ECMO that was stable on follow-up computed tomography (CT) scan and did not require intervention. She received a tracheostomy to facilitate rehabilitation and was discharged to a rehabilitation facility neurologically intact with a tracheostomy in place but no longer ventilator dependent.

Mycoplasma IgG remained positive on repeat workup. Extensive workup from a bronchoalveolar lavage (BAL) from the OSH revealed an acid-fast bacilli (AFB) culture growing nontuberculous mycobacteria, which was negative by DNA probe. She was also found to be *Histoplasma* antibody positive at the OSH but antigen negative in the urine and again negative upon repeat workup. All other cultures, including aerobic, anaerobic, fungal and viral cultures, and other infectious workup for pathogens, including *Pneumocystis jirovecii*, *Legionella*, *Blastomyces*, parvovirus, coxsackievirus, *Toxoplasma*, human immunodeficiency virus (HIV), Epstein-Barr virus (EBV), and cytomegalovirus (CMV) were negative. Due to pulmonary hemorrhage, she underwent testing for rheuma-

tologic disorders, including Goodpasture's syndrome, hemophagocytic lymphohistiocytosis (HLH), and macrophage-activating syndrome that were also negative.

ELSO Registry Data

Data on all patients who required ECMO and had an ICD9 code for *M. pneumoniae* infection from 1989 to 2015 were collected from the ELSO international registry.² A total of eight patients met these criteria with all cases reported between 2011 and 2015. They had a mean age of 21.6 (11–67) years with five females and two males and one case without a sex reported. There were three VA and four VV ECMO cases with one case not listing type of ECMO. The mean ECMO run was 232 hours/9.68 days. Survival of ECMO run was 75% (6/8); both deaths were reported in the patients with the longest ECMO runs, specifically runs > 350 hours (600 and 424 hours), and both were VV ECMO cases. Four cases used conventional ventilation, two cases used high-frequency oscillation, and two cases did not report type of ventilation prior to ECMO. Ninety percent of complications reported among all eight cases were reported in two cases that did not survive. The results are summarized in ►Table 1.

Literature Review

Medline and Embase (from January 1, 1974 to April 5, 2017) were searched using a combination of keywords and controlled vocabulary terms. The terms used were ECMO, *M. pneumoniae*, adult respiratory distress syndrome, ARDS and pneumonia, and the search was limited to the English language.

Fifteen cases were described in the literature. An additional five to nine cases were found within larger studies but without case-specific details.^{3,4} The results are summarized in ►Table 2.

Discussion

Mycoplasma pneumoniae is a common cause of community-acquired pneumonia (CAP), causing an estimated 15 to 20% of cases annually.⁵ Due to its typically unremarkable course, testing is not usually conducted and due to limitations, is often unreliable.⁵ Elevated cold agglutinin titers rise slowly over 2 to

Table 1 ELSO registry cases of *Mycoplasma pneumoniae*

Age (y)	Primary listed diagnosis	ECMO mode	ECMO (d)	Outcome
67.9	Acute respiratory failure	VV	25	Died
15.9	Acute respiratory failure	VV	17.7	Died
10.8	Chest pain	VA	5.5	Survived to discharge
17	Influenza with pneumonia	VA	4.7	Survived to discharge
4.8	<i>Mycoplasma</i> infection	VVDL	13	Survived to discharge
5.1	Acute respiratory failure	VVDL	4.6	Survived to discharge
34.2	Acute bronchitis	NR	6.8	Survived to discharge
17.6	Shock, unspecified	VA	9.8	Survived to discharge

Abbreviations: ECMO, extracorporeal membrane oxygenation; ELSO, Extracorporeal Life Support Organization; NR, not reported; VA, venoarterial; VV, venovenous; VVDL, venovenous double lumen.

Table 2 Reported ECMO cases in literature review with primary diagnosis of *Mycoplasma pneumoniae*

Article	Age (y)	Relevant history and listed complications	ECMO mode	ECMO (d)	Outcome
Peng et al ⁶	3.4	History of asthma	VA to VV	18	Survived to discharge
Peng et al ⁶	3.9	Not reported	VA to VV	10	Survived to discharge
Duke et al ⁷	6	Not reported	VV	50	Died
Daxboeck et al ⁸	18	Acute renal failure requiring dialysis, acute liver failure requiring extracorporeal liver support with a MARS, pericardial effusion, hemorrhagic pneumonia	Not reported	1	Died ^a
Garcia et al ⁹	13	Mild pulmonary hypertension and right ventricular dysfunction and experienced ataxia and left-sided hemiparesis prior to cannulation (no head CT due to instability). Developed bilateral multiple ischemic strokes with subfalcine and uncal herniation and loss of brain stem reflexes	VV	4.75	Died ^b
Goldman et al ¹⁰	1	History of tetralogy of Fallot and chronic lung disease	Not reported	NR	Not reported
Goldman et al ¹⁰	2.75	Not reported	Not reported	NR	Not reported
Hoffman et al ¹¹	34	Plastic bronchitis requiring bronchoscopic removal of casts, aerosolized tPA and rhDNase into airways	VV	7	Survived to discharge
Hopkins et al ¹²	17	Trisomy X, fetal alcohol syndrome, mild asthma, severe denuding of tracheal mucosa extending into the left mainstem bronchus	VV	22	Survived to discharge
Lindstrom et al ¹³	18	Not reported	VV	32	Survived to discharge
Masuda et al ¹⁴	32	Not reported	Not reported	Not reported	Died ^c
Patel et al ¹⁵	20	Diffuse alveolar hemorrhage unresponsive to high dose steroids and nitric oxide	VV	Not reported	Survived to discharge
Sultan et al ¹⁶	23	Sickle cell disease, acute chest syndrome, diffuse alveolar hemorrhage, RV dysfunction	VV	6	Survived to discharge
Yoshida et al ¹⁷	7	History of trisomy 21, pneumothorax	VV	6.3	Survived to discharge
Hsieh et al ¹⁸	6	Macrolide-resistant strain of <i>Mycoplasma</i> sibling also infected and improved with doxycycline	Not reported	12	Survived to discharge

Abbreviations: CT, computed tomography; ECMO, extracorporeal membrane oxygenation; MARS, molecular adsorption recirculating system; rhDNase, recombinant human deoxyribonuclease; RV, right ventricular; tPA, tissue plasminogen activator; VA, venoarterial; VV, venovenous.

^aDeath following diffuse hemorrhage and multiorgan failure.

^bCare withdrawn following postdecannulation brain herniation due to intracranial hemorrhage.

^cDeath following intracranial hemorrhage.

8 weeks, and serologic testing requires repeated measurements over time to differentiate past from acute infections.⁵ *Mycoplasma pneumoniae* is also difficult to culture and can require 3 or more weeks for growth.⁵ Polymerase chain reaction (PCR) testing is now available and increasingly sensitive.⁵ Limitations in laboratory studies to detect *M. pneumoniae* have made the diagnosis of active infection difficult, but improvements in diagnostic technique and sensitivity may explain the clustering of cases reported to ELSO and in the literature in the past 10 years. As *Mycoplasma* typically takes a benign course and is difficult to diagnose in real time, it may be

underdiagnosed, especially in cases of severe disease such as the case we presented and other cases reported in the literature and to ELSO. Importantly, in our case and others reported in the literature, severe disease occurs in immunocompetent patients despite appropriate antibiotic treatment and can require rapid escalation of therapy including respiratory and/or cardiovascular support through ECMO. The limitation of this review is the sparse and incomplete data available. In addition, some cases may have been unintentionally excluded due to these embedded within broader reports on other topics without case-specific details.

Conclusion

The overall survival rate for 22 cases of *Mycoplasma* requiring ECMO that reported outcome was 72.7% (16/22) demonstrating that ECMO may be safely and effectively be used to treat severe *Mycoplasma* infection. In the few cases of death reported, intracranial bleeding and/or multiorgan system failure were listed as the cause, which are common causes of ECMO-related mortality. In summary, in cases of severe ARDS as well as diffuse alveolar hemorrhage or other significant cardiopulmonary disease, the diagnosis of *Mycoplasma* ought to be considered and investigated, and atypical antimicrobial coverage should be instituted. ECMO should be reasonably considered in severe cases of *Mycoplasma* given relatively high rates of survival documented in the literature and ELSO database.

Conflict of Interest

None.

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