

#### Introduction

Community-acquired pneumonia is a leading cause of morbidity and mortality *Mycoplasma* pneumoniae with (M.pneumoniae) accounting for up to 30% of all cases.<sup>1-3</sup> *M. pneumoniae* usually presents with a benign course. Fewer than 10% of cases are clinically apparent and fewer than 5% of those cases requiring hospitalization.<sup>3-</sup> <sup>5</sup> Of those requiring hospitalization, 10% will require admission to an intensive care unit (ICU) with mechanical ventilation as a result of Acute Respiratory Distress Syndrome (ARDS).

The literature presents cases where a previously healthy subject, between the ages of 18 and 37, progressed to ARDS and the associated severe complications.<sup>4-8</sup> Many of these cases presented for medical treatment after up to 10 days of non-specific symptoms such as fatigue, myalgia, and low- to high-grade fever. The majority of these cases received appropriate medical care, including antibiotic therapy, at time of presentation. However, disease progression continued and sometimes resulted in patient demise.

Theories explaining how *M. pneumoniae* infection can require admission to an ICU for a young, previously healthy adult rely on the host's immune response rather than the microbial agent.<sup>3,9,10</sup> The immune response mounted by the host, a delayed hypersensitivity with an associated excessive

# Mycoplasma Pneumoniae Requiring Mechanical Ventilation

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host-cellular response involving neutrophils, IL-2, IL-8, IL-12, IL-18, causes the damage to the lung parenchyma that results in ARDS. Due to this hypothesis, the addition of high dose corticosteroids in conjunction with the appropriate antibiotic coverage is successful in treating this subpopulation.<sup>3,4,8</sup>

We present a case in which the appropriate antibiotic coverage was insufficient to prevent the progression of respiratory distress. After the patient was intubated and admitted to the ICU, corticosteroids were added to the treatment regimen and the patient made a complete recovery.

#### Case Report

A 46-year-old woman with a 19-month history of seizure disorder, secondary to a closed head injury, presented with altered mental status for the preceding 24 hours. Home medications included valproate, levetiracetam, hydrocodone/acetaminophen, propranolol, and alprazolam. Social history was significant for tobacco use and a monogamous long-term sexual relationship. Recent history included a flight to Atlanta one week earlier to visit a hospitalized and intubated relative diagnosed with AIDS and lymphoma.

The patient arrived via emergency medical services (EMS) with a Glasgow Coma Scale (GCS) of 7 (Eyes 2, Verbal 2, Motor 3). Associated signs and symptoms recorded by EMS included tachycardia (130 bpm), hypotension (70/36 mmHg), difficulty in breathing, productive cough for past four days, decreased appetite and oral intake, hypoglycemia (31 mg/dL), and four break-through seizures in the previous 24 hours. In the emergency department, the patient's vitals stabilized initially. Her oxygen saturation ( $O_2Sat$ ) then decreased to 89% and subsequently to 79%, requiring BiPAP of 10 cmH<sub>2</sub>O/5 cmH<sub>2</sub>O with FiO<sub>2</sub> of 1.00 to return to 100%  $O_2Sat$ .

On physical examination at time of admission, the patient was unresponsive with sluggish pupils constricted to 1 mm and bilateral crackles upon auscultation of the lungs. The patient was in shock and resuscitation was started. A chest x-ray was obtained (see Figure 1a).

Laboratory testing revealed leukocytosis  $(20.6 \times 10^3/\text{mm}^3)$  with a predominance of neutrophils (86%). Other significant laboratory findings included elevated INR (1.39) elevated liver enzymes (AST 1045 U/L; ALT 569 U/L) and ammonia (164 µmol/L), and evidence of hemolysis (LDH 1344 U/L).

Initial treatment included naloxone, dextrose, dexamethasone, and normal saline bolus with improvement in the patient's mental status. Empiric treatment included trimethoprim/sulfamethoxazole, ceftriaxone, azithromycin, and nystatin. Samples were cultured and serology testing was performed. The results were negative for influenza A and B. Streptococcus pneumoniae, viral hepatitis A, B, and C, legionella, human immunodeficiency virus cytomegalovirus (CMV), (HIV). and Pneumocystis jirovecii (P. jirovecii). Only the serology tests for Mycoplasma IgM and IgG were positive.

On the second day, respiratory distress progressed despite antibiotic treatment. The patient was intubated and transferred to ICU with oxygen saturation less than 80% and respiratory rate greater than 50. The chest x-ray at this time is presented in Figure 1b.

On the fifth day of admission, her clinical presentation had not improved and high dose corticosteroids were added to her regimen. The patient's respiratory function improved and she was extubated on the seventh day of admission. The chest x-ray at this time is shown in Figure 1c.

The patient was discharged the following day with prescriptions for azithromycin for three weeks and tapered prednisone for two weeks. She was scheduled for a follow-up appointment one week later.

## Discussion

This case highlighted the need to be aware of *M. pneumoniae* as an agent capable of causing a serious clinical picture. The patient presented as a medical resuscitation and that made many conditions more likely candidates than *M. pneumoniae* on the initial differential diagnoses. Suspicions of other causative agents mirrored the approach of others in similar instances.<sup>6</sup> Abnormal liver function tests initially were attributed to valproate use, but the values trended towards normal without discontinuation of valproate. Serum viral hepatitis titers also were negative suggesting the hepatitis was due most likely to the severe *M. pneumoniae* infection.<sup>3,6</sup> Elevated lactate dehydrogenase (LDH) suggested P. jiroveci, but sputum testing was negative and the patient was confirmed to be HIV negative. Elevated LDH has been reported in other cases of M. pneumoniae progressing to respiratory failure.<sup>3</sup> While elevated LDH and transaminase levels may be associated with severe *M. pneumoniae* infections, the contribution of multiple seizures and hemolytic anemia cannot be negated entirely. However, both of these clinical manifestations also were most likely the result of the M. pneumoniae infection.



Figure 1. Patient chest x-rays: (a) At admission, diffuse bilateral ground glass opacities without focal consolidation; (b) On  $2^{nd}$  day, worsening diffuse bilateral ground glass opacities; (c) On  $7^{th}$  day, persistent left lower lobe patchy infiltrates with interval slight improvement in the left perihilar region and right lower lobe.

Currently, antimicrobials are the sole therapy for *M. pneumoniae*, but this case and those in the literature demonstrated they are not always sufficient to halt the disease progression and prevent the need for mechanical ventilation.<sup>4,6-8</sup> Animal studies have shown that early treatment with corticosteroids and antibiotics is crucial in the successful resolution of symptoms and prevention of fulminant pneumonia and death.<sup>4,10</sup>

Of the 13 cases of fatal *M. pneumonia* infection reviewed by Chan and Welsh,<sup>4</sup> only two patients may have received corticosteroids with antibiotic treatment. One patient received only one dose and it is questionable whether the second patient received corticosteroids at all. Interestingly, 8 of 26 patients with non-fatal respiratory failure received combination therapy.<sup>4</sup>

Other case studies reported this successful combination.<sup>11</sup> Daxboeck et al.<sup>6</sup> presented a fatal case of respiratory failure due to *M. pneumoniae* in which the clinical deterioration progressed despite the "presumable eradication of the pathogen itself." Chan and Welsh's review<sup>4</sup> noted four cases of "unusually severe" M. pneumoniae infection in immunocompromised adolescents for which the chest x-ray demonstrated minimal or no changes. Furthermore, these same patients made a recovery with antibiotic treatment alone. For our immunocompetent patient, the combination of antibiotics and corticosteroids led to improvements in her status when antibiotics alone did not halt the progressive respiratory failure.

In retrospect, there were other factors to consider with this patient. The multiple seizures preceding hospitalization could have contributed to the ARDS. Aspiration of stomach contents during a seizure is not necessarily common but has been documented to occur.<sup>12</sup> In our case, the sputum samples did not provide evidence of stomach flora and the chest x-ray did not show a focal consolidation. Chemical damage from aspiration was unlikely to be the cause of failure in our case, but should be a consideration in similar instances.

The seizure activity was interesting. The patient reported compliance with her valproate regimen and the laboratory results supported the claim. Neurologic complications of *M. pneumoniae* infection include both central and nervous system involvement<sup>4,8,13,14</sup> and it is possible that our patient's seizures were a manifestation of these complications.

On autopsy of a previously healthy 27year-old woman who succumbed to ARDS secondary to M. pneumoniae infection, Tapyrik and Goldenberg<sup>8</sup> noted acute hemorrhagic leukoencephalitis (AHLE). One of the fatal cases of respiratory failure reviewed by Chan and Welsh<sup>4</sup> also demonstrated "multiple thrombi in leptomeninges" on autopsy and one of the nonfatal cases was noted to have "Guillain-Barre syndrome". Seales and Greer<sup>13</sup> presented a case of AHLE that occurred approximately seven days after the onset of M. pneumoniae infection. Their patient made a complete recovery with treatment including corticosteroids.

Our patient's anemia was not unusual. *M. pneumonia* has caused cold agglutinins and anemia even in mild cases of pneumonia.<sup>15</sup> While we did not have the data related to the patient's hematologic status prior to this case, we have reason to believe that her anemia was of new onset and hemolytic in nature. The size and hemoglobin concentration of the patient's red blood cells were within normal limits, but her LDH was elevated.

The final consideration is the judicious use of corticosteroids despite the demonstrated benefits with complications such as ARDS and AHLE.<sup>3,4,8,13</sup> Time is of the essence with evidence to suggest that the sooner corticosteroid treatment is initiated, the better the clinical outcome will be.<sup>3,4,8,10</sup> However, care must be taken to insure the appropriate antibiotic treatment continues as the immune response is suppressed to prevent further damage to the lungs and nervous system. This is of utmost importance for patients who are intubated for mechanical ventilation as they may be at an increased risk of acquiring a nosocomial infection.<sup>16</sup> The index of suspicion should be high as there is evidence that identifying a nosocomial infection in an ICU patient is difficult at the best of times.<sup>17</sup>

## Conclusion

M. pneumoniae infection often does not

## References

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require hospitalization or antibiotic treatment but our patient presented an example where hospitalization, ICU admission, and mechanical ventilation were all required. Antibiotic treatment alone was insufficient to halt the progression of the respiratory failure. Clinical improvement and resolution occurred in the setting of combination therapy with azithromycin and high-dose corticosteroids.

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