Reviewer’s report

Title: Increased serum IL-36β and IL-36γ levels in patients with neuromyelitis optica spectrum disorders: Association with disease activity

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Reviewer: Denis Bichuetti

Reviewer's report:

I have reviewed with interest the work by Drs. Yang and Zhand et al, on the possible effects and association of IL36 and NMO.

With the current knowledge it is assumed than NMO is not only a demyelinating disease, but an inflammatory disease that sarges the blood brain barrier. Please correct the statement in the introduction.

Table 1 discloses that 30% of the patients presented a topographic lesion as "others", I recommend specifying since this is such a small sample. Also, reporting the imunossupressive agents and dosage is importante, and I also recommend performing a correlation between time of imunossupression and IL36 dosage. At first, on might assume that levels are higher during an attack, but figure 3 shows that not all patients presente with reduction on its levels, and adequate imunossupression might be driving this effect, and not time distance from the relapse. Furthermore, it would also be interesting to include a control group with another CNS autoimmune disease, so to state if the elevation of IL36 is exclusive fo NMOSD or a common finding in CNS autoimmune disease. If this is not feasible, it must at least be discussed.

Although authors stated that they excluded MOG positive and other comorbidades immune diseases, only 56% of the sample is AQP4 positive. This is a slow number, unless tested under therapy, and I think it would be interesting to disclose when during disease course the antibody was tested.

These are small complementary analysis, but I think they would ad value to the study. Furthermore, I think it is to early to implicate IL36 in NMO pathogens, even earlier to propose a therapeutic target. The current study only reports an association, we do not know if cause-relation or not, and I recommend reviewing these statements.

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.

Yes

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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