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Testing for Myelin Oligodendrocyte Glycoprotein Antibody (MOG-IgG) in typical MS

Breza et al. (2019) reported a 31-year-old man who presented with a subacute mild sensory myelopathy, positive oligoclonal bands in cerebrospinal fluid and imaging findings of a short segment myelitis, conus medullaris involvement and ovoid shaped T2 hyperintense lesions located perpendicular to the ventricles. Serological evaluation was positive for MOG-IgG1 using live and fixed cell based assays. Nonetheless, the authors concluded that the patient didn't have MS but rather a MOG-associated disorder (MOGAD), although they acknowledge that MOG-IgG1 testing in this case was not indicated based on a recent international consensus recommendation (Jarius et al., 2018). Accordingly they suggest that MOG-IgG1 testing should be performed in all patients with typical MS.

The case lacks typical features for MOGAD (eg, acute disseminated encephalomyelitis ADEM or optic neuritis), but has many typical findings of MS (Filippi et al., 2019). The authors highlight the presence of a conus lesion as being able to distinguish MS from MOGAD, yet in a recent comparative study of a large cohort of myelitis patients with MOGAD, AQP4-IgG-associated NMOSD and MS (Dubey et al., 2019), involvement of the conus did not differ between MOGAD and MS. Axial MRI spine sequences (not included here) can help discriminate MS from MOGAD with MS typically causing wedge-shaped peripherally located lesions in the dorsal or lateral columns, while MOGAD often causes lesions sometimes restricted to grey matter more typical of MOGAD (Dubey et al., 2019; Ciron et al., 2019). Moreover, MOGAD patients often have both a longitudinally-extensive and short T2-hyperintense lesion and the presence of the former helps distinguish it from MS in which long lesions are extremely rare.

Large cohorts of MS patients have been tested for MOG-IgG1 and a small number of patients with MS have MOG-IgG1 positivity at low titer (Spadaro et al., 2016; Waters et al., 2019). While it is still unclear what the significance of low titer MOG-IgG1 in MS patients is, the consequences of a positive result are not insignificant as it may cause diagnostic uncertainty, lead to increased costs and result in withholding of proven medications for MS. Furthermore, MS likely far exceeds MOGAD in frequency. The false positive test rate for MOG-IgG, when evaluated in high pre-test probability setting, is low. However, when applied to a population with very low pre-test probability it may generate a high proportion of false positives potentially exceeding the proportion of true positives (Waters et al., 2019).

With the rapidly expanding number of diagnostic antibody biomarkers of neurologic disorders of varying specificity, neurologists should keep in mind that a positive result should not replace clinical judgement.

ASL and JJC no disclosures

SJP is a named inventor on patents (#12/678,350 filed 2010 and #12/573,942 filed 2008) that relate to functional AQP4/NMO-IgG assays and NMO-IgG as a cancer marker. Dr. Pittock has provided consultation to Alexion Pharmaceuticals, MedImmune LLC, and Chugai Pharma but has received no personal fees or personal compensation for these consulting activities. All compensation for consulting activities is paid directly to Mayo Clinic.

Brian Weinshenker receives royalties from RSR Ltd, Oxford University, Hospices Civil de Lyon, and MVZ Labor PD Dr. Volkmann und Kollegen GbR for a patent of NMO-IgG as a diagnostic test for NMO and related disorders, served on adjudication committee for clinical trials in NMO being conducted by MedImmune and Alexion, and consulted for Chugai regarding a clinical trial for NMO.

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