Severe diffuse interstitial pneumonia due to *Mycoplasma pneumoniae* in a patient with respiratory insufficiency

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**CASE REPORT**

A 25-year-old male with high fever, shortness of breath and somnolence was admitted to the emergency room of our hospital. His past medical history included physical and mental retardation due to asphyxia at birth, pneumonia of the right lower lobe in 1983 and laryngitis subglottica in 1985. Further history revealed weakness for one week and possible fever. He had developed a cough and started expectorating white sputum during the last few days. In the last 24 hours his rectal temperature rose to 40°C and he became somnolent. Suspecting acute bacterial bronchitis, the general practitioner started treatment with co-amoxiclav. The patient had not been abroad and had not been in contact with (swimming) water or birds. No infectious diseases were prevalent in his environment. On examination, we saw a very ill somnolent man. His temperature was 40.5°C, blood pressure 140/80 mmHg and pulse rate 125 beats/min. Pulmonary examination was normal. Nuchal rigidity could not be ruled out. Cerebrospinal fluid showed a glucose level of 4.1 mmol/l, a protein content of 0.17 g/l and no white cells. The ESR was 67 mm, with a C-reactive protein of 115 mg/l and a white-cell count of 9.4 × 10⁹/l with a normal differential. Haemoglobin was 7.3 mmol/l (MCV 85 fl). Values for serum asparate aminotransferase and alanine aminotransferase were slightly elevated, the lactate dehydrogenase level was 906 U/l, bilirubin 17 µmol/l and haptoglobin 4.41 g/l. Creatine kinase was 2141 U/l.
without elevation of CK-MB. The arterial pO₂ was 7.8 kPa, pCO₂ 4.7 kPa and oxygenation 92%, while the patient was given nine litres of oxygen a minute via a rebreathing mask. The chest X-ray showed a diffuse slightly intensified reticulonodular pattern without evidence of alveolar consolidation. The differential diagnosis consisted of the early phase of pneumonia or another infection possibly with incipient adult respiratory distress syndrome. After blood, sputum, cerebrospinal fluid and urine had been taken for culture, empirical treatment was started with co-amoxiclav 1200 mg four times a day intravenously and gentamycin once daily.

In spite of this treatment, the patient deteriorated during the next three days. His temperature remained elevated and a tachypnoea with a frequency of 40/min developed with a decline in the oxygenation of the blood. In arterial blood the pO₂ was 7.0 kPa, pCO₂ 3.4 kPa and oxygenation 89%, with an inspired oxygen fraction (FiO₂) of 40%. Chest X-ray showed a diffuse reticulonodular pattern, without evidence of alveolar consolidation (figure 1). High resolution CT scan of the chest showed, much more clearly than the X-ray, a very serious diffuse reticulonodular pattern with bilateral small consolidations (figure 2). The clinical picture consisting of an interstitial pneumonia, myositis and a high ESR with possible haemolysis (which raised the suspicion of cold agglutinins) made us think of a severe *M. pneumoniae* infection. Because of the threatening respiratory insufficiency and possible necessity for mechanical ventilation, the patient was admitted to the intensive care unit and received a rebreathing mask with a FiO₂ of 60% plus six litres O₂/minute by way of a nasal tube. Co-amoxiclav was discontinued and intravenous erythromycin 500 mg four times a day was started. The same day the diagnosis *M. pneumoniae* pneumonia was confirmed by a strongly positive complement fixation test for IgM antibodies directed against *M. pneumoniae* (titre 1:320), while the IgG was negative (titre <8), which confirmed an acute infection. The diagnosis was also supported by positive cold agglutinins (titre 1:128). This was an explanation for the high ESR, positive direct Coombs and subclinical signs of haemolysis. The microbiological investigations yielded no pathogens.

Our patient stayed in the intensive care unit for seven days. Mechanical ventilation could be avoided by means of a rebreathing mask and supplementary oxygen delivery. After three days erythromycin i.v. was converted to clarithromycin 500 mg orally twice a day for nine days. During his stay in the ICU he slowly recovered and his oxygen demand declined. He became more responsive and less somnolent. The laboratory abnormalities normalised. The patient was discharged in a good clinical condition one week later.

**DISCUSSION**

In this critically ill patient with a severe diffuse interstitial pneumonia, myositis and subclinical haemolysis, *Mycoplasma pneumoniae* infection was diagnosed. *M. pneumoniae* is one of the most common causes of non-pneumococcal community-acquired pneumonia. The frequency of this infection reported in ambulatory patients and hospitalised patients varies, probably due to the use of different diagnostic tests, lack of consensus with regard to diagnostic criteria, geographical differences and the existence of world-wide outbreaks with a four- to eight-year periodicity. The incidence of *M. pneumoniae* in severe ‘community-acquired pneumonia’ (CAP), requiring hospitalisation or even admission to an ICU, is approximately between 1 to 7%. However, the incidence of mycoplasma may be much higher in patients with milder disease that

**Figure 1**
Chest X-ray: bilateral reticulonodular pattern, without evidence of alveolar consolidation in a patient with *Mycoplasma pneumoniae* infection

**Figure 2**
High-resolution computer tomography of the chest: diffuse interstitial pneumonia with bilateral small consolidations in a patient with *Mycoplasma pneumoniae* infection
can be managed without hospitalisation. A recent study showed *M. pneumoniae* was the causative pathogen in 22.8% of the patients with mild CAP, which is much higher than the incidence of other atypical pathogens such as *Chlamydia pneumoniae* and Legionella species (10.7 and 0.7% respectively).\(^9\)

Infection by *M. pneumoniae* is seen at all ages, but most often in the first two decades of life. This infection occurs in any season, with a four- to eight-year periodicity for worldwide epidemics. Outbreaks are especially seen in places where many (young) people are brought together, like in schools, homes, military academies and universities. In our patient, his stay in a facility for the mentally retarded may have been important in this respect.

Transmission from person-to-person takes place via droplet nuclei after close and prolonged contact. The incubation period averages three weeks. Transmission from person-to-person takes place via droplet nuclei after close and prolonged contact. The incubation period averages three weeks. In our patient, his stay in a facility for the mentally retarded may have been important in this respect.

Clinical features caused by *M. pneumoniae* infection may be divided into those due to respiratory tract disease and those due to extrapulmonary disease. However, approximately 20% of *M. pneumoniae* infections are asymptomatic. The most common respiratory symptoms are a tracheobronchitis with a non-productive or mild productive cough (± 75% of patients), pharyngitis, rhinorrhea and earache. Up to 5% of patients have severe earache resulting from bullous myringitis. Only 5% of patients will develop pneumonia. The most common radiographic finding on chest X-ray is a bilateral peribronchial pneumonia pattern, which consists of thickened bronchial shadows, patchy alveolar consolidations with areas of plate-like atelectasis, and streaks of interstitial infiltration. It has been shown that the interstitial abnormalities in *M. pneumoniae* pneumonia are often difficult to recognise on plain X-rays of the chest but can usually been detected by high-resolution CT scan,\(^10\) as in our patient. The interstitial abnormalities can be localised, but diffuse involvement of both lungs has been described, even requiring mechanical ventilation. In those severe cases *M. pneumoniae* pneumonia can result in interstitial fibrosis and even bronchiolitis obliterans-organising pneumonia (BOOP) with long-term sequelae.\(^11\) The differential diagnosis of an interstitial pattern on chest X-ray is very extensive.

Extrapulmonary abnormalities are common in infections by *M. pneumoniae* and are usually superimposed on pulmonary disease so that mycoplasmal aetiology can be suspected. These include dermatological manifestations, central nervous system involvement, gastrointestinal symptoms and cardiac complications. Mild myositis is also frequently seen, as in our patient, and even rhabdomyolysis has occasionally been described.\(^12\) The most prominent extrapulmonary symptom is the presence of cold agglutinins. These are IgM antibodies directed against the glycolipid antigens of *M. pneumoniae* and cross-reacting with the I antigen of the red blood cell. Elevated cold agglutinin titres are seen in a variety of infections, including influenza, mononucleosis, psittacosis, rubella, adeno virus and measles, but usually occur at a higher titre in mycoplasmal infection. They are seen in up to 60% of patients with mycoplasmal infection. Cold agglutinins appear in the second week of illness, they peak at four weeks and disappear by two months. As in our case, they usually cause an elevated ESR and evidence of haemolysis, such as a positive direct Coombs’ test and an elevated reticulocyte count. The titre usually exceeds 1:128 in patients with *M. pneumoniae* pneumonia and overt haemolysis may arise. Although *M. pneumoniae* usually causes mild disease with a mortality rate of less than 1%, respiratory insufficiency, need for mechanical ventilation and death may occur. A severe course is strongly associated with comorbidity.\(^13\) Examples of pre-existing chronic diseases are chronic obstructive pulmonary disease, chronic cardiac insufficiency, diabetes mellitus and immunosuppressive diseases or therapies. Our patient did not have comorbidity but the disease definitely ran a severe course. Serious hypoxaemia, high oxygen demand and progressive somnolence necessitated admission to the ICU. Appropriate antibiotics, a high FiO\(_2\), and breathing supporting measures (physical therapy, assistance with expectoration, half-sitting position in bed) could just prevent intubation and mechanical ventilation. In most cases, it is not possible to point to the causative pathogen of a pneumonia just from the symptomatology. Nevertheless this case report illustrates that in some cases it is possible. Mycoplasma-specific IgM test and measurement of cold agglutinins may help to make the diagnosis and install appropriate antimicrobial treatment.

**REFERENCES**


