Reviewer's report

Title: A novel CCM1 mutation associated with multiple cerebral and vertebral cavernous malformations.

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Reviewer: Florence Riant

Reviewer's report:

The authors report a 4 generations CCM family with an unreported CCM1 intronic mutation leading to a splicing defect. They describe the clinical presentation in this family, in particular the association with vertebral hemangioma.

Major compulsory revisions:

The authors insist of the presence of vertebral hemangiomas in this family but they don’t discuss about the eventual importance. Why has a spinal MRI been done in the proband and in his relatives? What is the interest of doing it? What are the consequences of the presence of vertebral hemangioma, is there a special follow-up for the patients? What is the frequency of vertebral cavernoma in the general population?

Minor essential revisions:

1. The numbering of the exons is not concordant with the reference sequence used by the authors (the reported mutation is located in intron 5 close to exon 6 in ref seq NM_194454)

2. The presence or absence of the variant in polymorphisms databases should be given.

3. How do you look for the conservation of intronic regions?

4. There is no comment about the hepatic hemangioma. Is there an impact in the follow up?

5. There are some words to be corrected: “subjesct” page 2, “widespreas” page 5, “malfrmations”, “inleft”, “retrotrascibed” page 6.

In conclusion, the interesting points of this article are i) the association with vertebral hemangiomas but there is no comment about the incidence in the patients, ii) the new intronic mutation leading to a splice defect (interest for diagnostic laboratory). There is no real novelty in the other data and the article could be shortened in its presentation.

Level of interest: An article whose findings are important to those with closely related research interests.
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.