Author's response to reviews

Title: Chlamydia pneumoniae ARDS: successful treatment with extracorporeal membrane oxygenator; a case report and diagnostic review.

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Author's response to reviews: see over
Dear Professor Kidd,

We are submitting the revised material “*Chlamydophila pneumoniae* ARDS: successful treatment with extracorporeal membrane oxygenator; a case report and diagnostic review.” for publication in the *Journal of Medical Case Reports*. Please find a point-by-point response to the reviewers’ and editor concerns.

*English has been revised. All modifications have been highlighted in the manuscript.*

**Reviewer 1**

It is an interesting article that emphasizes that *C. pneumoniae* can cause ARDS even in otherwise healthy individuals and that the use of ECMO can be used in such patients as a salvage therapy. However, in the ‘Discussion’ section it is discussed in details only the diagnostic procedures, and briefly the ECMO. The topic of severe *C. pneumoniae* respiratory infections is hardly discussed. I suggest that the discussion should be enriched with such information (a brief review of the literature).

*The discussion section on the use of ECMO has been extended.*

Also, regarding the diagnosis, I suggest the authors to read the article Vaccine Immunol. 2008; 15:1508-31 and, if they think that adds information, to include it in the discussion.
Answer: IgM antibodies are interesting especially in a children’s population but seldom in adults as they have seldom a detectible titer of IgM (majority of reinfections, as in our case).

Line 2: Please rephrase the sentence: ‘Infection goes trough…’

Answer: this was done.

Abstract-Conclusion:-‘Chlamydophilia’ should be changed to ‘Chlamydophila’; -‘Definite diagnosis of Chlamydophilia is uneasy as specific and simple diagnostic tools still need to be developed.’

Answer: this was done.

Please, rephrase this sentence. I would suggest e.g.: ‘Simpler, more rapid and more specific methods for the definite diagnosis of Chlamydophila infections should be developed.’

Answer: this was done.

-Line 7: ‘…chronic obstructive pulmonary diseases…’ Do you mean ‘…exacerbations of chronic pulmonary disease…’? Please, clarify and add the corresponding reference(s).

Answer: this was done.

General comment: It should be clear in the description of the case the sequence of the events, using as reference the day of hospital admission (Day 1): Day of ICU admission, Day of the presentation of acute renal failure, Day of endotracheal intubation and initiation of mechanical ventilation, Day of ECMO initiation, Day of hospital discharge (if available).

Answer: this has been done.

-Par. 2, Line 1: ‘sequel’ should be changed to ‘sequela’

Answer: this was changed for ‘consequences’.

-Par. 2, Line 2: ‘gastric ulcus’ I would recommend the use of the term ‘gastric ulcer’

Answer: this has been done.

-Par.4, Line 1: ‘aeric bronchogram’ should be changed to ‘air bronchogram’

Answer: this has been done.
-Par.6, Line 1: ‘Samples obtained from the day of admission…’ should be changed to ‘Samples obtained on the day of admission…’

**Answer: this has been done.**

-Last par., Line 2: ‘…the patient was extubated a week later…’ Do you mean a week after ECMO withdrawal? Please, clarify.

**Answer: this has been done.**

-Par. 2, Line 4: ‘…diffuse symptomatic course of C. pneumonia …’ Please, rephrase. I would suggest e.g. ‘…unspecific symptoms of C. pneumoniae…’

**Answer: this has been done.**

-Par. 2, Line 4: ‘C. pneumonia’ should be changed to ‘C. pneumoniae’

**Answer: this has been done.**

-General comment: I would suggest an addition of very brief comment on other severe complications of C. pneumoniae that have been reported in the current literature (e.g. acute hepatitis, acute renal failure etc)

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Table I:

I would suggest instead using the dates 22/08/2009 - 03/09/2009 - 13/09/2009 presenting the days of sampling as Day 1 - Day 13 - Day 23

**Answer: this has been done.**

**Reviewer 2**

Authors described a severe case of ARDS due to C. pneumoniae infection and multi organ dysfunction syndrome treated by mechanical ventilation, Prone position, Nitric Oxide inhalation, ECMO and they conclude that the ARDS successfully treated by extracorporeal membrane oxygenation.
The weakness of the case is that pneumonia and sepsis are the most common triggers for ARDS, so a presentation of an ARDS due to pneumonia treated with the whole spectrum of well studied therapeutic options make the paper unsound.

Another problem is the discrepancy between the title << successful treatment with extracorporeal membrane oxygenator >> and the discussion, in which chapter the authors extensively discus only the different diagnostic tools for C. pneumoniae and not treatment.

**Answer: we kindly disagree with the above statements:**

*First, pneumoniae due to C pneumoniae has lead to ARDS, and anti-microbial treatment is rather specific; this has been added in the introduction. To our knowledge, there has been no report of chlamydophila ARDS successfully treated by ECMO. Extensive discussion of diagnostic tools is mandatory in such difficult to diagnose infection.*

**Reviewer 3**

On section "Case Report", 5th paragraph: Please indicate the exact values of laboratory parameters (i.e. creatinine, LDH, coagulation parameters etc) and specify severe hypoxia (ABGs, PO2/FiO2).

**Answer: this has been done.**

7th paragraph: Please write the cardiac hemodynamic data and a comment about SvO2 (septic profile? cardiac dysfunction?)

**Answer: this was done and a table 2 was added.**

8th; On what day of hospitalization / mechanical ventilation ECMO was applied?

*This was answered to with the remarks of reviewer 1.*

On "TABLE I" I think it is better to write the weeks after hospital admission (or initiation of symptoms) and not the exact date of the examination.
**Reviewer 4**

1. In INTRODUCTION: (at the end of the first paragraph) it would be advisable to specify the first-line antimicrobial treatment against Clamydophylia pneumonia

   *Answer: this has been done.*

2. In INTRODUCTION (at the end of the second paragraph) it would be prefferable to add the following ' STUDIES HAVE SHOWN THAT 35-47% of Chl. pneumonia pneumonia is mixed with other pathogens, the most common being str. pneumonia" Cin Infect Dis 1999;29:426 and Chest 2002;12:1776

   *Answer: this has been done and the articles have been added to the references.*

3. In CASE REPORT at the beginning of the 4th paragraph "arterial blood gas detemination..." You should specify the initial blood gas results

   *Answer: this has been done.*

4. In CASE REPORT at the beginning of 5th paragraph " Paired serum samples and Ag......." What does Ag stand for??

   *Answer: Ag = antigen; this has been changed in the paper.*

5. In CASE REPORT at the end of 6th paragraph It would be advisable to give the full cardio-respiratory data (formated in a table) before and after the ECMO

   *Answer: this has been done and added in table 2 (cfr. Reviewer 3).*

6. In DISCUSSION: In my opinion your case report is focused on two arms, firstly the successful use of ECMO and secondly the serologic diagnosis of the disease. Therefore I believe that you
should dedicate more space for the first arm dealing with the ECMO technique in much more details. You dedicated only half a page for the ECMO and more than two pages for the diagnosis.

*Answer: this has been changed and additional information has been given in the first part of the discussion.*

7. In DISCUSSION (second paragraph, six line) It would be better to specify the serious sequelae someone could get during the chronic course of the disease in case it remained undetected

*Answer: this has been done and a reference 17 has been added.*

8. In DISCUSSION (last paragraph) According to the diagnostic procedures you thoroughly analysed, in which state (current, reinfection, reactivation) do you classify the patient in the case report??

*Answer: In our patient reinfection was diagnosed because MIF were positive on admission, there was a four fold increase in anti-MOMP IgG, and finally a important rise and a rapid decline in anti-LPS IgA. This has been added in the discussion.*
We hope that the answers to the reviewers’ remarks make our paper more understandable and that it is now possible to accept it for publishing in the *Journal of Medical Case Report*.

Yours sincerely,

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