Reviewer’s report

Title: Mixed cerebrovascular disease in an elderly man with mixed vascular risk factors: a case report

Version: 1 Date: 22 Nov 2018

Reviewer: Svetlana Lorenzano

Reviewer's report:

The Authors have replied satisfactorily to most comments.

In the description of the case report, the Author stated "The degree of WMH was steady at Grade II on the Fazekas scale, and the mRS score maintained at 2 during the follow-up, with a stable status of cognition", however, for the sake of completeness, it should be specified that neurocognitive tests were not performed. In any case, it is known that neurocognitive tests are able to identify also mild cognitive impairment that may be not immediately clinically apparent.

At the end of the Discussion, the Authors made some final speculations on the possible etiopathogenetic mechanisms underlying the occurrence of multiple strokes in this patient. It is generally agreed that, due to the important familiarity of cardiovascular diseases and thrombotic events, hereditary protein S deficiency probably along with some undiagnosed specific genetic alterations and uncontrolled vascular risk factors may have played an important role in the development of both thrombotic and hemorrhagic cerebrovascular events in this patient. However, during the general discussion on the potential causes underlying the mixed cerebrovascular disease, the Authors should also briefly include the hypothesis of a potential association with occult cancer. It is known that cancer is associated with hypercoagulability but also with an increased risk of bleeding. It could be also possible that alterations of the immune system associated with an impairment of coagulation system could lead not only to recurrent cerebrovascular and systemic vascular events, including hemorrhagic and ischemic strokes and DVT, but also (in particular immune system abnormalities) to cancer development that not necessarily should be immediately detectable on regular diagnostic imaging.
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.

No

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:

Acceptable

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?
If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

Dr. Svetlana Lorenzano served as expert consultant for Boehringer Ingelheim from 2013 to 2014; she received two travel grants from Boehringer Ingelheim (one in 2016 one in 2017), one travel grant from Bayer (2014), Quintiles IMS (2017), Daichii Sankyo (in 2017).

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal