Reviewer’s report

Title: MACROPHAGE ACTIVATION-LIKE SYNDROME: AN IMMUNOLOGICAL ENTITY ASSOCIATED WITH RAPID PROGRESSION TO DEATH IN SEPSIS

Version: 0 Date: 14 May 2017

Reviewer: Miroslav Prucha

Reviewer's report:

The topic of the study is very interesting, however, I have the following comments on its content and implementation:

1. Background …poor definition of anakinra: anakinra is a recombinant, nonglycosylated form of the human interleukin-1 receptor antagonist (IL-1Ra).

2. Patients and Methods: Study design: Did the study involve patients with sepsis or infection? Line 6

3. P. 8 - study endpoints……Why did the authors divide the patients into two cohorts and subsequently use the Swedish validation cohort?

4. Definitions of MAS and MALS are confusing. What exactly is the difference between MALS definition here and MAS definition commonly used in the literature? And why were two definitions used to fulfill the criteria of MALS? (lit 5 a 15)

5. How is "immunodeficiency" defined in the authors’ HS score? In the original study referred to, it indicates clinical characteristics of the patients.

6. It is incorrect what the authors did in the case of MALS definition….i.e. compliance with the criteria for HS (p.8).

HS is based on a certain number of parameters, each of them having a specific point score. A certain number of points has 90% sensitivity for the compliance with the criteria of the syndrome. The authors, unable to measure one parameter, deducted the number of points assigned to this character and considered the total "diminished" in this way to be of equal value as the original. However, the evaluation of 9 parameters is not the same as the evaluation of 8 characters…In addition, I do not understand why 18 points were deducted, when bone marrow aspiration is associated with 35 points???.

The ratio of IL10/TNF - is not used in clinical practice. The measurement of HLA-DR expression on monocytes would be far more beneficial.
The following points should be discussed in more detail: In the studies published by Hotchkiss et al, dominant immunosuppression characteristic for patients with sepsis has been demonstrated. What is the authors’ opinion of the presence of MAS in the context of this immunosuppression and why is MAS present in such a small percentage of patients with sepsis? What explanation do the authors have for the dependence of this mortality on the decrease in ferritin on day 10?

Overall assessment: As has already been mentioned, the subject of the study is interesting but the general conception of the manuscript is confusing. It contains serious inaccuracies both in the form and content, and therefore requires substantial revision.

Are the methods appropriate and well described?  
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?  
If not, please specify which controls are required in your comments to the authors.

No

Are the conclusions drawn adequately supported by the data shown?  
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?  
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

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Please indicate the quality of language in the manuscript:

Not suitable for publication unless extensively edited

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