Mycoplasma pneumoniae Pneumonia with Worsening Pleural Effusion Despite Treatment with Appropriate Antimicrobials

Case report

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الالتهاب الرئوي الناتج عن الميكوبلازما الرئوية مع تدهور في الانصباب الجنبي بالرغم من العلاج المناسب بمضادات الميكروبات

تقرير حالة

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ABSTRACT: *Mycoplasma pneumoniae* is a common cause of community-acquired pneumonia. As *M. pneumoniae* pneumonia is usually a mild and self-limiting disease, complications such as pleural effusion occur only rarely. We report a 22-year-old woman who presented to the Emergency Medicine Department of the Sultan Qaboos University Hospital, Muscat, Oman, in 2017 with an eight-day history of fever associated with coughing, chills and rigors. She was diagnosed with *M. pneumoniae* pneumonia, but subsequently developed pleural effusion which worsened despite treatment with appropriate antimicrobials. The pleural effusion required drainage, which revealed that it was of the more severe exudative type. Following drainage, the patient improved dramatically. She was discharged and advised to continue taking antibiotics.

Keywords: Mycoplasma pneumoniae; Bacterial Pneumonia; Pleural Effusion; Antimicrobial Agents; Drainage; Case Report; Oman.

الملخص: الميكوبلازما الرئوية هي سبب شائع للالتهاب الرئوي المكتسب في المجتمع. بما أن الالتهاب الرئوي الناتج عن الميكوبلازما الرئوية هوعادة مرض خفيف ومحدود ذاتياً، فإن المضاعفات مثل الانصباب الجنبي لا تحدث إلا نادراً. نعرض هنا حالة امرأة تبلغ من العمر 22 عاماً تم إدخالها إلى قسم طب الطوارئ في مستشفى جامعة السلطان قابوس، مسقط، عُمان، في عام 2017 مع تاريخ مرضي من الحمى المرتبط بالسعال والقشعريرة وقسوة لمدة ثمانية أيام. تم تشخيص إصابتها بالتهاب رئوي ناتج عن الميكوبلازما الرئوية، ولكن بعد ذلك تطور إلى الانصباب الجنبي الذي ساء بالرغم من العلاج بمضادات الميكروبات المناسبة. احتاج الانصباب الجنبي إلى تفريغ والذي كشف على أنه كان من نوع نضحي شديد. بعد التفريغ، تحسن وضع المريضة بشكل كبير. وتم ترخيصها ونصحت بمواصلة تناول المضادات الحيوية.

الكلمات المفتاحية: الميكوبلازما الرئوية؛ الالتهاب الرئوي البكتيري؛ الانصباب الجنبي؛ مضادات الجراثيم؛ تفريغ؛ تقرير حالة؛ عمان.

M YCOPLASMA PNEUMONIAE ARE EXTREMELY small self-replicating free-living bacteria which can cause upper respiratory tract infections, including pharyngitis, sinusitis, ear pain, rhinorrhoea and pneumonia.[1,2] *M. pneumoniae* pneumonia is described as atypical and accounts for 1–29% of community-acquired pneumonia cases.[2] The causative bacteria can be transmitted through aerosols as well as in settings which promote close physical contact, such as homes, schools, military barracks and dormitories.[3] The post-exposure incubation period is between two to three weeks and infections are more prevalent among children and young adults.[4] Common risk factors include age (i.e. younger children or older adults), immune status (i.e. immunocompromised individuals with HIV or those undergoing chemotherapy or taking steroids), smoking and pre-existing lung disease.[5]

Classic symptoms of *M. pneumoniae* infection include fever, cough and the production of *sputum*; in most cases, the disease is self-limiting and results in a good prognosis.[6] However, *M. pneumoniae* pneumonia can be life-threatening, resulting in respiratory failure or acute respiratory distress syndrome in certain cases.[7] However, pulmonary complications such as parapneumonic effusion are rare and occur mainly in children and adolescents; most cases are unilateral, low-volume and resolve with appropriate antimicrobial therapy.[8–10]

M. pneumoniae pneumonia can be diagnosed by serology using an enzyme immunoassay. An acute infection is indicated by the detection of immunoglobulin (Ig) A and/or IgM, with a single titre of

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Table 1: Serial blood results of the current case

Investigation	Day 0	Day 2	Day 3	Day 6
Hb level in g/dL	11.9	10.9	12.6	11.1
WCC x 10⁹/L	-	6.9	7.0	8.7
ANC x 10⁹/L	-	6.9	5.7	5.8
Lp level x 10⁹/L	-	0.7	0.7	1.6
PC x 10⁹/L	-	142	157	208
Sodium level in mmol/L	134	137	-	140
Potassium level in mmol/L	3.9	3.6	-	4.0
Urea level in mmol/L	1.5	-	1.4	1.2
Creatinine level in µmol/L	59	48	-	59
Anion gap in mmol/L	19	16	-	14
Bicarbonate level in mmol/L	17	19	-	20
ALT level in U/L	-	-	136	33
AST level in U/L	-	-	118	36
Bilirubin level in µmol/L	-	-	6	5

Hb = haemoglobin; WCC = white cell count; ANC = absolute neutro-phil count; Lp = lipoprotein; PC = platelet count; ALT = alanine aminotransferase; AST = aspartate transferase.
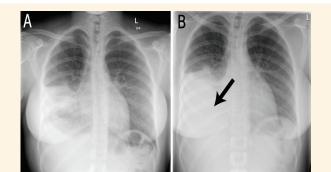
IgM greater than 1:64 or a four-fold rise in the IgG titre.[11,12] Polymerase chain reaction (PCR) analysis can also be used to detect *M. pneumoniae* in clinical samples of *sputum* and those of nasopharyngeal and throat swabs. However, microbial testing is not usually performed for outpatients with community-acquired pneumonia because empirical treatment is almost always successful.[13] This case report describes a patient with pneumonia who was not initially tested for *M. pneumoniae*. The patient deteriorated and developed severe pleural effusion, despite the administration of appropriate antimicrobials, necessitating drainage.

Case Report

A 22-year-old woman presented to the Emergency Medicine Department of the Sultan Qaboos University Hospital (SQUH), Muscat, Oman, in 2017 with an eight-day history of fever associated with coughing, chills and rigors. Although her coughing was initially dry, she had begun producing yellow-green *sputum* on day five and developed shortness of breath on day seven. The patient reported having recently undertaken a trip one week prior with her classmates, some of whom had also developed coughs. She was known to have the sickle cell trait and vitamin B_{12} deficiency and was taking weekly cyanocobalamin injections.

Upon initial examination, the patient appeared ill, dehydrated, febrile and tachycardic. Her temperature was 40.3 °C, her heart rate was 134 beats per minute and her respiratory rate was 18 breaths per minute. Pulse oximetry indicated an oxygen saturation of 97% in room air. Auscultation of the chest revealed reduced breath sounds in the right base. The results of initial and serial laboratory investigations are shown in Table 1. A chest X-ray showed consolidation of the right middle and lower lobes, with right-sided pleural effusion and partial lower lobe collapse [Figure 1A]. Subsequently, the patient was diagnosed clinically with community-acquired pneumonia. While awaiting the results of a respiratory viral screening panel and *sputum* culture, she was prescribed 2 g of ceftriaxone once daily and 500 mg of intravenous azithromycin and 75 mg of oseltamivir twice daily. However, the respiratory viral panel results were negative and the oseltamivir was discontinued. Three days later, the culture results of the *sputum* sample showed only upper respiratory commensals.

Two days after admission, the condition of the patient deteriorated. She was breathless at rest with a respiratory rate of 40 breaths per minute. Her heart rate had decreased to 120 beats per minute and she frequently vomited after episodes of coughing. A chest examination revealed absent breath sounds and

Figure 1: Chest X-rays of a 22-year-old female patient with *Mycoplasma pneumoniae* pneumonia on (**A**) the day of admission and (**B**) two days later, showing worsening pleural effusion (arrow).

stony dullness involving the middle and lower chest. A repeat chest X-ray confirmed that the right-sided pleural effusion had worsened [Figure 1B]. Accordingly, a drainage procedure was performed, during which 2 L of exudative fluid consisting predominantly of lymphocytes (80%) was drained via a pigtail catheter over a 24-hour period. In view of her worsening condition, a nasopharyngeal aspirate sample was sent for serological and PCR testing.

The PCR test results were positive for *M. pneumoniae*, while the serology was positive for IgA, IgM and IgG. As the serology test was qualitative, exact titres were not available. Treatment was continued with intravenous azithromycin for five days, after which the patient was discharged and advised to take moxifloxacin for six more days. She made a remarkable improvement and a chest X-ray four weeks later showed the complete resolution of the pneumonic patch and pleural effusion.

Discussion

Narita *et al.* described two types of *M. pneumoniae*-related pleural effusion with varying degrees of severity.[14] The first is characterised by a benign transient chest disease, is most probably reactive as evidence of the *M. pneumoniae* genome is usually undetectable and has lower but still abnormal concentrations of interleukin (IL)-18 and IL-8. The second involves more persistent disease, contains *M. pneumoniae* DNA and has significantly higher IL-18 and IL-8 concentrations.[14] It is possible that the presence of *M. pneumoniae* DNA elicits a stronger immunological reaction, thus causing greater lung damage and higher concentrations of IL-8 and IL-18. In addition, two major strains of *M. pneumoniae* clinical isolates have been reported to differ in adhesin gene sequence.[15] Of these, type 2 is more virulent, causing respiratory epithelial destruction, and has a more robust biofilm, presumably conferring increased resistance to host defence mechanisms and antimicrobial penetration.[15] In the current case, although the patient was not tested, it is likely that she had the more severe type with biofilm formation, especially as she did not improve following antimicrobial treatment. Drainage of the pleural effusion might have disrupted these biofilms, thereby aiding the recovery process.

Thrombocytosis can occur as a feature of *M. pneumoniae* infection and probably represents an acute phase response, while thrombocytopenia is unusual.[16] Another study found that children with severe *M. pneumoniae* pneumonia had prolonged fevers, higher C-reactive protein levels and lower lymphocyte and white cell counts (WCCs).[17] The patients with segmental/lobar pneumonia were usually older and had a longer fever duration and lower WCC and lymphocyte counts compared with those with bronchopneumonia.[17] *M. pneumoniae* infections have also been associated with acute chest syndrome and haemolytic anaemia in patients with sickle cell anaemia.[18] In the current case, the patient did not have haemolytic anaemia but did have the sickle cell trait. However, no particular association has been reported within this group in terms of the severity of the infection.

The diagnosis of an *M. pneumoniae* infection can be difficult. The Gram staining of *sputum* samples is not feasible to identify *mycoplasma* bacterium due to the absence of a cell wall; moreover, a *sputum* culture is time-consuming because of the slow growth rate of the pathogen *in vitro*.[1] Enzyme-linked immunoassay-based serology is the technique most frequently used to diagnose *M. pneumoniae* infections, although it can be confusing to interpret. Unfortunately, IgM antibodies can persist for months in some patients, thereby not necessarily indicating an acute infection, while others do not demonstrate an IgM response at all in cases of acute infection or reinfection.[19,20] Moreover, while IgA is reported to be more sensitive than IgM in diagnosing acute infections in adults, Yamazaki *et al.* reported a lower sensitivity in young children.[21,22] Therefore, the diagnosis of an *M. pneumoniae* infection relies on determining a four-fold increase in IgG titres taken two to four weeks apart.[23] Spuesens *et al.* reported no obvious differences between PCR positivity rates in the throat swabs of individuals with suspected cases of *M. pneumoniae* infections and those of healthy subjects.[24] This suggests that *M. pneumoniae* may colonise the upper airway without necessarily inducing disease. In the current case, the diagnosis of an *M. pneumoniae* infection was established by the IgA, IgM, IgG and PCR results of a nasopharyngeal swab. Furthermore, the patient's positive response to azithromycin treatment following drainage of the pleural fluid supports this diagnosis.

At SQUH, hospitalised patients with pneumonia are not routinely tested for *M. pneumoniae*; therefore, the current patient was tested only after she had deteriorated clinically. Nevertheless, the bacterial diagnosis of admitted cases of pneumonia is important, as patients with *M. pneumoniae* pneumonia require greater infection control measures for the duration of their illness, such as droplet isolation precaution measures.[25] Although physicians tend to empirically treat patients requiring admission for atypical pneumonia, testing for *M. pneumoniae* pneumonia might also allow for the better management of pleural effusion cases, should further intervention be required beyond antimicrobial therapy.[13]

Conclusion

M. pneumoniae is a common cause of community-acquired pneumonia. Patients requiring hospital admission should be tested for the presence of this bacteria, especially if they have pleural effusion.

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