Reviewer’s report

Title: INCREASED INCIDENCE OF SUSAC SYNDROME: A CASE SERIES STUDY

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Reviewer's report:

The manuscript „Increased incidence of SUSAC syndrome: a case series study” by Wilf-Yarkoni et al presents a single-center retrospective study on the incidence of Susac syndrome (SuS), a rare immune-mediated occlusive microvascular disease, in patients in the Surasky Medical Center in Tel Aviv, Israel. The authors report on 7 cases diagnosed and treated in their center from July 2017 to August 2018.

The main findings are (i) an increased incidence as compared to the reported incidence in a study from Austria and (ii) a putative correlation to infectious diseases as insinuated by positive CMV IgM antibody titers in 3 patients and increased anti-Streptolysin titer in one patient. Based on these observations, the authors conclude that is is worthwhile searching for a post-infectious state in newly diagnosed SuS patients as well as to screen for latent infections.

General critique:
This is an interesting case collection in a single center retrospective study, which highlights SuS as a rare yet important disease with therapeutic consequences in affected patients. Indeed, bringing this rare condition to the attention of physicians and translationally minded scientists is of great importance, which in this reviewer’s opinion constitutes the main value of this manuscript.

That said, serveral limitations on the study itself as well as the conclusions drawn emerge, which should be addressed in a revised version of the manuscript.

1. Most importantly, it is hard to accept the conclusion and supposed main finding of an increase in incidence based on the data presented. Comparing cohorts from another country with varying demographic and ethnic background may not represent the best way to conclude on an increase in incidence. Instead, could the authors present numbers for the last years of their center, maybe present them in a graphical yearly form to calculate the significance of their finding? Moreover, reasons for this potential increase in SuS incidence should be discussed (e.g. diagnostic criteria) in a revised version of the manuscript.

2. The authors point out in their discussion that there is no known correlation with infectious diseases and the occurrence of SuS. Yet, they postulate an infectious etiology due to IgM serum titers for CMV and increased anti-Streptolysin titer. However, this might be a mere co-incidence and in no way causal. Especially, did the authors measure IgM antibody titers in the CSF of these patients as well? Did the IgM antibodies in the serum convert to IgG over time? Were CMV PCRs done in the serum/PBMCs as well? In these lines, were there increased anti-Streptolysin titers in the CSF as well? Providing these data would be important to postulate an infectious etiology. If not, for sure the limitation of their conclusion (co-incidence, false positives etc) should be discussed in more detail in the discussion.
3. Did the authors check for serum and CSF anti-endothelial cell antibodies, a potential etiology of SuS brought forward in the discussion?

4. Since one potential aim of this report may be to increase the awareness about this rare disorder, it would be appreciated if the authors explained the standard diagnostic criteria and treatment regimen in more detail. A table based on the recent criteria might be useful to achieve that aim.

Minor points:
5. Please define abbreviations when first using them, e.g. BRAOs p.8, line 8
6. Please use complete sentences (p.9, line 5)
7. Table 2: please use generic pharmaceutical names instead of brand names (aspirin)

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Yes

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

Yes

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
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I am able to assess the statistics

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