Reviewer’s report

Title: Is neuromyelitis optica related to tuberculosis?

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Reviewer: Ilya Kister

Reviewer’s report:

I found the article to be well-written and interesting and am inclined to recommend it for publications despite a number of questions and comments for the authors.

My main concerns are two-fold:

1. The authors have not studied the association of TB and NMO, but only of ‘active pulmonary TB’ and NMO. This point needs to be emphasized. It is possible that history of distant or treated TB is a ‘risk factor’ for development of NMO later on in life. This paper does not address this broader association. If the authors have the data on ‘TB history” of their NMO pts and controls (and not just active PTB), it would be helpful to include it. Even if results are accepted, there may still be an association between TB and NMO.

2. It may be difficult, as the authors acknowledge, to know what the etiology of myelitis is in a patient with TB. Absence of NMO antibody in and of itself is insufficient to disprove that myelitis is not NMO related. As many 30% of NMO cases are NMO IgG negative (at least with ELISA tests), and it is not clear whether how many pts with TB myelitis/optic neuritis in this series were tested. Absence of relapses in TB myelitis cases is difficult to interpret as we don’t know how long the patients have been followed. Perhaps some of these ‘TB myelitis’ patients would relapse if followed long enough. I think duration of follow up is important to variable that needs to be included if available (or discussed explicitly even if unavailable).

It seems that the strongest argument against the 10 TB myelitis cases being related to NMO or other autoimmune disease was presence of meningeal enhancement and concomitant tuberculoma. It was not clear to me how many of these 10 pts had one or both of these findings.

Minor comments on ‘Methods’ section

“All patients with NMO fulfilled the 2006 Wingerchuk criteria 10 (the 1999 Wingerchuk diagnostic criteria were used for several cases owing to a lack of NMO-IgG data11).”

How many were diagnosed by 2006 criteria and how many by 1999 only?

“Because of distinct pathogenesis and therapy, the disorder related-“NMO-like” syndrome, which includes CNS infection and systemic autoimmune disorders
with a focus on the spinal cord and optic nerves, was excluded if there is.”
I am not sure what NMO-like syndrome refer to. Are these ‘NMO spectrum
disorders’ – eg recurrent myelitis +NMO ab, etc? The sentence is unclear overall.

Further questions:
Which test was used to determine NMO IgG? Cell-based, ELISA, etc?
What was duration of follow up?

Minor comments on ‘Results’ section

“Brain MRI showed small ischemic lesions” – Do authors mean ‘non-specific
white matter lesions’. These may or may not be ischemic.

“Some special MRI sequences including diffusion and magnetic resonance
spectroscopy (MRS) were not performed, as they were not available during that
period. However, considering the clinical data and consultations with the
neurosurgeon, intramedullary tuberculoma could be excluded.” Unclear how
consultation with neurosurgeon helped to exclude tuberculoma.

“serum positive” - seropositive

“tuberculoma (42.9%) in spinal cord was common” -it would be helpful to define
key imaging features of tuberculoma

“Six patients received additional immunosuppressants in remission” – this is
surprising. The standard of care in most countries is to treat all NMO patients
with immunosuppressants – any reason why only 6/92 pts were treated?

“All TBM patients received anti-tuberculosis therapy “ – what did it consist of?

Tables
“Linear sign” – what is it?

Comments on ‘Discussion’

“we report limited data showing that NMO-IgG was only detected in NMO
patients, and not in patients with TBM” – is there a degree of tautology involved?
le if a patient with myelitis had PTB and no NMO, he will likely be diagnosed as
TBM, while if he did have NMO Ab, he would be diagnosed as NMO?

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the
statistics.

Declaration of competing interests:
none