Case Report

Wien Klin Wochenschr (2007) 119/11–12: 379–384
DOI 10.1007/s00508-007-0810-7

WIENER KLINISCHE WOCHENSCHRIFT
The Middle European Journal of Medicine
Printed in Austria

Fatal *Mycoplasma pneumoniae* pneumonia in a previously healthy 18-year-old girl

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Received August 8, 2006, accepted after revision February 27, 2007

Letale Mykoplasmenpneumonie bei einer 18-jährigen Patientin ohne bekannte Risikofaktoren

Zusammenfassung. Ein Fall von Pneumonie durch *Mycoplasma pneumoniae* mit tödlichem Ausgang bei einer vorher gesunden 18-jährigen Frau wird dargestellt. Der Antikörpertiter gegen *M. pneumoniae* wurde am Tag 9 des Spitalsaufenthalts mit 1:512 (Komplementbindungsreaktion) bzw. 1:5120 (Mikropartikel-Agglutinationstest) gemessen. Nach 5-wöchiger Behandlung an der Intensivstation verstarb die Patientin an nekrotisierender hämorrhagischer Pneumonie mit Multiorganversagen. Während der Dauer der Intensivpflichtigkeit traten keine relevanten zusätzlichen Infektionen auf. Korticosteroide (ab dem 8. Tag der stationären Behandlung) konnten den Krankheitsverlauf nicht positiv beeinflussen. Bemerkenswert ist, dass wie auch in einigen früheren Fallberichten trotz adäquater antimikrobieller Therapie gegen *M. pneumoniae* (in diesem Fall seit 2 Tage vor der stationären Aufnahme) zu einer Verschlechterung des klinischen Zustands kam, trotz der Eradikation des Erregers aus dem Respirationstrakt (mittels PCR konnte am Tag 22 nach Aufnahme *M. pneumoniae* nicht aus der bronchoalveolären Lavage nachgewiesen werden). Es ist jedoch festzuhalten, dass die Erkrankung bereits einige Tage vor der stationären Aufnahme begonnen hat, sodass über den möglicherweise positiven Effekt einer adäquaten antimikrobiellen Therapie in einem sehr frühen Stadium der Erkrankung keine Aussage getroffen werden kann. Aufgrund des Fehlens anderer therapeutischer Optionen im Fall von schweren Verläufen scheint die frühzeitige Diagnose und Therapie der Mykoplasmenpneumonie wesentlich. Dies ist der dritte Fall von tödlicher Pneumonie durch *M. pneumoniae*, welcher während der letzten Jahre in Österreich veröffentlicht wurde, was die Bedeutung der potentiell schweren Verläufe der Mykoplasmenpneumonie unterstreicht.

Summary. A case of fatal *Mycoplasma pneumoniae* pneumonia in a previously healthy 18-year-old girl is reported. On hospital day 9, the antibody titer to *M. pneumoniae* was 1:512 in the complement fixation test and 1:5120 in the microparticle agglutination assay. After five weeks in the intensive care unit, the patient died from necrotizing hemorrhagic pneumonia with multi-organ failure. No significant superinfections occurred during ICU treatment. Corticosteroids (hospital day 8 onward) did not influence the course of the disease. It is noteworthy that, as in some previously reported cases, the clinical state deteriorated during presumably adequate antibiotic treatment (2 days before admission onward), and despite documented eradication of the pathogen from the respiratory tract (PCR from bronchoalveolar fluid on hospital day 22 was negative). However, the illness had lasted for several days before admission to the hospital, therefore the potentially beneficial effect of antibiotic treatment at an early stage of the disease cannot be assessed. Clearly, in default of other treatment options, correct diagnosis and early treatment of mycoplasma community-acquired pneumonia seems mandatory. This is the third case of fatal mycoplasma pneumonia reported from Austria in recent years, making this topic worthy of further scientific attention.

Key words: *Mycoplasma pneumoniae*, necrotizing pneumonia, multi-organ failure.

Introduction

Mycoplasma pneumoniae is a frequent cause of respiratory tract disease. The infection shows important epidemiological fluctuations, with peak incidences every four to seven years [1, 2]. A minority of *M. pneumoniae* infections (around 3%) lead to community-acquired pneumonia, the mycoplasma-associated disease of greatest clini-

cal interest, which will usually be diagnosed and treated [3]. In most cases mycoplasma pneumonia presents as a mild-to-moderate disease with a benign outcome. Comprehensive descriptions of the common clinical signs and symptoms of mycoplasma pneumonia have been reviewed by Clyde [3] and Denny et al. [4].

However, through hitherto unknown pathogenetic mechanisms, which most probably involve immunological cell-mediated tissue damage, *M. pneumoniae* causes severe-to-life-threatening pulmonary disease in some patients. *M. pneumoniae* pneumonia can present as bronchiolitis obliterans [5, 6], bronchiolitis obliterans with organizing pneumonia [7], acute respiratory distress syndrome (ARDS) [8, 9], chronic interstitial fibrosis [10], and necrotizing pneumonia [11]. A case of mycoplasma pneumonia requiring lung transplantation as the result of severe necrotizing pneumonia has been described [12]. The fatal and nonfatal cases of severe mycoplasma pneumonia published before 1995 have been reviewed by Chan and Welsh [13].

Although severe-to-life-threatening courses of mycoplasma pneumonia appear to be rare, the possibility has to be considered. Here we describe a case of fatal *M. pneumoniae* pneumonia in a previously healthy 18-year-old girl.

Case report

An 18-year-old previously healthy girl was admitted to a hospital in southern Austria with fever up to 40 °C and cough with yellowish expectoration. Significant laboratory values were an elevated serum level of C-reactive protein (CRP; 22.3 mg/dl, reference range: < 1.1 mg/dl), a mild leucocytosis (15.4 G/l, reference range: 3.8–11 G/l), and an elevated serum level of alanine aminotransferase (ALT 63 U/l; reference range: < 31 U/l). Two days before admission the patient had been prescribed moxifloxacin by her physician. Chest X-ray revealed pericardial patchy attenuation of the right lower lobe. A CT scan of the thorax showed a hazy consolidation that appeared more solid than on radiography. The diagnosis of community-acquired pneumonia was made and treatment with roxithromycin and ceftriaxone was initiated. During the next days, the patient showed undulating fever with no improvement of the general condition. On hospital day 6 the patient showed a Quick prothrombin time of 48%, which was considered as a sign of developing sepsis. The patient was therefore transferred to the local ICU. Antibiotic treatment was changed from roxithromycin to clarithromycin (plus cefepime). At that time the leucocyte count was 17.27 G/ml and serum CRP 33.9 mg/dl. A control CT scan of the thorax revealed progression of the pneumonic infiltrate with consolidation involving the posterobasal right lower lobe, but the patient still showed sufficient oxygenation with spontaneous respiration. On hospital day 7, the patient had respiratory failure and required intubation for mechanical ventilation. Acute renal failure with anuria developed, therefore hemodialysis was initiated. A pericardial effusion had developed between hospital days 4 and 7, and a discrete exanthema on the right arm, which had been visible at admission, had progressed to the trunk.

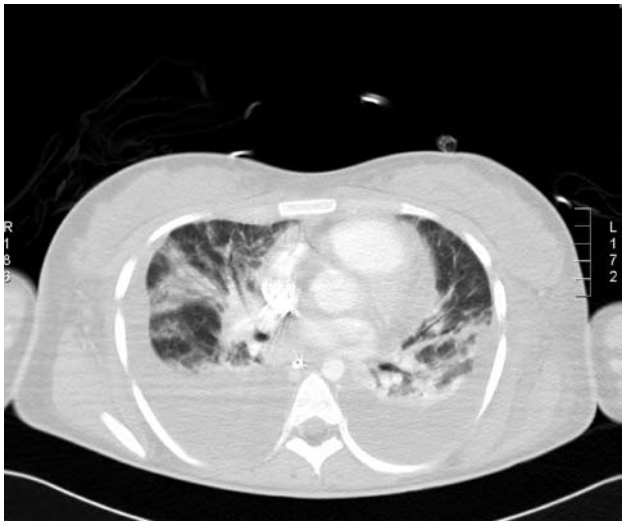

Fig. 1. Spiral-CT scan (hospital day 8) demonstrates bilateral upper lobe consolidation with air bronchograms and a large amount of pleural effusion

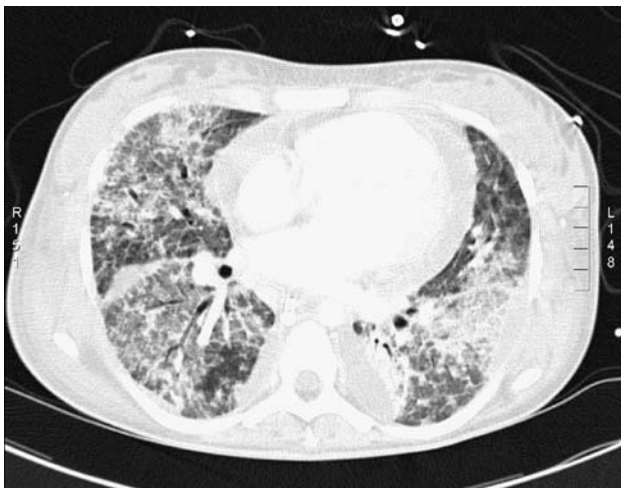

Fig. 2. Transverse thin-section CT scans of the chest (hospital day 17) show ground-glass opacities associated with smooth interlobular and intralobular septal thickening, with predominantly reticular pattern in lower lobes

On hospital day 8 the patient was transferred to Vienna General Hospital. On admission, a CT scan of the thorax showed progression of the pulmonary infiltrates, a large amount of bilateral pleural effusion and areas of hazy consolidation with air bronchograms, which now also included the apical part of both upper lobes (Fig. 1). In addition to respiratory failure, liver failure became evident, so that extracorporeal liver support with a molecular adsorption recirculating system (MARS) had to be initiated shortly after admission. Antimicrobial treatment with clarithromycin and cefepime was continued. Through the next four weeks anti-mycoplasma treatment was continued with alternating clarithromycin, azithromycin, ciprofloxacin, amikacin, and trimethoprim-sulfamethoxazole. From admission to Vienna General Hospital onward, the patient received hydrocortisone via a perfusor up to 30 mg/h (mostly 8 mg/h) throughout the hospital stay.

The pulmonary infiltrates were increasing and the CT scan showed areas of diffuse ground-glass attenuation and acinar attenuation of both lungs after hospital day 17 (Fig. 2). On hospital day 34 extracorporeal membrane oxygenation (ECMO) was initiated. On hospital day 35 the patient died from progressive hemorrhagic pneumonia and multi-organ failure. Pathological examination revealed septic dystrophy of the parenchy-

matous organs and fibrinous pericarditis. Cerebral bleeding of the parietal-temporal lobe and subpleural, pulmonary and diffuse gastrointestinal bleeding as a sign of hemorrhagic diathesis were also observed.

Microbiological investigations

Comprehensive investigations of the etiology of the pneumonia were performed. The results of serological tests are shown in Table 1. PCR assays for detection of CMV (serum, day 16) and *Chlamydia pneumoniae* (bronchoalveolar lavage, day 24) were negative.

Conventional bacteriological cultures were performed from blood (days 9, 14, 15, 26, 28, 29, 36), pleural fluid (d 9 and 13), pericardial fluid (d 35), ascites (d 15), urine (d 11), intravascular catheter tips (d 10, 24, 28, 29) and bronchial secretions (d 11, 14, 16, 18, 24, 36). All cultures remained nega-

Table 1. Results of serological tests

Pathogen	Day	Result	Assay
Legionella pneumophila	9	neg	Antigen/urine
Legionella spp. IgG	11	neg	ELISA
Legionella spp. IgM	11	neg	ELISA
Chlamydia psittaci IgG	11	neg	ELISA
Chlamydia psittaci IgA	11	neg	ELISA
Chlamydia psittaci	23	neg	CF
Chlamydia pneumoniae IgM	9	neg	ELISA[b]
Chlamydia pneumoniae IgM	9	neg	ELISA[b]
Chlamydia pneumoniae IgM	9	neg	ELISA[b]
Chlamydia pneumoniae IgA	18	neg	ELISA[b]
Chlamydia pneumoniae IgA	18	neg	ELISA[b]
Chlamydia pneumoniae IgA	18	neg	ELISA[b]
Chlamydia pneumoniae IgG	23	55 AU[b]	ELISA[b]
Chlamydia pneumoniae IgG	23	125 AU[b]	ELISA[b]
Chlamydia pneumoniae IgG	23	115 AU[b]	ELISA[b]
Bordetella pertussis IgA	11	neg	ELISA
Bordetella pertussis IgM	11	neg	ELISA
Pneumocystis jiroveci	24	neg	Antigen/BAL
Streptococcus pneumoniae	9	neg	Antigen/urine
Haemophilus influenzae	9	neg	Antigen/urine
Brucella abortus	9	<1:20	MAG
Brucella melitensis	9	<1:20	MAG
Francisella tularensis	9	<1:20	MAG
Weil Felix (OX-19, OX-2, OX-K)	9	<1:20	MAG
Leptospira spp.	9	<1:50	MAG
Borrelia burgdorferi IgG	11	neg	ELISA
Borrelia burgdorferi IgM	11	neg	ELISA
Salmonella spp. (OD, OA, OB, OC)	9	≤1:20	MAG
Hantaan virus IgG	16	neg	ELISA
Hantaan virus IgM	16	neg	ELISA
Adenovirus	9	neg	CF
CMV	9	1:16	CF[a]
CMV IgG	9	neg	ELISA[a]
CMV IgM	9	neg	ELISA[a]
CMV (serum)	16	neg	PCR
Enterovirus	9	1:8	CF
HSV	9	1:8	CF[a]
HSV IgM	9	neg	ELISA
Influenza A	9	1:8	CF[a]
Influenza B	9	1:4	CF[a]
Parainfluenza virus	9	1:4	CF[a]
VZV	9	1:8	CF[a]
VZV IgM	9	neg	ELISA
EBV IgM	9	neg	ELISA
Coxiella burnetii	23	neg	CF
RSV	23	neg	CF
HIV	9	neg	ELISA
HAV	9	neg	ELISA
HBV (Hbs-Ag)	9	neg	ELISA
HCV	9	neg	ELISA
Anti-A60-AK IgG to mycobacteria	24	neg	ELISA

[a]Repeated on hospital day 23 without significant change of the result; [b]*Chlamydia pneumoniae* ELISA plus, Medac, Wedel, Germany; cut-off value: 29 AU.

tive except an intravascular catheter tip removed on day 28, which yielded <100 colony forming units of *Staphylococcus epidermidis*. Bronchial secretions yielded low quantities of *C. albicans* (d 11, 14, 16, 18, 36).

Diagnosis of M. pneumoniae *infection*

On hospital day 9, antibody titers to *M. pneumoniae* were positive at 1:512 in the complement fixation (CF) test and 1:5120 in the microparticle agglutination (MAG) assay (Serodia Myco II, Fujirebio). These values were considered diagnostic for acute *M. pneumoniae* infection [14]. Two weeks later, the anti-*M. pneumoniae* titers had decreased to 1:128 in the CF test (day 23) and 1:640 in the MAG assay (day 24). PCR for detection of *M. pneumoniae* from bronchoalveolar lavage on hospital day 24 (after a total of 22 days of anti-mycoplasma therapy) was negative.

Discussion

There are several descriptions of severe cases of *Mycoplasma pneumoniae* pneumonia with and without associated multi-organ failure [15–19]. Clinically severe cases of *M. pneumoniae* pneumonia published before 1995 have been reviewed by Chan and Welsh [13]. In Austria, two cases of fatal mycoplasma pneumonia have been reported during recent years [12, 19].

Extremely severe or fatal cases of mycoplasma pneumonia may be underdiagnosed, because at the time of admission the patients are mostly critically ill, which does not raise suspicion of a mycoplasma etiology of pneumonia [20]. Furthermore, the possibility of comprehensive microbiological investigations, not only to diagnose *M. pneumoniae* infection but also to rule out other potential etiologies of pneumonia, may not be available in all healthcare settings. Nevertheless, clinically severe cases represent only a small minority of all cases of mycoplasma pneumonia.

In contrast to some published cases of severe *M. pneumoniae* pneumonia, the patient showed mild leucocytosis on admission [6, 10, 13]. However, it has been shown that leucocytosis in not uncommon in mycoplasma pneumonia [21]. CRP values have not been reported in most previous cases of severe mycoplasma pneumonia. The CRP serum level in the present case was considerably higher than in a patient collective from our institution [22] but lower than in our previously published case of fatal mycoplasma pneumonia with multi-organ failure [12].

In the present case, diagnosis of *M. pneumoniae* pneumonia was made from the results of serological tests. The patient showed highly elevated and diagnostic antibody titers in two different tests [14]. In addition to the high single titers, the fourfold decrease in titer between hospital days 9 and 23 is indicative of acute mycoplasma infection at the time of admission, because both tests mainly detect 'early' IgM antibodies [21, 22]. The negative PCR result on hospital day 24 after a total of 22 days of anti-mycoplasma therapy is not surprising. It is a shortcoming of the present report that no attempt was made to detect *M. pneumoniae* in the respiratory tract during an early stage of disease. However, it has been shown that the correlation between serology and PCR may be poor [25, 26]. One of the explanations for this finding may be a decrease of the bacterial load in the throat during the course of the illness [27]. With regard to moxifloxacin treatment from 2 days after admission onward, even a negative PCR result on admission would not have unambiguously ruled out a *M. pneumoniae* infection.

The urine antigen tests for detection of *S. pneumoniae* and *H. influenzae* were preformed relatively late in the course of the illness, after 11 days of potentially active antimicrobial treatment. IgG antibodies to *C. pneumoniae* in the medac ELISA plus were considerably elevated, but IgM and IgA antibodies were below the cut-off level for positivity. No evidence of *Legionella* sp. infection was obtained from the urine antigen test, or by antibody determination on hospital days 9 and 11. However, the antigen test enables the detection of exclusively *L. pneumophila* serogroup 1, and antibody determination within the first 11 days of hospitalization is quite early with regard to the slow mounting of *Legionella*-specific antibodies in the course of the illness. No anamnestic data on potential exposure to *Legionella* sp. were available. In the light of these considerations, the theoretic possibility of a co-infection including *M. pneumoniae* and an additional pathogen cannot be ruled out completely.

Both in the present case and in some previously reported cases of *M. pneumoniae*-associated ARDS, deterioration of the clinical state took place during presumably adequate antibiotic treatment [10, 13]. Clearly, from some stage of illness onward, the clinical course can no longer be influenced by antibiotics. However, in the present case, as well in previously described cases, the illness had lasted for several days before admission to hospital, therefore the effect of antibiotic treatment at an early stage of the illness cannot be assessed from the existing reports. Animal experiments have shown that significant inflammatory changes develop very early in the course of *M. pneumoniae* infection [28].

The development of pulmonary infiltrates in mycoplasma pneumonia is initially related to migration of mononuclear cells into the airways. Following cytokine release by macrophages, a mononuclear cell inflammatory response including mainly $CD4^+$ T cells, but also B cells and plasmocytes, contributes to infiltrate formation [29–31]. In human infection, lymphoplasmacytic bronchiolar wall infiltrates (cellular bronchiolitis) and bronchiolitis obliterans with organizing pneumonia (BOOP) have been described in open lung biopsy specimens from patients with nonfatal respiratory failure [8, 13].

There are data supporting the hypothesis that the severity of the disease and pulmonary infiltrates may be directly correlated with the strength of the individual immune response [20, 33]. There is also evidence that immunosuppressed patients with *M. pneumoniae* infection may lack pulmonary infiltrates [34]. In this context, corticosteroids, which down-regulate the cell-mediated immune response, may reduce immune-mediated pulmonary injury and may therefore be beneficial in extraordinarily severe mycoplasma pneumonia [10, 13]. The beneficial effect of corticosteroids has been described in some cases, although treatment failures have been reported in others. Previously published experiences with corticosteroid treatment of severe mycoplasma pneumonia have been summarized by Chan and Welsh [13]. In the present case the patient received corticosteroids from hospital day 8

onward, with progression of the pulmonary infiltrates despite presumable eradication of the pathogen itself.

To date, none of the potential treatment options for severe *M. pneumoniae* pneumonia has been evaluated in controlled clinical trials. Nevertheless, in default of other options, early diagnosis and treatment of community-acquired mycoplasma pneumonia seems mandatory. At present, one recommendable tool, among others, for the diagnosis of acute *M. pneumoniae* infection is ELISA detection of specific IgM and IgA antibodies [14]. If no rapid access to a well equipped laboratory is available, the bedside test Immunocard Mycoplasma (Meridian Bioscience, Cincinnati, OH, USA) for detection of specific IgM is a feasible though less sensitive alternative [35]. Studies on the pathogenesis of severe *M. pneumoniae* infections, which would enable conclusions on possible treatment options, are warranted.

References

1. Foy HM (1993) Infections caused by *Mycoplasma pneumoniae* and possible carrier state in different populations of patients. Clin Infect Dis 17 [Suppl 1]: S37–46
2. Daxboeck F, Bauer CC, Assadian O, Stanek G (2006) An unrecognized *Mycoplasma pneumoniae* epidemic in Vienna. Wien Klin Wochenschr 118: 208–211
3. Clyde WA Jr (1993) Clinical overview of typical *Mycoplasma pneumoniae* infections. Clin Infect Dis 17 [Suppl 1]: S32–36
4. Denny FW, Clyde WA Jr, Glezen WP (1971) *Mycoplasma pneumoniae* disease: clinical spectrum, pathophysiology, epidemiology, and control. J Infect Dis 123: 74–92
5. Waites KB, Talkington DF (2004) *Mycoplasma pneumoniae* and its role as a human pathogen. Clin Microbiol Rev 17: 697–728
6. Chan ED, Kalayanamit T, Lynch DA, Tuder R, Arndt P, Winn R, Schwarz MI (1999) *Mycoplasma pneumoniae*-associated bronchiolitis causing severe restrictive lung disease in adults. Chest 115: 1188–1194
7. Prabhu MB, Barber D, Cockcroft DW (1991) Bronchiolitis obliterans and Mycoplasma pneumonia. Respir Med 85: 535–537
8. Llibre JM, Urban A, Garcia E, Carrasco MA, Murcia C (1997) Bronchiolitis obliterans organizing pneumonia associated with acute *Mycoplasma pneumoniae* infection. Clin Infect Dis 25: 1340–1342
9. Van Bever HP, Van Doorn JWD, Demey HE (1992) Adult respiratory distress syndrome associated with *Mycoplasma pneumoniae* infection. Eur J Pediatr 151: 227–228
10. Radisic M, Torn A, Gutierrez P, Defranchi HA, Pardo P (2000) Severe acute lung injury caused by *Mycoplasma pneumoniae*: potential role for steroid pulses in treatment. Clin Infect Dis 31: 1507–1511
11. Oermann C, Sockrider MM, Langston C (1997) Severe necrotizing pneumonitis in a child with *Mycoplasma pneumoniae* infection. Pediatr Pulmonol 24: 61–65
12. Daxböck F, Brunner G, Popper H, Krause R, Schmid K, Krejs GJ, Wenisch C (2002) A case of lung transplantation following *Mycoplasma pneumoniae* infection. Eur J Clin Microbiol Infect Dis 21: 318–322
13. Chan ED, Welsh CH (1995) Fulminant *Mycoplasma pneumoniae* pneumonia. West J Med 162: 133–142
14. Daxboeck F, Krause R, Wenisch C (2003) Laboratory diagnosis of *Mycoplasma pneumoniae* infection. Clin Microbiol Infect 9: 263–273
15. Takiguchi Y, Shikama N, Aotsuka N, Koseki H, Terano T, Hirai A (2001) Fulminant *Mycoplasma pneumoniae* pneumonia. Intern Med 40: 345–348
16. Chian CF, Chang FY (1999) Acute respiratory distress syndrome in Mycoplasma pneumonia: a case report and review. J Microbiol Immunol Infect 32: 52–56
17. Baum H, Strubel A, Nollert J, Layh-Schmitt G (2000) Two cases of fulminant *Mycoplasma pneumoniae* pneumonia within 4 months. Infection 28: 180–183
18. Turi L, Herbecq P, Vignozzi G, Lemaire C (1996) Respiratory distress syndrome in an adult secondary to *Mycoplasma pneumoniae* infection. Presse Med 25: 127
19. Graninger W (2005) Tödliche Mykoplasmenpneumonie mit Multi-Organ-Versagen. 8. Kongress für Infektionskrankheiten und Tropenmedizin, Hamburg, S57
20. Cassell GH (1995) Severe Mycoplasma disease – rare or underdiagnosed? West J Med 162: 172–175
21. Lieberman D, Schlaeffer F, Lieberman D, Horowitz S, Horovitz O, Porath A (1996) Mycoplasma pneumoniae community-acquired pneumonia: a review of 101 hospitalized adult patients. Respiration 63: 261–266
22. Daxboeck F, Gattringer R, Mustafa S, Bauer C, Assadian O (2005) Elevated serum alanine aminotransferase (ALT) levels in patients with serologically verified Mycoplasma pneumoniae pneumonia. Clin Microbiol Infect 11: 507–510
23. Jacobs E (1993) Serological diagnosis of *Mycoplasma pneumoniae* infections: a critical review of current procedures. Clin Infect Dis 17 [Suppl 1]: S79–82
24. Barker CE, Sillis M, Wreghitt TG (1990) Evaluation of Serodia Myco II particle agglutination test for detecting *Mycoplasma pneumoniae* antibody: comparison with mucapture ELISA and indirect immunofluorescence. J Clin Pathol 43: 163–165
25. Wubbel L, Jafri HS, Olsen K, Shelton S, Barton Rogers B, Gambill G et al. (1998) *Mycoplasma pneumoniae* pneumonia in a mouse model. J Infect Dis 178: 1526–1529
26. Waris ME, Toikka P, Saarinen T, Nikkari S, Meurman O, Vainionpaa R, Mertsola J, Ruuskanen O (1998) Diagnosis of *Mycoplasma pneumoniae* pneumonia in children. J Clin Microbiol 36: 3155–3159
27. Tjhie JHT, van Kuppefeld FJM, Roosendaal R, Melchers WJ, Gordijn R, MacLaren DM, Walboomers JM, Meijer CJ, van den Brule AJ (1994) Direct PCR enables detection of *Mycoplasma pneumoniae* in patients with respiratory tract infections. J Clin Microbiol 32: 11–16
28. Dorigo-Zetsma JW, Zaat SA, Vriesema AJ, Dankert J (1999) Demonstration by a nested PCR for *Mycoplasma pneumoniae* that *M. pneumoniae* load in the throat is higher in patients hospitalised for *M. pneumoniae* infection than in non-hospitalised subjects. J Med Microbiol 48: 1115–1122
29. Opitz O, Piestch K, Ehlers S, Jacobs E (1996/1997) Cytokine gene expression in immune mice reinfected with *Mycoplasma pneumoniae:* the role of T cell subsets in aggravating the inflammatory response. Immunobiology 196: 575–587
30. Fernald GW (1973) Role of host response in *Mycoplasma pneumoniae* disease. J Infect Dis 127 [Suppl]: S55–58
31. Pietsch K, Jacobs E (1993) Characterization of the cellular response of spleen cells in BALB/c mice inoculated with *Mycoplasma pneumoniae* or the P1 protein. Med Microbiol Immunol (Berl) 182: 77–85
32. Ito S, Abe Y, Kinomoto K, Saitoh T, Kato T, Kohli Y, Kuriyama M, Sakai T, Ishizaki T (1995) Fulminant *Mycoplasma pneumoniae* pneumonia with marked elevation of serum soluble interleukin-2 receptor. Intern Med 34: 430–435

33. Tanaka H, Honma S, Abe S, Tamura H (1996) Effects of interleukin-2 and cyclosporine A on pathologic features in *Mycoplasma* pneumonia. Am J Respir Crit Care Med 154: 1908–1912
34. Foy HM, Ochs H, Davis SD, Kenny GE, Luce RR (1973) *Mycoplasma pneumoniae* infections in patients with immunodeficiency syndromes: report of four cases. J Infect Dis 127: 388–393
35. Beersma MF, Dirven K, van Dam AP, Templeton KE, Claas EC, Goossens H (2005) Evaluation of 12 commercial tests and the complement fixation test for *Mycoplasma pneumoniae*-specific immunoglobulin G (IgG) and IgM antibodies, with PCR used as the "gold standard". J Clin Microbiol 43: 2277–2285

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