International Journal of Multidisciplinary Research and Growth Evaluation.

It is possible a co-infection with two atypical pathogens? A strange case report

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Article Info

ISSN (online): 2582-7138
Volume: 05
Issue: 05
September-October 2024
Received: 10-08-2024
Accepted: 14-09-2024
Page No: 732-735

Abstract
"Atypical" pneumonias are clinically distinct and fo not tipically present with high fever, productive cough or lobar consolidation. The primary etiological agents include Mycoplasma Pneumoniae, Chlamydia Pneumoniae and Legionella Pneumophila. This case report details a young asthmatic patient who developed a dual infection with Chlamydia Pneumoniae and Mycoplasma Pneumoniae, which exacerbated the patient's asthma symptoms, resulting in significant complications. A literature review highlights the potential for such atypical infections to aggravate respiratory conditions in patients with pre-existing asthma. Clinical management involving antibiotic therapy and respiratory support, led to a gradual resolution of symptoms. This case underscores the importance of considering atypical infections in differential diagnosis of asthmatic patients experiencing acute symptom worsening.

DOI: https://doi.org/10.54660/.IJMRGE.2024.5.5.732-735

Keywords: Atypical pneumonia, Mycoplasma Pneumoniae, Chlamydia Pneumoniae, Legionella Pneumophila

Introduction

Respiratory infections caused by atypical pathogens such as C. pneumoniae and M. pneumoniae, pose significant diagnostic and therapeutic challenges, particularly in patients with chronic respiratory conditions such as asthma. These microorganisms are known to cause lower respiratory tract infections that can mimic other respiratory conditions, complicating the clinical course of asthmatic patients [1]. Co-infection with both pathogens result in severe clinical manifestations, including acute respiratory distress syndrome (ARDS). In this article, the case of a young asthmatic patient with a co-infection with involving C. pneumoniae and M. pneumoniae has been reported, and the clinical and therapeutic implications based on evidence from the literature have been discussed [2].

Case report

A 39-year-old Caucasian man presented to my pulmonology clinic "Ambulatorio La Madonnina" in March 2024, with reported episodes of fever, reaching up to 38.5°C, lasting approximately 2 weeks, accompanied by cough with yellowish mucus, dysphonia, and dyspnoea. The patient also visited the Polistena emergency room (Italy) in March due to abdominal pain, described as unspecified gastralgia. A computed tomography (CT) scan of the abdomen revealed a small hernia of epiploic fat in the transverse mesocolon.A subsequent cardiac examination indicated sporadic ventricular extrasystoles, and atrioventricular valve incontinence, primarily affecting the mitral valve, along with left atrial enlargement.The patient's medical history, includes being a non-smoker, having obesity (Body mass index : 33 kg/m2), and a prior episode of bronchopneumonia at 9 years of age. His Surgical History includes at 5 years of age, adenoidectomy and tonsillectomy at 5 years of age, meniscectomy, ankle surgery, and inguinal cyst removal.

He has documented allergies to iodinated contrast medium, intolerance to high doses of cortisone, and allergies to aeroallergens, specifically (dust mites.) Notably, there was no professional exposure to dust or asbestos. Chest radiography performed in mid-March showed no pleuro-parenchymal lesions. Physical examination revealed a cylindrical chest, clear pulmonary sounds, and hypotransmitted tactile vocal fremitus bilaterally. A respiratory vesicular murmur characterised by crackling rales was noted at the right lung base, with associated expiratory wheezing. Consequently, the patient was advised to start empirical broad-spectrum antibiotic therapy with azithromycin, amoxicillin/clavulanic acid, and oral cortisone, with adequate gastric protection. The patient was also recommended the administration of inhaled corticosteroids/long-acting beta-agonists at two inhalations twice daily as maintenance therapy, along with a chest CT scan, and laboratory tests for M. Pneumoniae, and C. Pneumoniae, Legionella, and Pneumococcus (Table 1). Spirometry results indicated normal findings, with a negative bronchoreversibility test for bronchial asthma. However, serial assessments showed significant variations in forced expiratory volume in one second and forced expiratory flow 25–75%, as illustrated in Table 2. The chest CT revealed minimal bilateral fissural thickening without pleuro-pericardial effusion (see Fig. 1 panels A— C). Based on the laboratory results, the patient was treated with doxycycline 40 milligrams/day for 30 days, along with an additional course of azithromycin, followed by re-evaluation. At the follow-up visit, the following diagnoses were established: asthma exacerbation due to atypical microorganisms and radiological signs of bilateral scissuritis.

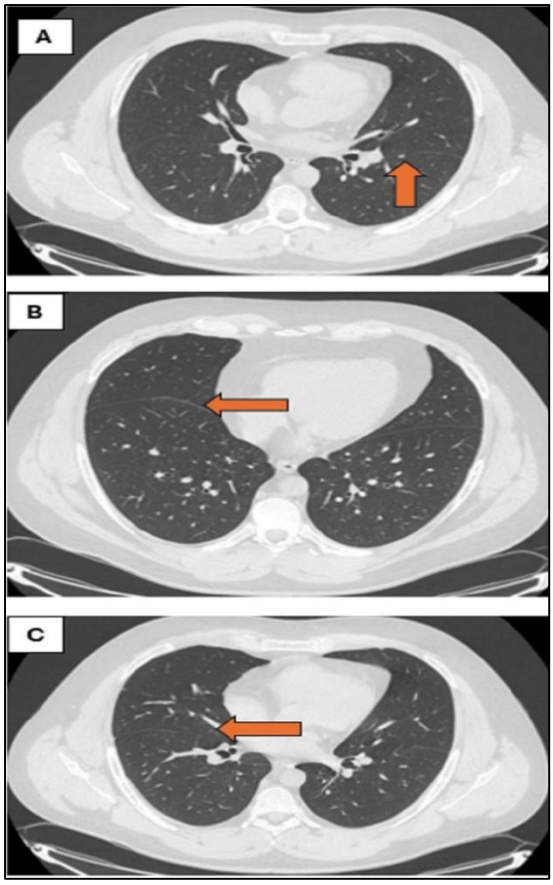

Fig 1: Panels A–C. Panels A–C illustrate the presence of an intrascissural micronodule and bilateral thickening of the fissures. These findings suggest infection by atypical pathogens

Discussion

The presence of respiratory co-infections in asthmatic patients represents a significant area of research, as it can profoundly affect clinical management and patient outcomes. Co-infection with C. pneumoniae and M. pneumoniae has been associated with more severe clinical manifestations, particularly when accompanied by concurrent viral infections, such as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), as reported in various scientific studies during the pandemic [3, 4]. This is particularly relevant in the context of coronavirus disease 2019 (COVID-19), where co-infections can complicate the clinical presentations and therapeutic approaches. Several authors documented cases of ARDS resulting from co-infection with these atypical pathogens, highlighting the need for timely and accurate diagnosis to prevent adverse outcomes [5, 6]. Diagnosing infections caused by C. pneumoniae and M. pneumoniae can be challenging due to their clinical presentation, which often overlaps with other respiratory infections, and the need for specific diagnostic tests, such as polymerase chain reaction(PCR) and serology [7, 8]. Scientific literature indicates that these infections could lead to lower respiratory tract diseases in paediatric patients, a finding that is also applicable to young adults with chronic respiratory conditions. Several studies have emphasised that co-infection with SARS-CoV-2 can significantly exacerbate the clinical course in patients infected with C. pneumoniae and M. pneumoniae [9, 10]. In the clinical case discussed, the patient, a young adult with a history of well-controlled asthma, experienced an acute exacerbation of respiratory symptoms [11]. Chest radiography and CT scans revealed bilateral infiltrates, while microbiological tests confirmed the presence of both pathogens [12]. Clinical management required a combination of specific antibiotics and respiratory support therapy, with careful monitoring to prevent severe complications. Several scientific studies have underscored the importance of identifying acute M. pneumoniae and C. pneumoniae infections in children experiencing wheezing episodes, suggesting that timely antibiotic therapy could improve clinical outcomes [13, 14]. This principle also applies to young adults, where appropriate treatment can prevent progression to more severe conditions [15].

Conclusion

Acute respiratory infections are a leading trigger of asthma exacerbations, with viral infections being the predominant cause of infection-associated exacerbations in adults. During severe acute exacerbations, it is crucial to treat infectious agents promptly and empirically, though initial treatment regimens can vary significantly, encompassing bacterial, atypical, and viral pathogens depending on regional epidemiology. This case highlights the importance of considering atypical pathogens, such as *C. pneumoniae* and *M. pneumoniae*, in asthmatic patients experiencing acute symptom exacerbations. Early diagnosis and appropriate treatment are essential to prevent severe complications and improve clinical outcomes. The literature review emphasises the need for heightened awareness and a targeted diagnostic and therapeutic approach in patients with respiratory co-infections, particularly in the context of the COVID-19 pandemic. Future studies should focus on optimising diagnostic and therapeutic strategies for effectively managing these infections in patients with chronic respiratory diseases.

Table 1: The table displays elevated IgM and IgA levels, which gradually decrease with serial laboratory monitoring and specific antibiotic therapy. Urinary antigen tests for Legionella and Pneumococcus were negative. Normal values Ig C. Pneumoniae: Women: For IgA < 10 negative; >=10 and < 13 doubtful; >= 13 positive For IgG< 10 negative; >=10 and < 12 doubtful; >= 12 positive For IgM < 10 negative; >=10 and < 15 doubt; >= 15 positive Men: For IgA< 10 negative; >=10 and < 13 doubtful; >= 13 positive For IgG < 10 negative; >=10 and < 12 doubtful; >= 12 positive For IgM < 10 negative; >=10 and < 15 doubt; >= 15 positive. Normal values Ig M. Pneumoniae: women: < 10 negative >= 10 positive Men: < 10 negative >= 10 positive

Laboratory examinations	29/03/2024	30/04/2024	29/05/2024
IgA *M. pneumoniae*	*21 AU/mL*	*18 AU/mL*	*10 AU/mL*
IgG *M. pneumoniae*	*9 AU/mL*	*10 AU/mL*	*5.2 AU/mL*
IgM *M. pneumoniae*	*21 Index*	*13 Index*	*8.8 Index*
IgA *C. pneumoniae*	*21 AU/mL*	*17 AU/mL*	*13 AU/mL*
IgG *C. pneumoniae*	*13 AU/mL*	*15 AU/mL*	*28 AU/mL*
IgM *C. pneumoniae*	*21 Index*	*17 Index*	*0.3 Index*
Urinary antigen *Legionella*	*Negative*	/	/
Urinary antigen *Pneumococcus*	*Negative*	/	/

Legend Tab. 1: Ig, immunoglobulin; M. pneumoniae, Mycoplasma pneumoniae; C. pneumoniae, Chlamydia pneumoniae

Table 2: Global spirometry results using PulmOne MiniBox+ Medgraphics(Italy). The spirometry values show a significant increase in FEV1 (+240 mL post-BD after 3 months of therapy with ICS/LABA. There is also a reduction in mid-expiratory flows (74% of the predicted value), indicative of lower airway pathology responsive to salbutamol. These findings are consistent with bronchial asthma in the context of a lower airway infection

Spirometry parameters	Predicted value (pre-BD)	Predicted value (post-BD)	Percentage change from the predicted value	Predicted value after 3 months of ICS/LABA
FEV1	*88%*	*92%*	*+4%*	*93%*
FVC	*92%*	*93%*	*+1%*	*93%*
FEV1/FVC	*76.24%*	*78.79%*	*+3%*	*79.41%*
FEF 25–75	*74%*	*85%*	*+15%*	*87%*
PEF	*115%*	*114%*	*-1%*	*124%*
TLC	*82%*	/	/	*84%*
RV	*62%*	/	/	*66%*
RV/TLC	*77%*	/	/	*80%*
IC	*113%*	/	/	*121%*

Legend Tab. 2: BD, bronchodilator; ICS/LABA; inhaled corticosteroids/long-acting beta-agonists FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; FEV1/FVC, FEV1/FVC ratio; FEF 25–75, forced expiratory flow 25–75%; PEF, peak expiratory flow; TLC, total lung capacity; RV, residual volume; RV/TLC, RV/TLC ratio; IC, inspiratory capacity

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