

CASE REPORT

Bridging treatment for antibiotic efficacy in respiratory failure caused by *Mycoplasma Pneumoniae* infection

Simona Tantillo¹, Francesca Franzoi², Manuel Losito², Martina Guarnera¹, Irene Ottaviani¹, Nicola Cilloni¹

¹AUSL di Bologna, Ospedale Maggiore Carlo Alberto Pizzardi, Terapia Intensiva e HUB Maxiemergenze

²Dipartimento di Medicina e Chirurgia, Alma Mater Studiorum of Bologna

Corresponding Authors:

Simona Tantillo

email: Simona.tantillo@ausl.bologna.it

Abstract

Community-acquired pneumonia (CAP) is a common respiratory infectious disease, in 7.5% of cases the responsible pathogen is represented by *Mycoplasma Pneumoniae*, 4% of these patients require hospitalization in Intensive Care Unit (ICU). We describe two cases of two young male patients with acute respiratory failure caused by *Mycoplasma pneumoniae*. They were admitted to the ICU with a high risk of requiring intubation, but this was avoided through an individualized treatment. The first case underscores the potential efficacy of high-flow nasal oxygen, supported by esophageal pressure swing (ΔP_{es}) monitoring, evaluating the patient's respiratory effort and titrating the oxygen therapy administered. In the second case, the patient's hypoxemia was treated with high-flow oxygen therapy with inhaled nitric oxide guided by a high shunt fraction. Through the analysis of these two cases, we emphasize the crucial importance of personalized management of hypoxemia in severe instances, as a bridge treatment while waiting for antibiotic therapy to be effective. Additionally, despite the patients not requiring intubation, it is imperative to admit and manage severe cases in ICU. This approach facilitates close monitoring and the potential for therapeutic escalation, ensuring comprehensive care for optimal patient outcomes. Further research is warranted to elucidate the optimal approach to non-invasive respiratory support and prevention of patient self-inflicted lung injury in the early stages of acute hypoxemic respiratory failure. Further researches are needed to assess the efficacy of inhaled nitric oxide in preventing tracheal intubation.

© Tantillo S. et al. | MSJ 2024 | 2(1):e202445

This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made.

Received: July 8, 2024

Revised: July 31, 2024

Accepted: August 4, 2024

Published: October 11, 2024



Article information are listed at the end of this article.

Introduction

Community-acquired pneumonia (CAP) represents a frequent respiratory infectious disease, with general incidence ranges between 1 and 25 cases per 1000 inhabitants per year. Approximately 40% of patients with CAP require hospitalization, and 5% of these patients require hospitalization in intensive care unit (ICU), due to septic shock or the need for invasive or non-invasive mechanical ventilation [1].

Streptococcus pneumoniae is the most common pathogen (20.0%), followed by *Haemophilus influenzae* (10.8%), *Mycoplasma pneumoniae* (7.5%) and *Chlamydia pneumoniae* (3.3%); less common are *Moraxella catarrhalis* (2.0%), *Staphylococcus aureus* (1.9%) and Influenza Virus (0.7%) [2]. *Mycoplasma pneumoniae* infection is more common in children than in adults; in a recent review the proportion of infection between children and adult is 24,5% versus 3,9% [3]. Only 4% of *Mycoplasma pneumoniae* patients need ICU admission for acute respiratory failure.

Mycoplasma pneumoniae can progress to acute respiratory distress syndrome (ARDS) and potentially lead to a fatal outcome, particularly when diagnosis and treatment are delayed or respiratory support is inadequate [4]. According to the latest international guidelines for CAP, high-flow nasal oxygen (HFNO) is recommended for patients with acute hypoxemic respiratory failure (AHRF) due to CAP, provided intubation is not immediately required [5]. Evidence indicates that HFNO offers superior oxygenation and reduces respiratory rate compared to standard oxygen therapy. Additionally, a multicenter trial demonstrated that patients with a $\text{PaO}_2/\text{FiO}_2$ ratio ≤ 200 mmHg treated with HFNO had a lower intubation rate compared to those receiving standard oxygen therapy, and even non-invasive ventilation (NIV) via facial mask [6]. However, patient self-inflicted lung injury (P-SILI) may occur when the inspiratory effort in spontaneous breathing is excessive [7]. This effort can be evaluated by measuring the esophageal pressure swing (ΔPes) using a specialized nasogastric tube equipped with an esophageal balloon, with low and high inspiratory efforts defined as $\Delta\text{Pes} \leq 10$ cmH₂O and >15 cmH₂O, respectively [6,8].

Assessing a patient's respiratory effort is crucial to prevent non-invasive treatment failure and subsequent delayed intubation [9-10].

The utilization of inhaled nitric oxide (iNO) has been demonstrated to play a role in enhancing oxygenation in AHRF by improving the ventilation-perfusion mismatch [11]. However, this does not translate into a statistically significant benefit in mortality. This lack of impact on survival may be attributed to the fact that nitric oxide (NO) does not directly influence lung function, reduce lung injury, or resolve the underlying cause of acute respiratory failure, rendering its benefits transient [12]. This topic has attracted considerable attention during the recent COVID-19 pandemic, with evidence suggesting its efficacy as a rescue therapy in moderate-to-severe acute respiratory distress syndrome (ARDS) [13]. Nonetheless, its application as an early intervention in spontaneously breathing patients remains relatively underexplored.

We describe two cases of acute respiratory failure caused by *Mycoplasma pneumoniae* pneumonia in two young men. They were admitted to the ICU with a high risk of requiring intubation due to hypoxemia, dyspnea, and rapid clinical deterioration [14], but this was avoided through an individualized bridge treatment. Informed consent was obtained from the patients for the use of the data for scientific research purposes.

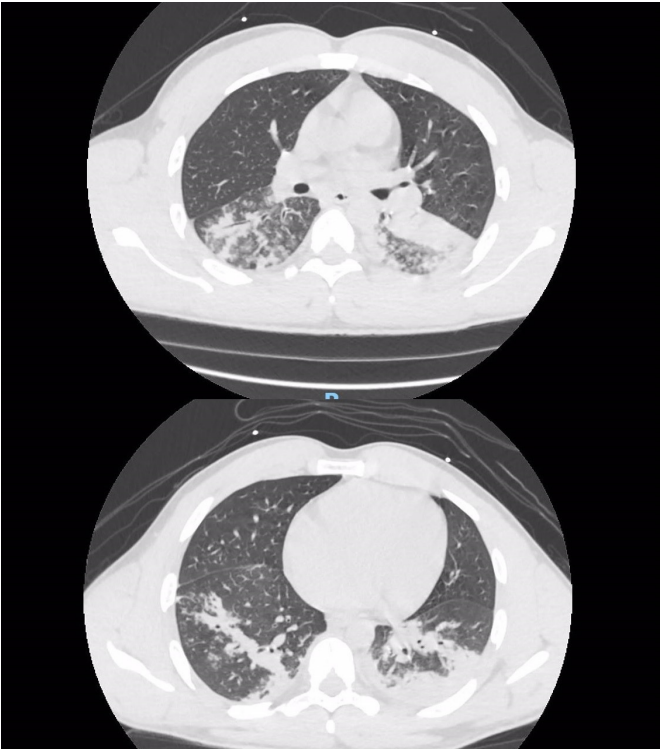
Clinical case 1

A 20-year-old personal trainer, with a history of hypothyroidism and an allergy to clarithromycin, developed flu-like symptoms following a recent trip to Spain. After a week of persistent high fever, cough, and worsening tachypnea, he presented to the emergency department, where a CT scan revealed bilateral pneumonia with a tree-in-bud pattern. Empirical broad-spectrum antibiotic therapy with Levofloxacin and Ceftriaxone was initiated.

Arterial blood gas analysis (ABG) demonstrated hypoxemic respiratory failure without hypercapnia (PH 7.57 PaO_2 44.7 mmHg PCO_2 25.6 mmHg, FiO_2 30%). AHRF did not respond to oxygen therapy with a reservoir mask, with a respiratory rate (RR) of 35-40 breaths per minute.

An angio-TC scan was performed, showing a worsening bilateral pneumonia. (Figure 1)

FIGURE 1



Subsequently, the patient was admitted to the ICU and HFNO (50l FiO2 50%) was initiated. A nasogastric tube with an esophageal pressure transducer was inserted to measure ΔPes. After the placement of the nasogastric tube, the initial esophageal pressure value was 14; we evaluated all factors that can contribute to an increase in swing, such as agitation, fever, and hypoxia. After initiating mild sedation, managing hyperpyrexia, and increasing the inspiratory fraction of oxygen to 65%, the esophageal pressure rapidly decreased to values between 10 and 12. Over a 12-hour period of HFNO treatment, a reduction in ΔPes from 10-12 to 8 cmH20 was observed. Additionally, arterial blood gas analysis demonstrated progressive improvement in PaO2/FiO2 ratio (P/F) from 147 to 204 mmHg with a reduction in FiO2 to 50%, while maintaining normocapnia. The patient’s respiratory discomfort decreased with resolution of fever and tachypnea, and oxygen therapy was transitioned to low-flow nasal cannula. (Table 1)

During the ICU stay, a PCR test for Mycoplasma pneumoniae on a nose-throat swab returned positive. Targeted therapy with Levofloxacin was continued, and the patient was transferred to the internal medicine department the following days.

TABLE 1

	Start	30min after mild sedation and treatment of hyperpyrexia	12h Treatment	24h Treatment	30h Treatment
	HFNC 50L/min FiO2 50%	HFNC 50L/min FiO2 65%	HFNC 50L/min FiO2 65%	HFNC 50L/min FiO2 50%	HFNC 50L/min FiO2 50%
TC °C	38	37	37	36	36
pH	7.45	7.44	7.45	7.45	7.45
pCO2	36.9	38.5	37	36	36
P/F	124	147	183	184	204
ΔPes	14	10-12	8	8	8
RR	35		15	14	13

Clinical case 2

A 26-year-old obese man with a history of insulin resistance managed with metformin therapy presented to the emergency department with persistent cough and fever, which worsened despite antibiotic therapy with ceftriaxone. In the previous days, he also experienced an episode of acute urinary retention, necessitating the placement of a urinary catheter. Blood tests revealed neutrophilic leukocytosis with a slight elevation in serum C-reactive protein (CRP) but not procalcitonin (PCT). A CT scan showed right lobar lung consolidation and a bilateral dorso-basal tree-in-bud pattern. (Figure 2) His ABG shows: PH 7.45 PaO2 64.1 mmhg PCO2 41 mmHg, with FiO2 60% and RR 30 breaths per minute.

FIGURE 2



Initial attempts at low-flow oxygen administration via Ventimask and then via a mask with a reservoir led to further deterioration with tachypnea and desaturation to SpO2 88%, causing patient exhaustion and necessitating ICU admission. Broad-spectrum antibiotic treatment with amoxicillin/clavulanate and clarithromycin was initiated. A subsequent CT scan revealed worsening lung consolidation with a widespread bronchiolitis pattern and areas of air trapping in the superior lobes. In the ICU, High Flow Nasal Cannula (HFNC) oxygenation was initiated concurrently with nitric oxide administration, starting at 20 ppm, guided by a high shunt fraction (calculated as PaO2/PAO2 < 0.2). iNO therapy had no haemodynamic impact on the patient; assessment of respiratory effort was not available in this patient. Multiplex PCR examination of a nasal swab confirmed Mycoplasma pneumoniae infection on the first day of ICU stay, leading to the discontinuation of penicillin derivatives and continuation of macrolide antibiotic therapy. Despite the severity of his condition, orotracheal intubation was not required during the ICU stay. Following an initial phase of worsening oxygenation and PaO2/FiO2 ratio, the patient exhibited significant clinical improvement, disappearance of subjective dyspnea and normalization of sensorium, stabilization of vital parameters, and a reduction in shunt fraction on the second day. This allowed for the gradual reduction of oxygen support and nitric oxide until their discontinuation. The patient was transferred to a low-intensity care unit on the same day with low-flow oxygen via Ventimask. (Table 2)

TABLE 2

	Basal	6h of treatment	12h of treatment	24h of treatment	36h of treatment
	Ventimask FiO2 60%	HFNC 50L/min FiO2 50%	HFNC 40L/min FiO2 40%	HFNC 40L/min FiO2 40%	HFNC 40L/min FiO2 30%
TC °C	36,2	36,3	36,1	36,3	36
pH	7,45	7,47	7.45	7.46	7.4
pCO2	41	36,1	43,6	40,5	45,9
PaO2/PAO2	0,17	0,25	0,37	0,27	0,57
P/F	106	161	215	160	302
iNO (ppm)	-	20	10	5	5
RR	30	11	13	24	16

Discussion

There are no clinical cases in the literature regarding individualized treatments for *Mycoplasma pneumoniae* infection while awaiting the efficacy of antibiotic therapy; with appropriate respiratory support and anti-mycoplasmal therapy, all patients had a rapid clinical improvement.

This is the first case series that describes two different treatments for two distinct clinical presentations, protecting patients from potential damage due to hypoxemia and non-invasive ventilation.

The first case underscores the potential efficacy of HFNO, supported by Δ Pes monitoring, in the management of severe pneumonia complicated by AHRF. The utilization of non-invasive respiratory support in the early management of acute hypoxemic respiratory failure remains a topic of debate. There is evidence suggesting that HFNO may reduce the need for endotracheal intubation, particularly in patients with a $\text{PaO}_2/\text{FiO}_2$ ratio (P/F) ≤ 200 mmHg [5]. Spontaneous breathing may offer multiple benefits in patients with AHRF, including decreased need for sedation, preserved diaphragm activity, improved cardiovascular function, prevents complications associated with endotracheal intubation and invasive mechanical ventilation. However, excessive effort to breathe due to high respiratory drive may lead to P-SILI. High transpulmonary pressure during inspiration and large tidal volumes determine an increase in lung stress and strain [15]. To mitigate this risk, the assessment of inspiratory effort can be performed through measurement of esophageal pressure swing (Δ Pes). As the Δ Pes values indicated normal to low inspiratory effort, HFNO treatment could be continued leading to an improvement in oxygenation without lung damage and with patient's comfort.

Instead, the second case describe how the use of iNO in spontaneously breathing patients could be a bridge of treatment waiting the response to the antibiotics. While iNO has been extensively evaluated as a rescue therapy in mechanically ventilated patients with ARDS, the effects on patients outcomes in spontaneously breathing patients with AHRF due to causes other than Covid-19 are not well described [16]. INO with its property to improve the ventilation-perfusion mismatch, may serve as an alternative or as a bridge to gain time for lung healing; it also has a potential bronchodilator, anti-inflammatory and potentially direct antimicrobial effect [11].

However, this case highlights its potential early

application in acute respiratory failure, potentially averting the need for mechanical ventilation.

Conclusion

Mycoplasma pneumoniae is characterized by its atypical clinical and radiological presentation. Through the analysis of these two cases, we emphasize the crucial importance of personalized management of hypoxemia in severe instances, using a continuous monitoring of effort by Pes and the use of a selective vasodilator that may optimize ventilation/perfusion matching increasing oxygenation, while awaiting the effect of antibiotic therapy. Additionally, despite the patients not requiring intubation, it is imperative to admit and manage severe cases in ICU. This approach facilitates close monitoring and the potential for therapeutic escalation, ensuring comprehensive care for optimal patient outcomes. Further research is warranted to elucidate the optimal approach to non-invasive respiratory support and prevention of P-SILI in the early stages of AHRF. Further researches are needed to assess the efficacy of inhaled nitric oxide in preventing tracheal intubation.

References

1. Martin-Loeches I, Torres A, Nagavci B et al. ERS/ESICM/ESCMID/ALAT guidelines for the management of severe community-acquired pneumonia. *Eur Respir J*. 2023 Apr 3;61(4):2200735. doi: 10.1183/13993003.00735-2022.
2. Fujikura Y, Somekawa K, Manabe T et al. Aetiological agents of adult community-acquired pneumonia in Japan: systematic review and meta-analysis of published data. *BMJ Open Respir Res*. 2023 Sep;10(1):e001800. doi: 10.1136/bmjresp-2023-001800.
3. Lv YT, Sun XJ, Chen Y, Ruan T, Xu GP, Huang JA. Epidemic characteristics of *Mycoplasma pneumoniae* infection: a retrospective analysis of a single center in Suzhou from 2014 to 2020. *Ann Transl Med*. 2022 Oct;10(20):1123. doi: 10.21037/atm-22-4304.
4. Ding L, Zhao Y, Li X et al. Early diagnosis and appropriate respiratory support for *Mycoplasma pneumoniae* pneumonia associated acute respiratory distress syndrome in young and adult patients: a case series from two centers. *BMC Infect Dis*. 2020 May 24;20(1):367. doi: 10.1186/s12879-020-05085-5.
5. Frat JP, Thille AW, Mercat A, et al. FLORALI Study Group; REVA Network. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. *N Engl J Med*. 2015 Jun 4;372(23):2185-96. doi: 10.1056/NEJMoa1503326.

6. Bellani G, Laffey JG, Pham T et al. Noninvasive Ventilation of Patients with Acute Respiratory Distress Syndrome. Insights from the LUNG SAFE Study. *Am J Respir Crit Care Med*. 2017 Jan 1;195(1):67-77. doi: 10.1164/rccm.201606-1306OC.
7. Brochard L, Slutsky A, Pesenti A. Mechanical Ventilation to Minimize Progression of Lung Injury in Acute Respiratory Failure. *Am J Respir Crit Care Med*. 2017 Feb 15;195(4):438-442. doi: 10.1164/rccm.201605-1081CP.
8. Tonelli R, Fantini R, Tabbi L et al. Early Inspiratory Effort Assessment by Esophageal Manometry Predicts Noninvasive Ventilation Outcome in De Novo Respiratory Failure. A Pilot Study. *Am J Respir Crit Care Med*. 2020 Aug 15;202(4):558-567. doi: 10.1164/rccm.201912-2512OC..
9. Yoshida T, Brochard L. Esophageal pressure monitoring: why, when and how? *Curr Opin Crit Care*. 2018 Jun;24(3):216-222. doi: 10.1097/MCC.0000000000000494.
10. Sklienka P, Frelich M, Burša F. Patient Self-Inflicted Lung Injury-A Narrative Review of Pathophysiology, Early Recognition, and Options. *J Pers Med*. 2023 Mar 28;13(4):593. doi: 10.3390/jpm13040593.
11. Redaelli S, Magliocca A, Malhotra R et al. Nitric oxide: Clinical applications in critically ill patients. *Nitric Oxide*. 2022 Apr 1;121:20-33. doi: 10.1016/j.niox.2022.01.007.
12. Karam O, Gebistorf F, Wetterslev J, Afshari A. The effect of inhaled nitric oxide in acute respiratory distress syndrome in children and adults: a Cochrane Systematic Review with trial sequential analysis. *Anaesthesia*. 2017 Jan;72(1):106-117. doi: 10.1111/anae.13628..
13. Al Sulaiman K, Korayem GB, Altebainawi AF, et al. Evaluation of inhaled nitric oxide (iNO) treatment for moderate-to-severe ARDS in critically ill patients with COVID-19: a multicenter cohort study. *Crit Care*. 2022 Oct 3;26(1):304. doi: 10.1186/s13054-022-04158-y.
14. Grieco DL, Menga LS, Cesarano M et al. Effect of Helmet Noninvasive Ventilation vs High-Flow Nasal Oxygen on Days Free of Respiratory Support in Patients With COVID-19 and Moderate to Severe Hypoxemic Respiratory Failure: The HENIVOT Randomized Clinical Trial. *JAMA*. 2021 May 4;325(17):1731-1743. doi: 10.1001/jama.2021.4682.
15. Spinelli E, Mauri T, Beitler JR, Pesenti A, Brodie D. Respiratory drive in the acute respiratory distress syndrome: pathophysiology, monitoring, and therapeutic interventions. *Intensive Care Med*. 2020 Apr;46(4):606-618. doi: 10.1007/s00134-020-05942-6.
16. Chandel A, Patolia S, Ahmad K et al. Inhaled Nitric Oxide via High-Flow Nasal Cannula in Patients with Acute Respiratory Failure Related to COVID-19. *Clin Med Insights Circ Respir Pulm Med*. 2021 Sep 29;15:11795484211047065.doi: 10.1177/11795484211047065.