Reviewer’s report

Title: CNS vasculitis and stroke as a complication of DOCK8 deficiency: a case report

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Reviewer: Muhammad Chohan

Reviewer's report:

Abstract

In the background paragraph, it would be helpful to include a sentence like "DOCK8 immunodeficiency syndrome is the autosomal recessive form of hyperimmunoglobulin E syndrome" just to give readers a quick understanding of what DOCK8 deletion does. The paragraph as it exists now seems to suggest that the primary result of DOCK8 mutation is CNS vasculitis, which I don't believe is the point you are trying to make. Rather, DOCK8 deletion results in hyperimmunoglobulin E syndrome, and can occasionally be associated with CNS vasculitis. Without the quick description of DOCK8, this paragraph is rather misleading.

Background

The phrase "despite this lethal relationship" seems out of place, as you have not mentioned any statistics regarding the outcomes (rate of death) of patients with HIES and vasculitis, or even simply of patients with vasculitis

Saying "the only known approach," suggests that the Hutchinson approach was designed with immunocompromised patients in mind, which is precisely the opposite of what you say later in the sentence. It would be more accurate to say something like "the currently accepted approach for treating these patients is an immunosuppressive protocol developed by Hutchinson et al in order to treat patients with primary CNS vasculitis; however this protocol may, in fact, be inappropriate for patients with an underlying immunodeficiency." This way it doesn't sound like you are claiming that the Hutchinson approach was designed specifically for your purposes but may be inappropriate.
Case Presentation

"Magnetic resonance imaging demonstrated the presence of white matter and basal ganglia hyperintensities consistent with previous infarcts in the right frontal white matter and basal ganglia." This sounds a bit redundant.

Discussion

The discussion is certainly the strongest part of this paper. It very clearly and thoroughly readdresses the currently accepted treatment for CNS vasculitis in children, developed by Hutchinson et al, and then discusses the reasons that treatment may not be appropriate for this particular population of patients. You address the treatment you chose for this patient, including the reasons you deviated from the published therapy, and the reasons for choosing the therapy that you did. Your discussion of the associated ischemic stroke was appropriate, and thorough. Your suggestion that prophylactic antiplatelet therapy should be considered early, especially if platelet counts are high is a reasonable conclusion to make based on this one case, though I don't think there is published evidence to back it up, and could even be a harm to some patients if they are already prone to hemorrhage. This detail underscores the primary problem with this discussion, and with the treatment recommendations made therein: that these suggestions are based on theory and the successful treatment of a patient group with N=1. Obviously conducting large, randomized trials, or even case series is limited when the disease process or patient population being studied is rare. And it may never be feasible for a large-scale randomized trial to corroborate your claims that this is a safe and effective treatment for these types of patients. But I think it is worth publishing this paper, as its methodology is clear, and the decisions in treatment were made using best-available evidence, with good theoretical reasoning backing decision-making. Perhaps other medical professionals across the globe with similar patients will be able to validate or invalidate the claims made in this paper. But as it is, I believe that this is a well written paper describing a well thought-out treatment for an unusual condition, and it could potentially impact the outcomes of these patients for the better.

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?**
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Yes

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Not relevant to this manuscript

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Please indicate the quality of language in the manuscript:

Acceptable

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