Reviewer's report

Title: Mycoplasma pneumoniae pneumonia revisited within the German Competence Network for Community-acquired pneumonia (CAPNETZ)

Version: 1 Date: 22 September 2008

Reviewer: Katherine Loens

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Major compulsory revisions:

General Comments

The authors studied the incidence, clinical characteristics, and outcome of patients with M. pneumoniae pneumonia. The diagnosis was based on a positive PCR result from respiratory samples and/or a positive IgM titer from an acute phase serum sample. On the other hand IgA and IgG tests were performed on the acute phase serum as well (see M&M) but the correlation between the combination of different serology results with PCR (if a respiratory specimen was available) is not shown in the manuscript.

The applied IgM test has a sensitivity in early and middle phase sera of 37%, an overall sensitivity (early, middle and late phase) of 71% and a specificity of 88% (Beersma 2005).

The gold standard for diagnosis a M. pneumoniae infection by serology is still a 4-fold rise or seroconversion of IgG. According to the ERS guidelines (Woodhead 2005), serologic tests for the management of the individual patient with LRTI are not recommended. Serology for infections caused by M. pneumoniae is more useful in epidemiologic studies than in the routine management of the individual patient.

Respiratory specimens were available from 33.6% of patients. In a previous publication from the CAPNETZ project (Wellinghausen 2006) an expanded gold standard (PCR positive in at least 2 different laboratories) was used to define a C. pneumoniae infection (MIF was done as well) which is scientifically more correct. The definition used in this manuscript is less stringent. Why?

According to Nilsson et al (Nilsson 2008) PCR is superior to serology for diagnosis of a M. pneumoniae infection. Additionally, Daxboeck et al. recommended the combination of serology and direct pathogen detection for diagnosis of a M. pneumoniae infection. (Daxboeck 2003).

In conclusion, it’s a pity that not all patients had both a respiratory sample and serum sample available.

Specific comments

Abstract

1. Page 2, line 12: Why only a positive IgM result and no IgG and/or IgA? Paired
sera were not collected? A major limitation of an IgM-specific test is that
detectable levels of IgM antibodies may not be present if the serum sample is
obtained too early in the infection, and only 14 to 27% of acute-phase sera tested
positive by the various IgM kits in a study by Talkington et al. (Talkington 2004).
Additionally, in the diagnosis of infection in adults and in cases of adult
reinfections where IgM is not always produced, the detection of specific IgM
antibodies alone may be problematic. Adults may produce only IgG antibodies.
False positive IgM results have been reported as well. The use of serology alone
for the diagnosis of a M. pneumoniae infection on single serum samples is more
and more open for discussion. Nir-Paz et al. (Nir-Paz, R. 2006), and others
(Petitjean 2002, Waites et al. 2004), re-emphasised the need to use paired sera
for the diagnosis of M. pneumoniae infections, as well as the need for more
accurate and reliable diagnostic kits.

Introduction

2. Page 4, line 7: Chlamydia should be replaced by Chlamydophila

3. Page 4, line 15: M. pneumoniae pneumonia is usually a mild pneumonia, as is
also shown in this study, and not very often the cause of death.

Materials and Methods

4. Page 6, line 19: other respiratory secretions: Did it depend on the opinion of
the physician whether or not a respiratory specimen was collected in case the
patient was not able to provide a sputum? There was no standardized respiratory
sampling foreseen in the study?

5. Page 7, line 3: how were samples transported to Ulm?

6. Page 7, line 5: how long were they stored before NA extraction? Were all
samples retrospectively analysed (both respiratory specimens and sera)? Were
physicians aware of the test results to enable them to change therapy?

7. Page 5, line 16: IgG and IgA tests were performed but results are not
specifically mentioned.

8. Page 5, line 18: crude antigen, enriched antigen, recombinant antigen?

Results

9. Page 10, line 1: How do IgM, IgA, IgG and PCR results correlate with each
other?

10. Page 10, line 16: which test was used for L. pneumophila detection? uAg,
serology, PCR, culture?

11. Page 11, 1st paragraph: is there a difference in outcome/recovery between
patients that received appropriate AB-therapy and those that received
inappropriate AB-therapy? This is not clear from the text. According to Table 1,
2% of patients had a change of AB-therapy.

Discussion

12. Page 13, line 14-20: Another study or more detailed correlations between all
serological tests and PCR should be presented to support this paragraph.

13. Page 14, line 21-24: should be more emphasized in the results section.
Figures and Tables
14. Table 2: what about IgM+, IgA+, IgG+ but PCR- etc? If the numbers of positive combinations (PCR and serology) are counted, the total number of PCR positives is 170, whereas the results section mentions 148 PCR + patients probably due to the fact that some patients had 2 positive serological tests. This should be clarified.
15. Fig 1: the abbreviation should be S. pneumoniae in stead of Str. pneumoniae

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I have no competing interests