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Case Report

Acute Respiratory Distress Syndrome Caused by Mycoplasma Pneumoniae Diagnosed by Polymerase Chain Reaction

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ABSTRACT

Mycoplasma pneumoniae (M. pneumoniae) is a common pathogen in cases of atypical pneumonia. Most individuals with Mycoplasma pneumonia run a benign course, with non-specific symptoms of malaise, fever and non-productive cough that usually resolve with no long-term sequelae. Acute lung injury is not commonly seen in Mycoplasma pneumonia. We report a case of acute respiratory distress syndrome cause by *M. pneumoniae* diagnosed by quantitative real-time polymerase chain reaction (RT-PCR).

CASE REPORT

A previously well 15-year-old female presented with a one week history of dry, non-productive cough and a three-day history of occipital headache, photophobia, sore throat and fever. She was a smoker of 0.5 pack years. She was a student and lived in an urbanised area with her family. There was no history of recent foreign travel, no known exposure to moulds and no exposure to birds or farm animals. Physical examination was unremarkable. Investigations revealed that the white cell count (WCC) was raised at 12.6 X 10^9/L (neutrophils 9.89 X 10^9/L , lymphocytes 1.32 X 10^9/L) and the C-reactive protein (CRP) was elevated at a level of 192 mg/L. Admission chest X-ray (CXR) was normal. She was empirically treated with IV ceftriaxone 2g BD for presumed meningitis. She had declined lumbar puncture prior to initiation of antibiotic therapy. There was initial improvement with intravenous fluid and antibiotic administration however, on day 3 of her hospital admission, she deteriorated with a raised respiratory rate and high temperatures. Her throat was noted to be inflamed and IV benzylpenicillin 1.2g q4hrs was added empirically to cover for tonsillitis. She continued to deteriorate the following day with a fall in $p0_2$ of 7.5 kPa on room air arterial blood gas. CRP remained elevated at 205 mg/L. Repeat CXR revealed a dense, left-sided consolidation. She was transferred to the High Dependency Unit (HDU) for supportive ventilation on day 3 of her admission and initial antibiotics were changed to IV meropenem 2g BD and IV clarithromycin 500mg BD for broader antimicrobial cover. Despite aggressive management, there was further clinical deterioration with worsening CXR changes involving the right lung base within 24 hours of HDU admission. She was tachypnoeic with a respiratory rate of up to 50 breaths per minute and remained pyrexial. She continued to deteriorate and required intubation and ventilation within 24 hours of HDU admission due to exhaustion. She was diagnosed with acute respiratory distress syndrome (ARDS) based on CXR findings which showed bilateral alveolar infiltrates and pO2 of 6.9 kPa on high flow oxygen.

Blood and urine cultures were negative. Sputum sample cultures were negative on direct culture. Legionella and pneumococcal urinary antigens were negative. A previously published real-time PCR for detection of *M. pneumoniae* specific P1 cytadhesin was modified to quantify *M. pneumoniae DNA* in 10µl assay volumes[1,2]. Her throat swab contained 7780 copies/ml of mycoplasmal DNA. Mycoplasma pneumonia was diagnosed and PO doxycycline 100mg BD was added for additional atypical pneumonia cover at day 10 of her admission. A bronchoalveolar lavage (BAL) was performed at day 6 of intensive care stay because of persistently raised inflammatory markers and high ventilator requirements.

Real-time PCR of her BAL detected 6440 copies/ml of *M. pneumoniae* DNA. Cold agglutinins were also detected in serum at a dilution of 1/32. Serum for Mycoplasma IgM, taken at day 9 of the presentation, was negative however a subsequent sample taken at day 18 of the presentation was positive. These serological results support the PCR findings in confirming *Mycoplasma pneumonia* as the cause of her acute respiratory distress syndrome. She improved over the course of her ten day admission to the Intensive Care Unit, was weaned off ventilator support and was transferred back to a General Medical ward to finish her treatment. She completed a two-week course of clarithromycin and doxycycline. Repeat chest X-ray prior to discharge showed marked improvement. She was discharged and has since made a complete recovery after 21 days in hospital.

DISCUSSION

Mycoplasma pneumonia is the commonest cause of atypical community acquired pneumonia (CAP). It has a worldwide prevalence which tends to occur in epidemics. In the UK, epidemics were always described as occurring every 3 – 4 years; the last proper epidemic was late 1997-1998. Since then, less infection has been seen than expected, hence the

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previously observed 3 – 4 year cycle pattern has broken down[3]. It is well recognised that the vast majority of Mycoplasma infection is undiagnosed. Mycoplasma pneumonia tends to occur primarily in young adults but may occur in any age. Symptoms of mycoplasma pneumonia include fever, sore throat and a non-productive cough[4]. Central nervous system involvement due to mycoplasma infection is well documented in the literature which ranges from aseptic meningitis, encephalitis, cerebral ataxia and transverse myelitis[5]. Our patient presented with headache and photophobia and was initially treated as meningitis.

Radiological findings in cases of mycoplasma pneumonia are usually an interstitial pattern as opposed to lobar type pneumonia, as seen in Streptococus pneumoniae infection[6]. Techniques for laboratory diagnosis of mycoplasma pneumonia include culture, serological and molecular methods. As *M. pneumoniae* is a bacteria which lacks a cell wall, culturing this organism is difficult. She et al. assessed the utility of culture for *M. pneumoniae* for the diagnosis of respiratory tract infections and found that culture was less sensitive and had low yield when compared to other laboratory techniques such as PCR and IgM serology[7]. When comparing between PCR and IgM serology for the diagnosis of mycoplasma infection during the acute phase of infection, Nilsson et al. found that PCR was superior to serology. This study also found that following an acute infection, persistent and sometimes long-term, carriage of *M. pneumoniae* DNA in the throat is common following an acute infection which is not affected by antibiotic therapy[8].

Cold agglutinin is a non-specific laboratory investigation which is raised in about 75 percent of cases of mycoplasma pneumonia. Serum titre levels of more than 1:64 in a person with a lower respiratory tract infection would highly suggest Mycoplasma pneumonia infection. Another feature in patients with *M. pneumoniae* infection is acute thrombocytosis which usually occurs 1-2 weeks into the illness[9]. This patient had serum platelet levels exceeding above 700 during the course of her illness which returned to normal levels during the recovery period.

M. pneumoniae is a bacterium that lacks a cell wall, hence cell wall acting antibiotics such as penicillins and cephalosporins have no action. Tetracycline, clarithromycin or erythromycin remain as the mainstay treatment for *M.pneumonia* and should be used empirically in treating community-acquired pneumonia[4]. Most Mycoplasma pneumonia infections resolve without complications however, some cases can progress to acute respiratory distress syndrome (ARDS). Cell-mediated immune response is thought to be the pathogenesis of pulmonary injury in mycoplasma infection, for which steroids may have a role in the treatment of severe cases. Radisic et al. described a case of mycoplasma infection complicated by ARDS which improved on prednisolone treatment[10].

CONCLUSION

Mycoplasma pneumonia is an uncommon cause of acute respiratory distress syndrome. This case report shows the advantage of using PCR for detection of *M. pneumoniae* DNA in throat swabs and respiratory tract secretions in acute infection. PCR is superior to serology which requires acute and convalescent samples to confirm the diagnosis of *Mycoplasma pneumoniae* infection. Mycoplasma pneumonia should be considered in patients who do not respond to broad-spectrum antimicrobials and empirical atypical cover with a macrolide such as clarithromycin should be started. We consider PCR as the front-line investigation for the diagnosis of acute *Mycoplasma pneumoniae* infection. Clinicians suspecting mycoplasma infection should send respiratory secretions for *Mycoplasma pneumoniae* PCR.

The authors have no conflict of interest

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