

A CASE OF EXTRA-PULMONARY MYCOPLASMA PNEUMONIAE INFECTION

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Abstract

Mycoplasma pneumoniae is a common atypical pathogen causing community-acquired pneumonia (CAP), mostly in children and young adults with age between 5 and 40 years old. Beyond respiratory symptoms, extra-pulmonary features are described, such as skin rash, arthralgia, gastrointestinal symptoms, and heart disease, occurring in less than 5% to 10% of patients⁽¹⁾. This case refers to a 26-year-old patient, without significant medical history or background treatment, immunocompetent, who is presenting to the emergency room for prolonged fever, and conjunctival suffusions. Following the investigations, pneumonia, and conjunctivitis due to atypical bacteria are suspected and appropriate treatment is administered. Along with other multiple infectious agents that could precipitate a respiratory febrile infection with ocular involvement, we should consider also *Mycoplasma pneumoniae* as a possible cause. Appropriate antibiotic therapy may result in a favorable, but delayed course of the disease.

Keywords: *Mycoplasma pneumoniae*, infection, conjunctivitis, pneumonia, atypical bacteria.

Abstract

Mycoplasma pneumoniae este un agent patogen atipic frecvent care cauzează pneumonie dobândită în comunitate (PAC), mai ales la copii și adulți tineri cu vârsta cuprinsă între 5 și 40 de ani. Dincolo de simptomele respiratorii, sunt descrise caracteristici extra-pulmonare, cum ar fi erupția cutanată, artralgie, simptomele gastrointestinale și afecțiunile cardiace, care apar la 5% până la 10% dintre pacienți⁽¹⁾. Acest caz prezintă un pacient de 26 de ani, fără antecedente medicale semnificative sau tratament de fond, imunocompetent, care se prezintă la camera de gardă pentru febră prelungită și sufuziuni conjunctivale. În urma investigațiilor se suspectează pneumonie și conjunctivită cauzate de microorganisme atipice și se administrează terapia adecvată. Alături de mulți alți agenți infecțioși care ar putea precipita o infecție respiratorie febrilă cu afectare oculară, ar trebui să luăm în considerare, ca o posibilă cauză, și *Mycoplasma pneumoniae*. Terapia adecvată cu antibiotice poate determina evoluția favorabilă, deși întârziată, a bolii.

Cuvinte cheie: *Mycoplasma pneumoniae*, infecție, conjunctivită, pneumonie, bacterii atipice.



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Introduction

Of all the cases of community-acquired pneumonia, more than 15% of them are caused by an atypical pathogen, zoonotic (*Chlamydia psittaci*, *Fancisella tularensis*, *Coxiella burnetti*) or non-zoonotic (*Chlamydia pneumoniae*, *Mycoplasma pneumoniae*, *Legionella*)⁽²⁾.

Mycoplasma pneumoniae is the smallest bacteria with a self-limiting capacity⁽³⁾, without a wall cell that makes this organism unresponsive to beta-lactam anti-microbial agents⁽³⁾ Usually, *M. pneumoniae* infection is self-limited ranging from asymptomatic to mild forms. *M. pneumoniae* infection affects the upper and lower respiratory tract, and can have extrapulmonary involvement⁽³⁾.

The aim of this paper is to raise awareness of the importance of the differential diagnosis in a febrile illness, and the role of a multi disciplinary team in managing the case.

Case report

A 26-year-old male patient living in the country, with no significant medical history, no ongoing treatment, no travel history in the past three months, presented to the emergency room for persistent high fever (38.9°C), fatigability, mild headache, myalgia predominantly in the lower limbs, and hyperemic conjunctives with a three-day

earlier onset. He has been under treatment with antibiotics for 2 days, set by a generalist practitioner for a probable bacterial pharyngitis. On physical examination, the patient had an altered general condition, fever, myalgia, and hyperemic conjunctivae (Figure 1). There was no evidence of pulmonary rales, additional heart murmurs, or lymph nodes enlargement.



Figure 1. Hyperemic conjunctivae

Although the clinical exam suggested a viral etiology, laboratory findings detected elevated levels of muscle enzymes and inflammatory markers, with negative serology for VHC, VHB, HIV, and syphilis. Imaging investigations revealed minimal right basal pleural thickening with pulmonary ventilation disturbances (Figure 2, 3), and also slightly enlarged mediastinal lymph nodes (Figure 4). Considering the above, the diagnosis of community-acquired pneumonia with atypical bacteria is very probable and serological tests for *Coxiella burnetii*, *Leptospira*, *Chlamydia pneumoniae*, and *Mycoplasma pneumoniae* were requested. A combination therapy with Ceftriaxone and



Figure 2. Thoracic radiography - asymmetric findings in the lower lobes due to the interstitium changes in the right lung



Figure 3. Computed tomography of the lungs - interstitium changes in the right base

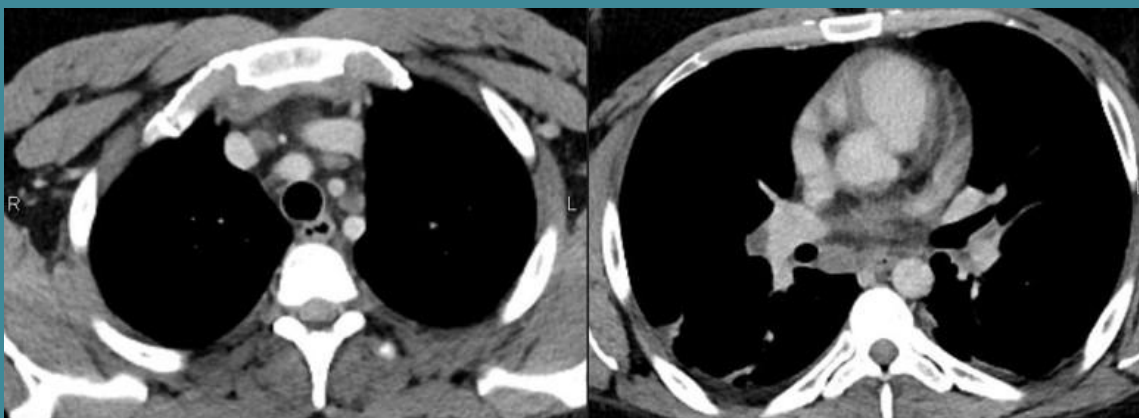


Figure 4. Computed tomography of the lungs - mediastinal slightly enlarged lymph nodes



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Doxycycline was initiated. The fever and myalgias persisted even after 4 days of therapy (Figure 5), accompanied by an increase in the inflammatory syndrome (Table 1). The antimicrobials were then switched to Doxycycline associated with Meropenem and a non-infectious cause was suspected.

A multidisciplinary team was required in order to expand the differential diagnosis. The ophthalmological examination confirmed conjunctivitis in an infectious context without advocate a specific etiology.

The hematological exam excluded a hemato-oncological pathology, and the rheumatological consultation raised the suspicion of Still's Disease in the adult. Serology investigations for cANCA, pANCA, ANA, and ferritin were supplemented, with the possibility of initiating corticosteroid therapy.

On the 6th day of admission, the result for *M. pneumoniae* serology came positive. Thus, the final diagnosis was CAP due to *Mycoplasma pneumoniae* and associated conjunctivitis. Antibiotic therapy was then de-escalated to monotherapy with Doxycycline. The patient became afebrile on the 9th day of admission with no cortisone intake.

Differential diagnosis

In the presented case, the initial diagnosis was erythematous pharyngitis. Faced with a febrile syndrome associated with

conjunctivitis and significant inflammatory syndrome, several probable diagnoses should be considered (Table 2).

A) Infectious causes

Conjunctivitis might be associated with autoimmune conditions, infections, or medication consumption⁽⁴⁻⁷⁾. Viral conjunctivitis is often caused by multiple adenoviral serotypes infection, characterized by bilateral pink eyes although may be a 1 to 3 days delay between the first and fellow eye, foreign body sensation, watery discharge, preauricular lymphadenopathy, high fever, myalgias, pharyngitis, and sore throat⁽¹¹⁾.

Dengue and Zika viruses are transmitted through the bite of an infected mosquito from tropical and subtropical areas. These can involve acute onset fever, conjunctivitis, headache, arthralgia, myalgia, and maculopapular rash, although conjunctivitis is more frequently associated with Zika disease⁽¹²⁾.

Leptospirosis was taken into consideration, given its similar clinical picture, especially when living in the country but the diagnosis was ruled out by serology. Infective endocarditis, caused by bacteria or fungi can associate conjunctival hemorrhages⁽¹³⁾. This presumption has been ruled out due to negative blood cultures and a trans-esophageal echocardiography that did not detect vegetation on the heart valves.

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 24 - follow up
Leukocyte (*10 ³ /mmc)	13.5	14.5	15.5	13.8	12.8	/	N
Neutrophil (%)	82	77	80.2	78.8	74.6	/	N
Fibrinogen (mg/dL)	972.00	1013.00	941.00	872.00	710.00	/	N
CRP (mg/dL)	27.7	20.3	17.2	13.2	/	/	N
CK total (U/L)	188.00	46.00	49.00	/	59.16	/	N
TGO U/L	34.00	/	/	26.00	/	22.00	/
TGP U/L	26.00	46.00	54.00	51.00	/	53.00	/
Rheumatoid factor (UI/mL)	/	/	513.30	/	/	/	/
cANCA	/	/	Negative	/	/	/	/
pANCA	/	/	Negative	/	/	/	/
ANA	/	/	Negative	/	/	/	/
Ferritin (ng/ml)	/	/	15.20	/	/	/	/
IgG and IgM Mycoplasma pneumoniae	/	/	/	/	/	IgM positive IgG negative	IgM negative IgG positive
Clamydia pneumoniae IgG and IgM	/	/	/	/	/	Negative	/
Coxiella burnetii IgG and IgM	/	/	/	/	/	Negative	/
Leptospira IgG and IgM	/	/	/	/	/	Negative	/

Table 1. Laboratory findings
N - normal value

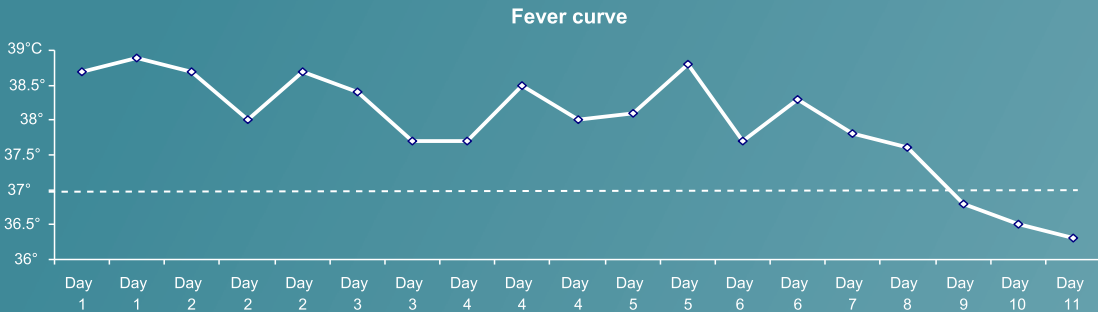


Figure 5. Fever curve



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Infectious

- **Viral^(4,5)**
 - Adenovirus infection
 - Herpes simplex
 - Shingles⁽⁸⁾
 - Enteroviruses infection
 - Dengue fever
 - Zika fever
 - Syphilis⁽⁹⁾
 - HAV, HBV, HCV
 - COVID-19⁽⁷⁾
- **Bacterial⁽⁴⁾**
 - Staphylococcal infections (*S.aureus*)
 - *Streptococcus pneumoniae*
 - *Haemophilus influenza*
 - *Leptospira* infection
 - *Coxiella burnetii*
 - *Clamydia pneumoniae*
 - Bacterial Endocarditis
- **Fungal**
 - Fungal endocarditis (uncommon)
- **Parasitic**

Non-infectious

- **Allergy⁽⁴⁾**
Seasonal allergies, medications, dust and mites, chemicals
- **Autoimmune disease^(6,8)**
 - Adult onset Still disease (AOSD)⁽⁸⁾
 - Rheumatoid Arthritis⁽⁶⁾
 - Systemic Lupus Erythematosus⁽⁶⁾
- **Hematologic and oncologic conditions⁽⁹⁾**
 - Neoplasms (Hodgkin's lymphoma, leukemia)
- **Toxic⁽¹⁰⁾**

B) Non-infectious etiology

The patient denied the consumption of any medications, prolonged exposure to toxic substances, or the presence of any allergies. The rheumatology exam raised the concern about Adult-onset Still's disease, an autoimmune illness classified on Yamaguchi criteria by daily fever for more than a week, pharyngitis, sore throat, arthralgia,

hepatosplenomegaly, lymphadenopathy, altered liver enzyme levels, elevated ferritin levels and C-reactive protein⁽⁸⁾.

Negative results of cANCA, pANCA, ANA immunological markers, and the ferritin value excluded Still disease (Table 1).

The correlation between *Mycoplasma pneumoniae* infection and conjunctivitis

Infection with atypical bacteria, usually manifested as respiratory tract illness, can associate extrapulmonary manifestations such as CNS affection, digestive tract disease (nausea, vomiting, diarrhea), musculoskeletal damage (myalgia, arthralgia), skin damage (cutaneous rash, bullous erythema), cardiovascular diseases such as myocarditis, heart failure, pericarditis, ocular damage characterized by swelling of the optic disc, optic nerve atrophy, retinal exudates and hemorrhages, cranial nerve paralysis, keratitis, and uveitis)⁽³⁾.

To our knowledge, there are few case reports in the literature concerning *Mycoplasma pneumoniae* associated conjunctivitis. Still, some studies showed that nonproductive cough, nasal congestion, and the altered general condition due to *M. pneumoniae* were followed by conjunctivitis⁽¹⁴⁾ and even subconjunctival hemorrhage⁽¹⁵⁾ with potential poor outcome, despite antibiotic treatment and corticosteroids⁽¹⁴⁾. Several cases of eye infections caused by *M. pneumoniae* have been reported, such as anterior uveitis or papillitis⁽¹⁶⁾. In addition, some authors have questioned the fact that conjunctivitis or uveitis along with positive results for *M. pneumoniae* infection may be also due to systemic inflammation or immunological reactions towards bacterial aggression⁽¹⁶⁾.

Delayed response to appropriate treatment in pneumonia with atypical bacteria

In the past, respiratory infections with *Mycoplasma* sp were considered completely self-limited and did not require antibiotic treatment. Subsequently, it was

demonstrated that adequate antibiotic therapy shortens the symptomatic period and speeds up the healing process⁽¹⁷⁾.

In our case, treatment with Doxycycline has been initiated since the first day of hospitalization. However, the initial clinical course got worse with the persistence of 2-3 febrile episodes daily and increasing inflammatory markers. Facing a persistent febrile syndrome associated with an important inflammatory syndrome, the guidelines recommend the administration of immediate empirical antibiotic treatment⁽¹⁸⁾, adapted to the most likely diagnosis.

Cortisone was delayed, although it was suggested by the rheumatologist when persistent fever was associated with myalgia and headache after a few days of Doxycycline. The escalation of treatment with broadening spectrum of action did not improve clinical or biological parameters. The patient became afebrile on day 9 of treatment with Doxycycline, and the inflammatory syndrome has faded without cortisone administration. Thus, the clinical and biological outcome was slowly favorable in a 26-year-old immunocompetent patient who received appropriate therapy from the first day of hospitalization.

Because *Mycoplasma* spp are organisms with a slow growth rate, respiratory tract infections are expected to respond better to longer treatment courses than other infections. Antibiotherapy for 7-10 days of parenteral or oral administration seems to have the same efficiency as 14-21 days of oral therapy⁽¹⁹⁾.

Conclusion

The case stands out due to the delayed response to antibiotic treatment for pneumonia caused by atypical bacteria in a



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young immunocompetent patient. At the 14 days follow-up, the patient presented in good general condition, but with persistent hyperemic conjunctivitis for which he was undergoing topical ophthalmic treatment and had no inflammatory syndrome.

Along with the extrapulmonary manifestations of infection with *Mycoplasma pneumoniae*, occurring in less than 25% of cases, the ocular involvement is less frequent, but usually implies conjunctivitis findings⁽²⁰⁾.

Rigorous investigations are needed for both infectious and non-infectious causes of a prolonged febrile syndrome, in the multidisciplinary team made up of microbiology, immunology, and hematology⁽¹⁶⁾ specialists, in order to reach the appropriate antibiotic or anti-inflammatory treatment.

Conflict of Interest disclosure: The authors declare that there are not conflicts of interest.

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Ethics: The study presented in this article was carried out following the recommendations of the Helsinki Declaration of 1975, revised in 2013, and the Taipei Declaration of 2016. The approval of the ethics committee was not necessary given the retrospective nature of the study and that the findings are the description of a single case report. The patient involved in the research agreed to participate and agreed to

provide details about the case and publish the research results.

Informed consent: The patient included in this study signed the informed consent.

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