Reviewer's report

Title: Hypogelsolinemia, a disorder of the extracellular actin scavenger system, in patients with multiple sclerosis

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Reviewer: Hayrettin Tumani

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In this manuscript, Kulakowska et al. measured gelsolin (GSN) and Vitamin D binding protein (DBP) as indicators of the actin scavenger system in blood and cerebrospinal fluid (CSF) of patients with multiple sclerosis (MS).

The authors used Western blot for analysis of GSN and ELISA for DBP.

The authors found that decreased serum levels of GSN are associated MS, and conclude that this protein may be involved in chronic inflammation associated with neurodegeneration.

Although the preliminary character of the study does not allow drawing a meaningful conclusion yet, the findings of this study warrant systematic longitudinal and prospective studies to further understand the role of GSN in the pathogenesis of MS.

Major concerns:

Main methodological limitations of this study are
1. cross sectional nature (longitudinal changes can not be excluded),
2. small cohort of patients (MS is a heterogenic disease),
3. lack of detailed clinical description of relapse activity,
4. lack of data on MRI brain lesions,
5. lack of other MS subtypes representing early (first attack) and advanced disease (secondary progressive MS) stages, and finally
6. lack of other inflammatory disease controls.

Minor concerns:

1. Numbers of samples or patients should be given in the abstract.
2. To get an impression of the clinical activity presence of relapse or time between sampling and last relapse would be of interest.
3. In Table 1, presence or prevalence of oligoclonal IgG bands should be included, since this diagnostic parameter is the only indicator of the inflammatory process found in the CSF of MS patients.
4. If possible data on the CSF/serum ratio of albumin to assess the state of the blood-CSF-barrier function in MS and control patients should be given in Table 1.
This would be more appropriate than total protein, especially since mobilization effect of the actin scavenger system across the blood-CSF barrier is discussed as a potential mechanism for the reduced GSN in blood of MS.

5. Potential causes for the reduced GSN should be discussed more cautiously, since there is no convincing evidence from the data presented or from the literature. In contrast, the authors offer an argument against by “However, accumulation of EASS protein in the CNS would probably result in the presence of significantly higher intrathecal gelsolin and DBP levels, which was not observed.”

6. Please discuss the limitations of Western blot assay, as it is more difficult than ELISA to standardize. Furthermore Western blot data have to be regarded semiquantitative rather than quantitative.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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

Declaration of competing interests:

'I declare that I have no competing interests'