Reviewer’s report

Title: Novel ANKRD11 gene mutation in an individual with a mild phenotype of KBG syndrome associated to a GEFS+ phenotypic spectrum: a case report.

Version: 0 Date: 14 Nov 2018

Reviewer: Ilaria Parenti

Reviewer’s report:

The authors present an interesting case report describing two siblings with GEFS+, with one of the sibling showing a more complex phenotype reminiscent of a neurodevelopmental disorder. The identified mutation in SCN9A explains the GEFS+ phenotype, whereas the additional ANKRD11 variant clarifies the more complex phenotype of the most severely affected sister. The report underlines the importance of identifying multiple molecular diagnoses for the interpretation of disease phenotypes and for an appropriate surveillance and treatment of human diseases.

The variant in SCN9A p.Lys655Arg appears to be quite frequent in the population, and also ClinVar suggests a conflicting interpretation of pathogenicity for this variant. The authors could expand their discussion and speculate on the reason-why the same variant does not cause the same phenotype in the unaffected father (e.g. Incomplete penetrance? Existence of an additional causative variant in the siblings? Existence of a protective variant in the father?)

The authors should name the kit and the companies used for DNA extraction and array-CGH. Also, the different stages of the genetic analysis should be discussed in more detail.

The authors should check the references throughout the manuscript, since some references are not included in the references list (e.g. Swols 2017).

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.

Yes
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.

Not relevant to this manuscript

Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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