Two cases of concurrent syphilis infection and MOG antibody-associated disease: Causation or coincidence?

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Background
Myelin oligodendrocyte glycoprotein (MOG) antibody-associated disease (MOGAD) is a rare demyelinating disease of the central nervous system which is frequently preceded by infections. The underlying pathomechanism, however, remains poorly understood.

Objective
Here, we present clinical data of two MOGAD patients with concurrent syphilis infection and investigate the reactivity of patient-derived antibodies to MOG and Treponema pallidum (T. pallidum) with in vitro techniques.

Methods
Longitudinal serum samples and soluble immunoglobulins in single B cell supernatants were measured for MOG-reactivity by a live cell-based assay. Reactivity against T. pallidum was assessed by enzyme-linked immunosorbent assay.

Case 1
A 43-year-old man experienced numbness in the genital area and lower limbs. He had been living with HIV for five years and maintaining viral suppression since. Previous diagnoses of treated latent tuberculosis and latent syphilis, were also reported. Lower limb hypoaesthesia with a sensory level at T12 without motor or autonomic dysfunction. Spinal cord MRI revealed a gadolinium-enhancing T2-signal hyperintense lesion at the C4 and C5 level. Serologies for syphilis with the VDRL test presented a titer of 1:16, which had been negative for over a year, and an increased TPPA titer of 1:20'480 after being stable at 1:640 for more than a year. The CSF TPPA was 1:1.6. The patient was diagnosed with latent syphilis reinfection/reactivation associated with short cervical myelitis. He was treated with IV penicillin. A MOG-IgG test in serum at the two-month follow-up was reconfirmed. Lower limb hypoesthesia with a sensory level at T12 without motor or autonomic dysfunction. Spinal cord MRI revealed a gadolinium-enhancing T2-signal hyperintense lesion at the C4 and C5 level. Serologies for syphilis with the VDRL test presented a titer of 1:16, which had been negative for over a year, and an increased TPPA titer of 1:20'480 after being stable at 1:640 for more than a year. The CSF TPPA was 1:1.6. The patient was diagnosed with latent syphilis reinfection/reactivation associated with short cervical myelitis. He was treated with IV penicillin. A MOG-IgG test in serum at the two-month follow-up was clear-positive, and a MOGAD diagnosis was given. At the 6-month follow-up, no new lesions were detected on the MRI. Serum NfL and MOG-IgG levels remained high. The patient was diagnosed with monophasic MOGAD.

Case 2
A 44-year-old man experienced vision loss and pain in the right eye. Ophthalmological examination revealed a right eye visual acuity of 20/50 with red color desaturation. Brain MRI showed papilledema, and a gadolinium-enhancing T2-signal hyperintensity of the intraorbital and intracanalicular segment of the right optic nerve, nerve sheath, and adjacent fatty tissue suggesting a diagnosis of optic neuritis. Serological investigation revealed chronic HBV infection and suspected optic neuritis. At follow-up, a MOG-IgG result in serum sampled at disease onset was clear-positive, leading to the diagnosis of MOGAD. At the 8-month follow-up, no new lesions were detected on the MRI. Serum NfL and MOG-IgG levels remained high. The patient was diagnosed with monophasic MOGAD.

Experimental Results
A total of 2622 enriched MOG-recognition B cells from the first patient were sorted and single-plated, of which seven supernatants recognized MOG, and two showed reactivity to T. pallidum antigens. From the second patient, 540 enriched MOG-recognition B cells were sorted and single-plated. Of these, reactivity to MOG was identified in 15 supernatants, whereas reactivity to T. pallidum antigens was detected in five supernatants. Notably, of these supernatants, one showed reactivity to both MOG and T. pallidum. Measurements of positive B cell supernatants were repeated and validated in independent experiments. We cannot exclude that the respective co-existing infection antigens (e.g., HIV and HBV antigens) may have contributed to MOGAD pathogenesis.

Discussion
Among infections associated with the development of MOGAD, respiratory infections (including SARS-CoV-2), Zika virus, mumps, herpes simplex virus, Borrelia, Epstein-Barr virus, and tuberculosis have been described. Further, three cases of syphilis infection and MOGAD have previously been reported: one latent syphilis patient with meningencephalomyelitis associated with MOG-IgG seropositivity, one patient with acute neurosyphilis (presenting with papillitis and uveitis) with positive MOG-IgG results in the CSF, and a case of co-existing neurosyphilis and MOGAD manifesting as ON, which is a rare manifestation of neurosyphilis that show similarities to ON in MOGAD. The current study expands on the existing literature by reporting two additional cases of concurrent latent syphilis infection and MOGAD, and provides data indicating a potential link between syphilis and the development of post-infectious autoimmunity.

References

Funding
The study was funded by an ECTRIMS Clinical Fellowship and a Swiss Government Excellence Scholarship to A.B.A.G.R.G., a doctoral fellowship from the Goldschmidt Jacobson Foundation (to P.L.), and a Swiss Young Talents in Clinical Research Fellowship to J.F. The study was further funded by the Swiss National Science Foundation (SNF EcoleLuscolo Professorship: 194609; SNF Starting Grant: 211310), the National MS Society (FO-1708-26871), the Fondation Pierre Mercier pour la Science, the Propatient Foundation, the Goldschmidt Jacobson Foundation, and the Gottfried and Julia Bangerter Rhyner Foundation (all to A.-K.P.).