Reviewer's report

Title: Moyamoya Disease: A Clinical Spectrum Literature Review and Case series from a Tertiary care hospital in Pakistan.

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Reviewer: Edward Smith

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The manuscript "Moyamoya Disease: A Clinical Spectrum; Literature Review and Case Series from a Tertiary care hospital in Pakistan" by Shoukat et al., presented as a clinical studies article, describes a group of 13 patients identified with "moyamoya disease" from a single center in Pakistan over an 18 year period. Patients were identified by ICD-9 codes in a hospital database and the series represents the largest experience with moyamoya patients from Pakistan to date. The authors describe their experience with these patients and provide a limited literature review of moyamoya in their discussion.

As written, this manuscript provides an important view into the diagnosis and treatment of patients with moyamoya in Pakistan, but requires a number of minor and major revisions to be completed before publication.

Major compulsory issues include:

1 - A lack of a consistent method of diagnosis of moyamoya. The diagnosis is made by angiogram, and – in some papers – with MRI/MRA. However, in this paper it is unclear, but appears that these authors have patients that were diagnosed without either of these modalities. In addition, it is unclear that the authors make a distinction between moyamoya disease (the idiopathic presentation of bilateral angiographic moyamoya findings) and moyamoya syndrome (the presence of angiographic moyamoya in the setting of associated conditions, such as congenital cardiac disease, unilateral changes or other syndromic conditions). This has implications for what is actually being treated, particularly where the authors suggest that differences may exist in Pakistani patients as compared to patients in other parts of the world. (for example, on p. 6, the statement “the classical smokey appearance of moya vessels was seen only in 4 patients.”)

The imaging provided is concerning (at least on the limited resolution images available) in at least in one case for the possibility of aneurysmal or dissection-related subarachnoid hemorrhage (Figure 1) – suggesting a need for more convincing images or questioning the diagnosis.

All in all, a much more robust method of confirming the diagnosis – using the accepted international diagnosis of moyamoya syndrome/disease – needs to be provided, with correlative images and - ideally – further data such as Suzuki grade.
2 – There is a profound absence of any meaningful follow-up data on these patients, with only 3 (p. 7) with any “long-term” follow-up. While the authors appropriately comment on the inherent difficulties on treating complex patients and obtaining follow-up in Pakistan, it nonetheless significantly limits the ability of the authors to make any meaningful statements on natural history, surgical outcomes or the role of “conservative management” – as discussed in their paper. If these follow-up data are not available, perhaps the focus of the paper should be on presentation and diagnosis – not speculative comments on management.

3 – There is an absence of discussion regarding methods of how patients were identified for treatment and why a particular method of management was selected. Although a rationale must have been present in each case, the reader is left without any information about why a particular strategy (surgical, medical, etc.) was selected for a given patient.

4 – This paper is overly speculative, with numerous statements made without adequate documentation. Comments about genetic basis of disease, differences in etiology in the Pakistani population and the mechanism of intellectual deterioration in moyamoya patients are not able to be substantiated with the data provided. While it is useful to offer hypotheses to tie data together, the findings here are too thin to support this level of pervasive speculation. A more focused approach delineating the data collected and specifically discussing the limitations of treating and managing patients in Pakistan would be of greater value.

5 – The literature review is of limited utility here and is better suited to just providing data directly relevant to the Pakistan experience – rather than a truncated attempt at a global review of moyamoya. The discussion should be significantly shortened and redirected to addressing the issues specific to Pakistani patients with moyamoya (difficulties with diagnosis, follow-up, differences in presentation, etc.)

Minor issues include:

1 – A need to provide percentages as well as absolute numbers.

2- Providing a definition of moyamoya disease vs. syndrome (see above).

3 – A discussion of the CSF analysis. (Differences were mentioned, but not discussed.)

4 – Stylistic changes, such as grammatical review and perhaps changing the use of some less-commonly used words and phrases (“dumb” perhaps to “aphasic”) or removal of imprecise terms (“a good period”).

In summary, this article provides important insights into the presentation of moyamoya in a previously under-reported area. The authors are to be lauded for their attempts to compile this case series and it is important to document similarities and differences in this clinical entity in different geographic areas.
around the world. A redirection of this paper to focus on the presentation of these patients – and the specific challenges faced by clinicians treating them in this environment – would be a potentially valuable contribution to the literature.

The authors are to be commended for this series, but significant changes in style and substance are needed to make this manuscript suitable for publication.

**Level of interest:** An article of limited interest

**Quality of written English:** Needs some language corrections before being published

**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.