Reviewer's report

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

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Reviewer: giorgio boncoraglio

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Authors report the case of a 49-year-old man that was diagnosed with multiple supratentorial cavernous angiomas and multiple vertebral hemangiomas; they studied also four generations of his family and found other six members with multiple cerebral cavernous malformations. In two of them, spinal MRI was performed and was normal.

Given the autosomal dominant pattern of inheritance, CCM1, 2 and 3 were sequenced in the proband and two affected relatives. A new c.263-10A>G variant in the CCM1 gene was found in the 3 affected subjects. This mutation produces an alteration in the transcript.

Authors conclude that their findings support the pathogenicity of c.263-10A>G mutation and expand the spectrum of genetic defects associated with the pathogenesis of vertebral hemangiomas and cerebral cavernous malformations.

Up to 2007, more than 90 distinct CCM1 mutations have been published.

For this paper, I see two major compulsory revisions that should be done:
1. none of the healthy relatives has been tested for the c.263-10A>G variant. At least one of the healthy (clinically and radiologically) should be.
2. vertebral hemangiomas are relatively common benign dysplasias or vascular tumors affecting the vertebral column, with an estimated incidence of 10% to 12% in the population [Acosta FL Jr, et al. Comprehensive management of symptomatic and aggressive vertebral hemangiomas. Neurosurg Clin N Am. 2008;19:17-29]. Therefore, unless authors will find at least an other affected members with vertebral hemangiomas, they should not conclude that their findings expand the spectrum of genetic defects associated with the pathogenesis of vertebral hemangiomas and cerebral cavernous malformations.

Level of interest: An article of limited interest

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