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Case Report

Not-so-walking pneumonia: challenges in managing mycoplasma complicated by autoimmune hemolytic anemia in a young female

Sanket P. Bharadwaj[1], Rachit Sharma[2], Yatri S. Patel[1], Dhruvi A. Shah[2], Aneeket T. Marwah[1]*

[1]Department of General Medicine, Smt. N.H.L. Municipal Medical College, Ahmedabad, Gujarat, India
[2]Department of General Medicine, GMERS Medical College, Sola, Ahmedabad, Gujarat, India

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***Correspondence:**
Dr. Aneeket T. Marwah,
E-mail: aneeketmarwah95@gmail.com

ABSTRACT

Mycoplasma pneumoniae (Eaton agent) is a leading cause of atypical community-acquired pneumonia and can present with serious complications like acute respiratory distress syndrome (ARDS), acute respiratory failure and a variety of extrapulmonary manifestations including significant hemolysis. In this case report, we describe a case of a 17-year-old female with *Mycoplasma pneumonia* accompanied by major complications including hemolysis and possible macrolide resistance and explore the clinical obstacles faced in its diagnosis and treatment. The patient presented to the emergency room with a 10-day history of high-grade fever, coryza and dry cough with worsening dyspnea and palpitations since one day. Along with routine hematological and radiological workup, molecular and serological investigations confirmed the diagnosis. The patient was managed by a multidisciplinary team and had a prolonged hospital stay. She was primarily managed with antibiotics followed by glucocorticoids. She was discharged with oral prednisolone in tapering doses and showed a favorable recovery on follow-up. This case highlights the importance of including Mycoplasma in the differential diagnosis for a young adult with pneumonia and extrapulmonary manifestations especially in cases of non-responsiveness to conventional beta lactam therapy. Macrolide resistant *M. pneumoniae* strains have increasingly become prevalent in Asia. The case also emphasizes the significance of early diagnosis and prompt intervention to reduce complications and aid quick recovery.

Keywords: Atypical pneumonia, Mycoplasma pneumoniae, Autoimmune hemolytic anaemia, Macrolide resistance, Glucocorticoids

INTRODUCTION

Mycoplasma pneumonia also known as "walking pneumonia" is a well-recognized form of atypical pneumonia caused by *Mycoplasma pneumoniae* in 3-13% of infected cases, particularly among middle-aged school students. It typically results in a mild upper respiratory infection including pharyngitis, tracheobronchitis or reactive airway disease that seldom requires antimicrobial treatment. However, severe pneumonia leading to respiratory failure and hospitalization can occur.[1]

Non-productive cough is the predominant symptom, along with fever, headache and malaise seen in the majority of patients. Around a quarter of patients may also experience extrapulmonary complications including neurological, dermatologic, cardiac, rheumatologic, renal, gastrointestinal and hematologic- such as encephalitis, skin rashes, myocarditis to name a few. Hematological manifestations include autoimmune hemolytic anemia (AIHA), hemophagocytosis, thrombotic thrombocytopenic purpura and disseminated intravascular coagulation.[2] These manifestations can manifest before, during, after, or independently of pulmonary symptoms.[3]

Acute infection can be diagnosed by polymerase chain reaction (PCR) detection of the organism in respiratory tract secretions - oropharyngeal, nasopharyngeal and

pulmonary specimens are acceptable. Serological tests for IgM and IgG antibodies against the organism by enzyme linked immunosorbent assay (ELISA) in paired serum samples combined with PCR remains the most sensitive and rapid approach for diagnosis.

Mycoplasma pneumoniae infection is often linked with the presence of IgM cold agglutinins, resulting in hemolysis. However, severe hemolysis due to *Mycoplasma* infection is exceedingly uncommon. Macrolide resistance to the tune of >90% in a few countries of the Asian continent has been described in literature and such patients typically experience a significantly longer duration of symptoms, as was the case with our patient.

Here, we present an unusual case of *Mycoplasma pneumoniae* pneumonia causing autoimmune hemolysis, with probable macrolide resistance in an immunocompetent patient.

CASE REPORT

A 17-year-old female presented to our hospital with a 10-day history of high-grade fever associated with dry cough, coryza and sore throat. The patient had developed breathlessness at rest associated with palpitations one day before presentation. The patient had no known co-morbidities and was not using any drugs. There was no significant travel history. Prior to admission to our hospital, laboratory investigations done at an outside setup were suggestive of anemia with normal white blood cell counts. The patient had received oral antibiotics-amoxicillin-clavulanic acid 625 mg thrice a day along with azithromycin 500 mg once a day for 5 days before presenting to our hospital.

Upon examination, the patient appeared pale, sick and dyspneic. Physical examination revealed temperature of 100.4 F, heart rate 140 beats/min, respiration 32 times/min, blood pressure 118/80 mm Hg, and transcutaneous oxygen saturation 91% on ambient air. Respiratory auscultation showed right sided crepitations coupled with decreased air entry. There was no organomegaly or lymphadenopathy. The rest of the examination was unremarkable. Urine pregnancy test was negative.

A nasopharyngeal swab was taken and was found negative for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and all strains of influenza virus. Initial investigations (Table 1) were suggestive of a Hb of 6.7 g/dl, with mean corpuscular volume of 83 fl, total leukocyte count of 10,500/ul with 83% neutrophils, 7% lymphocytes, and erythrocyte sedimentation rate (ESR) 7 mm/hour.

Peripheral smear was suggestive of microcytic polychromatic red blood cells (RBCs) with anisopoikilocytosis and clumping of RBCs. Malaria by paracheck, dengue NS-1, IgM and Widal test were negative. The serology for HIV, hepatitis B, and C was negative. Serum IgE levels were within normal limits. Corrected reticulocyte count was 4% with a strongly positive (4+) direct and indirect Coombs test, suggestive of autoimmune hemolytic anemia (AIHA).

Urine for routine examination was normal. Blood cultures were negative for microbial growth. Bedside echocardiography was suggestive of left ventricular ejection fraction (LVEF) of 55% with no regional wall motion abnormalities, mild mitral and tricuspid regurgitation, no clot/vegetation/effusion and an inferior vena cava (IVC) diameter of 1.5 cm-collapsible with respiratory variability.

Chest X-ray (Figure 1a) was suggestive of patchy air space opacities in the right lower zone, suggestive of changes of consolidation. High-resolution computed tomography (HRCT) thorax (Figure 1b) was suggestive of active infective etiology in the form of dense area of consolidation with internal air bronchogram with adjacent nodular infiltrates in the right lower lobe.

Table 1: Hematological investigations at the time of initial admission.

Investigations	Results	Reference range
Hemoglobin (Hb) (g/dl)	6.7	12-18
Total leukocyte count (TLC) (/ul)	10,500	4000-10000
Absolute platelets count (APC) (/ul)	2,50,000	150-410
Urea (mmol/l)	25.9	15-40
Serum creatinine (mg/dl)	0.92	0.6-1.2
Na+ (mEq/l)	129	135-145
K+ (mEq/l)	4.32	3.5-5.5
SGPT (U/l)	124	10-49
SGOT (U/l)	115	10-34
ALP (U/l)	218	45-150
Total/direct bilirubin (mg/dl)	1.62/0.61	0.1-1.2/0-0.3
Total proteins/serum albumin (gm/dl)	6.75/3.39	6-8/3.5-5.5
CRP	151	Negative (<5)

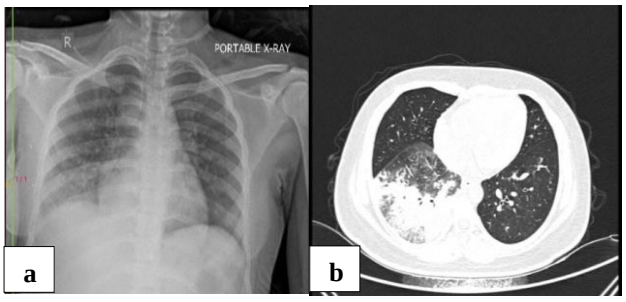

Figure 1: (a) X-ray chest anteroposterior view, and (b) HRCT thorax on admission.

She was supported with 2 l/min of oxygen via face mask and was started on empirical antibiotics for community acquired pneumonia- intravenous ceftriaxone 2 gram/day plus oral azithromycin 500 mg once daily with empirical antiviral oseltamivir 75 mg twice daily.

One unit of packed red cells was transfused in view of anemia. In view of persistent fever spikes and oxygen requirement, ceftriaxone was switched over to piperacillin+tazobactam two days later. Five days later, piperacillin-tazobactam was discontinued and intravenous meropenem and linezolid were initiated for added Gram negative and methicillin resistant *Staphylococcus aureus* (MRSA) coverage. Departmental 2D echocardiography was done in order to rule out valvular pathology/ vegetations in view of persistent tachycardia. A repeat X-ray chest and HRCT thorax (Figure 2) done a week later showed mild reduction in nodular infiltrates.

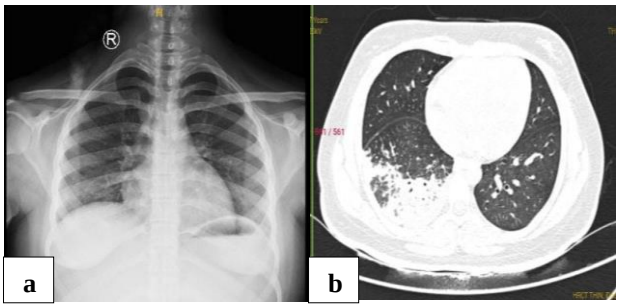

Figure 2: (a) X-ray chest postero-anterior view, and (b) HRCT thorax done one week later.

Atypical pneumonia panel by immunofluorescence from serum showed *Mycoplasma pneumoniae* IgM positive (3+ intensity). In view of persistent oxygen requirement and fever spikes, pulmonology reference was done and bronchoalveolar lavage (BAL) was performed. Real time PCR from BAL fluid showed the presence of *Mycoplasma pneumoniae*. Suspecting macrolide resistance, the patient was started on second line drugs for the detected organism-intravenous moxifloxacin 400 mg once a day with oral doxycycline 100 mg twice a day and continued for a total of 14 days, following which the patient gradually became afebrile and improved.

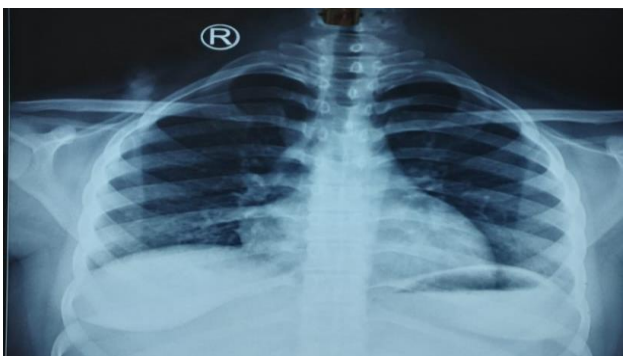

Figure 3: X-ray chest postero-anterior view two weeks after discharge.

Hematology opinion for AIHA was taken and in view of resolving sepsis the patient was started on oral steroids-prednisolone 40 mg per day for one week followed by gradual tapering. The patient was discharged 17 days after admission. Complete blood counts on follow-up were normal.

DISCUSSION

This was an unusual case of *Mycoplasma pneumoniae* pneumonia causing autoimmune hemolysis, with probable macrolide resistance in an immunocompetent patient. Mycoplasma pneumonia is often referred to as "walking pneumonia" due to its typically mild nature and tendency to resolve without complications either spontaneously or with supportive care alone. Patients commonly present with fever, cough, myalgias, headache and gastrointestinal symptoms. It can cause a wide range of extrapulmonary manifestations. One such complication seen in our patient is the development of hemolytic anemia, which has been reported in association with severe pneumonia caused by this organism. The pathogenesis of this phenomenon is not fully understood, but it is thought to involve both local vascular effects and systemic immune-mediated mechanisms.[4]

In the West, *Mycoplasma pneumoniae* is a well-known respiratory pathogen, but data on its prevalence in India is limited due to challenges in rapid and reliable diagnostic techniques across healthcare facilities, as well as insufficient awareness of severe presentations.[5] Vascular thrombosis and infarctions, attributed to cold agglutinin-induced hemolysis and a hypercoagulable state, are reported in nearly half of fulminant infection cases.[5] Approximately 0.5–2% of *Mycoplasma pneumonia* cases can progress rapidly to life-threatening complications, such as respiratory failure, particularly in young, otherwise healthy adults, possibly due to host-related factors and an exaggerated cellular immune response.[6]

Severe disease is often associated with cytokine release, contributing to significant pulmonary injury and clinical illness severity. This immune-mediated injury underscores the consideration of immunomodulatory therapies in addition to conventional antimicrobial treatments.[7] Severe pneumonia can lead to diffuse alveolar damage with fibrinous exudates within alveolar lumens, resulting in consolidation. Co-existing conditions such as diabetes, cancer, and heart disease further complicate the clinical course.[8]

Given the variability of radiographic findings and their overlap with other conditions, a high index of suspicion is crucial for Mycoplasma pneumonia diagnosis. Definitive diagnosis relies on a combination of clinical assessment, radiographic findings, PCR, and serological testing. Enzyme-linked immunoassay-based serology targeting IgM, IgA, or IgG against *Mycoplasma pneumoniae* aids in diagnosis, as bacterial isolation from sputum is often unreliable.[9]

Recent advances in nucleic acid amplification tests and multiplex PCR have revolutionized respiratory infection diagnosis, offering high sensitivity and simultaneous detection of a broad range of pathogens, including viruses and atypical bacteria (*Mycoplasma pneumoniae, Chlamydophila pneumoniae, Legionella pneumophila, Bordetella pertussis*), thereby enabling prompt treatment initiation.[10]

Due to the lack of a cell wall, *Mycoplasma pneumoniae* is not visualized on gram staining and is insensitive to beta-lactam antibiotics. Empirical antibiotic therapy for community-acquired pneumonia should cover both "typical" (e.g., *Streptococcus pneumoniae*) and "atypical" (e.g., *Mycoplasma pneumoniae*) organisms due to challenges in predicting the specific etiological agent.[11] For severe, life-threatening *Mycoplasma pneumonia*, early administration of anti-mycoplasma drugs (macrolides such as erythromycin, clarithromycin, and azithromycin) has been recognized as beneficial.[12] Data from Chinese and Japanese studies reveals an increasing proportion of macrolide resistant isolates.[13] Treatment with second-line drugs including tetracycline and fluoroquinolones in suspected macrolide resistance leads to successful recovery, as was seen in this patient.

CONCLUSION

This case was challenging on multiple grounds of conventional therapeutics, including intractable tachycardia due to the dual trouble of infective etiology with severe anemia, unavailability of donor blood due to non-matching and agglutination, continuous fever spikes due to presumed macrolide resistance and delayed introduction of steroids after beginning of resolution of septic parameters. A multidisciplinary team including internal medicine, pulmonary medicine, infectious disease and hematology were involved in the management of this patient. *M. pneumoniae* should be considered a leading differential in pneumonia with hematological abnormalities. A low threshold of suspicion and timely diagnostic and therapeutic interventions are vital in the treatment of this condition.

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REFERENCES

1. Widén J, Jönsson G, Karlsson U. Mycoplasma pneumonia with severe cold agglutinin hemolysis, thrombocytosis, leukemoid reaction and acute renal failure. IDCases. 2023;31:e01689.
2. Kumaravel Kanagavelu A, Nagumantry S, Sagi S, Oyibo S. A rare case of severe hemolytic anemia and pulmonary embolism secondary to Mycoplasma pneumoniae infection. J Med Cases. 2022;13.
3. Waites KB, Talkington DF. Mycoplasma pneumoniae and its role as a human pathogen. Clin Microbiol Rev. 2004;17(4):697-728.
4. Narita M. Two unexpected phenomena in macrolide-resistant Mycoplasma pneumoniae infection in Japan and the unique biological characteristics of Mycoplasma pneumoniae. J Infect Chemother. 2011;17(5):735-6.
5. Salama A. Acquired immune hemolytic anemias. Ther Umsch. 2004;61(2):178-86.
6. Unni A, Hidayathulla PK, Kavitha KP, Paloth MN, Nair PR, Kumar P J, et al. A fulminant pneumonia due to Mycoplasma pneumoniae - Case report and literature review. IDCases. 2022;29:e01552.
7. Kumaravel Kanagavelu A, Nagumantry S, Sagi S, Oyibo S. A rare case of severe hemolytic anemia and pulmonary embolism secondary to Mycoplasma pneumoniae infection. J Med Cases. 2022;13.
8. Zhang T, Han C, Guo W, Ning J, Cai C, Xu Y. Case Report: Clinical Analysis of Fulminant Mycoplasma pneumoniae Pneumonia in Children. Front Pediatr. 2021;9:741663.
9. Talkington DF, Shott S, Fallon MT, Schwartz SB, Thacker WL. Analysis of eight commercial enzyme immunoassay tests for detection of antibodies to Mycoplasma pneumoniae in human serum. Clin Diagn Lab Immunol. 2004;11(5):862-7.
10. Calderaro A, Buttrini M, Farina B, Montecchini S, De Conto F, Chezzi C. Respiratory tract infections and laboratory diagnostic methods: A review with a focus on syndromic panel-based assays. Microorganisms. 2022;10(9):1856.
11. Thibodeau KP, Viera AJ. Atypical pathogens and challenges in community-acquired pneumonia. Am Fam Physician. 2004;69(7):1699-706.
12. Matsumoto M, Nagaoka K, Suzuki M, Konno S, Takahashi K, Takashina T, et al. An adult case of severe life-threatening Mycoplasma pneumoniae pneumonia due to a macrolide-resistant strain, Japan: a case report. BMC Infect Dis. 2019;19(1):204.
13. Okazaki N, Narita M, Yamada S, Izumikawa K, Umetsu M, Kenri T, et al. Characteristics of macrolide-resistant Mycoplasma pneumoniae strains isolated from patients and induced with erythromycin in vitro. Microbiol Immunol. 2001;45(8):617-20.

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