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Response to correspondence: Testing for myelin oligodendrocyte glycoprotein antibody (MOG-IgG) in typical MS

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We thank Lopez-Chiriboga et al. for their interest in our recently presented case entitled "MOG antibody-associated demyelinating disease mimicking typical multiple sclerosis: a case for expanding anti-MOG testing?" (Breza et al., 2019). We appreciate their comments regarding MOG-antibody associated demyelinating disease (MOGAD), drawing attention to some important aspects of MOGAD that remain to be elucidated (Lopez-Chiriboga et al., 2019). A few of the concerns raised were also addressed in our paper, such as the need to fine-tune clinical criteria for testing anti-MOG antibodies. It is noteworthy that despite extensive studies, the phenotypic spectrum, clinical relevance and prognosis of anti-MOG antibody-associated demyelination are not yet fully defined. We described a case of MOGAD initially diagnosed as typical MS, and, at presentation, not fulfilling the proposed recommendations for anti-MOG antibody testing (Jarius et al., 2018).

We completely agree with Lopez-Chiriboga et al. that a positive result for anti-MOG antibodies should not replace clinical judgement, particularly in this ever-growing era of diagnostic antibody biomarkers in neurology. However, we should note that MOGAD is a rare disease deciphered when neuroimmunological diseases were re-defined using their antigen specificity rather than clinical manifestations (Levy, 2019). Since the clinical spectrum is still evolving, we believe that very stringent criteria for anti-MOG antibody testing could result in missing atypical MOGAD cases. A wider screening, particularly until universally accepted testing criteria are established, provides the chance to unravel the different phenotypes and the frequency of MOGAD disease.

Concerning anti-MOG testing, one should also consider that diagnosing anti-MOG antibody-associated demyelination has important treatment implications. Although a false positive result can limit patient access to wider treatment, as the authors correctly note, a missed true positive can also have deleterious effects on MOGAD patient care.

Certainly, our case is rare and not among the most common MOGAD cases. However, most features of our case have been previously reported in MOGAD. Regarding MRI features, conus medullaris lesions are in fact a recommended MRI indication for MOG-IgG testing by Jarius et al. (2018). More specifically, the aforementioned authors, comment that conus medullaris lesions were present at onset in MOGAD patients in several studies (Jarius et al., 2018; Baumann et al., 2018). We acknowledge, however, that in a recent study the percentage of conus lesions identified in MOGAD versus MS was not significantly different (Dubey et al., 2019).

The most atypical feature for MOGAD in our case was the presence of periventricular lesions perpendicular to the corpus callosum (Dawson's fingers type). However, lesions in the corpus calosum have been previously reported in rare MOG-positive cases (Baumann et al., 2018; Cobo-Calvo et al., 2018). Nevertheless, the mostly centrally located spinal cord lesions and the flair up during steroid sparing in our patient, further suggested MOGAD. Probably, only a lesion biopsy could further support MOGAD, identifying markers of demyelination, complement and IgG deposits (Jarius et al., 2018).

We presented a case positive for anti-MOG antibodies using several techniques (both live and fixed CBAs for total IgG and IgG1 anti-MOG antibodies). We wish to stress that anti-MOG antibodies in this patient were positive, not low as was the case in other MS patients that we have also identified. The patient remained positive after retesting a month later. Three different cell-based assay (CBA) techniques were used: (a) serum dilution titer 1/80 with a live CBA for IgG1 anti-MOG (cut-off limit 1/20), (b) titer 1/360 with a live CBA for total IgG anti-MOG (cut-off limit 1/160), and (c) titer >1/10 with a commercial (Euroimmun) fixed-cell CBA for total IgG anti-MOG (1/10).

A live CBA is the current gold standard for anti-MOG antibody testing. Anti-MOG abs testing should be done using the best available method. However, the international recommendations currently do not impose the aforementioned technique. Although, the superiority of the live CBA with anti-IgG1 antibody versus fixed CBA with total anti-IgG has been recently proved (Waters et al., 2019), the issue remains uncertain concerning the evaluation of cases with low titers of MOG antibodies.

In conclusion, the point raised by our report was not to suggest that all patients with typical MS should be screened for anti-MOG antibodies, but rather to alert clinicians to the fact that very stringent criteria for anti-MOG antibody testing could result in missing atypical MOGAD cases. As we highlight in our case, MOGAD is a new emerging

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diagnostic entity (Ramanathan et al., 2018). Further studies are urgently needed to fully define when testing for MOG-antibodies is appropriate. The aim should be to avoid false positives within the large pool of MS, without sacrificing atypical MOGAD cases.

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Declaration of Competing interest

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