Letter to the Editor of Annals of Neurology

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MOG-IgG-associated bilateral optic neuritis in temporal relation to monkeypox vaccination

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Dear Editors,

with great interest we read the article by Money et al. reporting three cases of monkeypox virus disease (MPXV) associated central nervous system (CNS) disease which raised the question if this reflects a parainfectious injury or a viral invasion of the CNS.[1]

The reported cases strikingly resemble antibody-mediated CNS myelin oligodendrocyte glycoprotein-IgG-associated disease (MOGAD) in many aspects[2]: (1) Patients presented with typical phenotypes including prodromal phases with fever and myalgia followed by acute disseminated encephalomyelitis (ADEM), longitudinally extensive transverse myelitis (LETM) or encephalopathy with seizures, (2) cerebrospinal fluid (CSF) pleocytosis, (3) prompt treatment response to plasma exchange only, and (4) almost complete clinical and radiographic recovery. The authors' differential diagnosis included MOGAD, but MOG-IgG was negative (tested in 2/3), however crucial information regarding time point and method is lacking.

In this context, our observation of MOGAD in temporal relation to MPXV vaccination adds interesting information.

In our case, ten days after smallpox vaccination as a preventive measure against MPXV, a 52-year-old immunocompetent man developed headache, fever and shortly after bilateral optic neuritis with papilledema, reduced visual acuity and normal brain MRI besides T2 hyperintensities in both optic sheaths. CSF revealed pleocytosis (11/µl) but negative oligoclonal bands. MOG-IgG (initially 1:100 by fixed cell-based-assay and 1:160 by live cell-based-assay at follow-up (FU) 5 weeks later and after high-dose corticosteroids) tested positive in serum and MOGAD was diagnosed.[2] Repeated corticosteroid therapy yielded clinical recovery. FU at 22 weeks showed typical bilateral thinning of GpRNFL thickness on optical coherence tomography (Fig. 1), MOG-IgG had turned negative.

Intriguingly, almost a century prior the advent of MOG-IgG testing, several cases of optic neuritis in relation to compulsory smallpox vaccination have been reported.[3] Along this line, MOGAD manifestation is known to be triggered by infections and vaccinations, such as the SARS-CoV-2 vector-based vaccine.[4]

Induction of MOG-IgG after smallpox vaccination could be triggered by molecular mimicry or bystander activation of pre-existing MOG-specific memory B cells, which can be detected in MOGAD patients, but occasionally in healthy donors, and can differentiate into MOG-IgG producing plasmablasts by TLR engagement.[5] Induction of MOG-IgG after different vaccines as well as transient appearance of MOG-IgG (anti-vaccine antibodies are longer lasting) would be compatible with a bystander activation of autoreactive

B cells.[4] MOG-IgG are pathogenic, but they require an opening of the blood-brain barrier to enter the CNS, which may be caused by inflammatory cytokines produced after infection or vaccination. [6]

Author Contributions:

DE and LAG contributed to the conception and design of the study; DE, SF, MR, JH, TK and LAG contributed to the acquisition and analysis of data; DE, SM, JH, EM, TK and LAG contributed to drafting the text or preparing the figures.

Potential Conflicts of Interest:

All authors have nothing to report in relation to this Letter to the Editors.

Informed consent:

Written informed consent was obtained from the patient for publication of the deidentified data.

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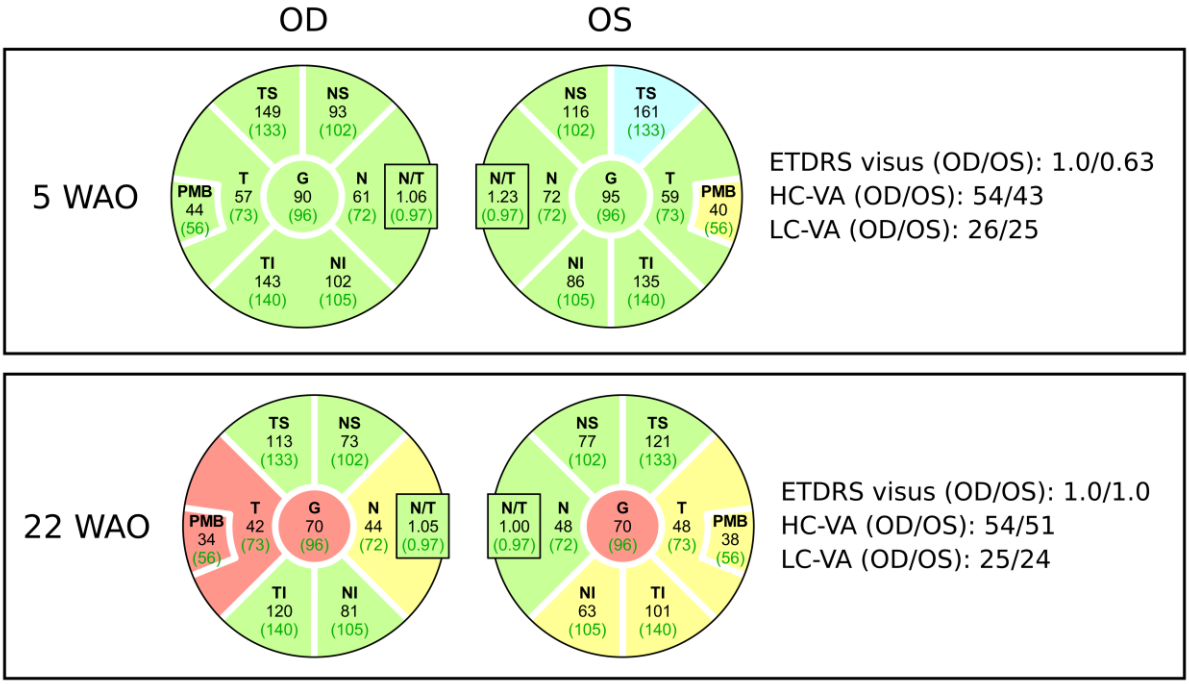

Figure 1: Optical coherence tomography (OCT) and visual acuity (VA). OCT and VA at 5 and 22 weeks after MOGAD onset. Global (G) and segment-specific (T: temporal, N: nasal, S: superior, I: inferior, PMB: papillomacular bundle) color-coded peripapillary retinal nerve fiber layer (pRNFL) thickness. Numbers represent the actual (black) and expected (green) thickness in µm in each segment (WAO: weeks after onset). VA was measured with ETDRS (Early Treatment Diabetic Retinopathy Study, at 2 m distance), high-contrast (HC, 100 %) and low-contrast (LC, 25 %) visual acuity charts.