An interesting variety

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This issue of *Neurology®: Neuroimmunology and Neuroinflammation* (N2) includes a wide variety of exciting articles. As usual, I had difficulty selecting the articles to highlight in this Editor's Corner, which is aimed to reflect the range of topics rather than imply a higher quality of the selected manuscripts.

One of the treatments frequently used in neuro-myelitis optica (NMO) is rituximab. Nosadini et al.¹ provide interesting information on monitoring and redosing rituximab in 16 pediatric patients with NMO. Overall, the patients received a total of 76 rituximab courses; the mean time from rituximab dosing to last documented B-cell depletion and initial repopulation (defined as CD19 $\geq 10 \times 10^6$ cells/L) was 4.5 and 6.8 months, respectively, with large interpatient variability. The authors found a significant reduction between prerituximab and postrituximab annualized relapse rate. Twenty-one relapses occurred in 10 patients (65% during repopulation, 15% during depletion, and 20% as a result of depletion failure). Important causes of repopulation relapses included inadequate monitoring and delayed redosing after detecting repopulation. This study shows that in children with NMO, rituximab is effective in relapse prevention and that careful monitoring of B-cell repopulation and appropriate redosing could reduce relapses.

In multiple sclerosis (MS), most immunotherapies (interferon- β , glatiramer, steroids) do not appear to increase the prevalence of JC virus (JCV) serology. In contrast, the recent identification of progressive multifocal leukoencephalopathy (PML) among patients treated with natalizumab indicates that studies on the effects of this treatment on JCV are needed. Schwab et al.² examined a large cohort of patients with MS treated with natalizumab in order to determine any influence on JCV serology. The study, accompanied by an editorial comment by Drs. Javed and Reder,³ reveals that treatment with natalizumab was associated with a 15.9% rise in JCV index values in 14.8 months (12.9% per year), suggesting that

JCV seroconversion and index values are influenced by natalizumab. The findings emphasize the importance of monitoring patients' JCV serology, and that seroconversion or rising JCV index alter the risk of PML in these patients.

Zivadinov et al.⁴ hypothesized that in patients with MS dysregulated Epstein-Barr virus (EBV)-infected B cells may induce meningeal inflammation, contributing to cortical pathology. This process was suggested by studies showing that cortical gray matter pathology is associated with subpial cortical lesions, ectopic lymphoid-like structures, and retrograde Wallerian degeneration. Based on these data, the authors investigated a large cohort of patients with MS and appropriate controls to determine if antibody responses to EBV were associated with cortical pathology. The findings showed that the presence of antibodies to EBV viral capsid antigen (VCA) and nuclear antigen-1 (EBNA-1) were associated with more advanced cortical atrophy and accumulation of chronic T1 black holes and focal white matter lesions in patients with MS. The authors conclude that further research aimed at modulating the response of patients with MS to EBV via drug and vaccine strategies is warranted.

Makranz et al.⁵ describe the clinical features of sandfly viruses (SFV) in 9 patients diagnosed during 2008–2013 in the Jerusalem area. These viruses (phleboviruses) represent a genus within the *Bunyaviridae* family. Patient age ranged from 1.5 to 85 years (5 female). Clinical features included acute development of fever, change in consciousness and behavior, seizures, headache, meningitis, limb paresis, and, in 4 cases, myelitis. In 5 of 6 patients, brain MRI showed symmetrical abnormalities in the basal ganglia, thalami, and other deep structures, and in 3 cases there were additional findings in the spinal cord. Clinical follow-up was available in 7 patients; 4 recovered and the other 3 had residual deficits, 1 with severe brain damage. Some of the patients' family members were seropositive but asymptomatic. Two of the patients were tourists from nonendemic regions. Given that

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SFV-induced meningitis is less frequent among residents in endemic zones (likely due to Toscana virus immunity), the authors suggest that tourists from regions in which Toscana virus is not endemic are the target population.

Minocycline is a synthetic tetracycline and its use may result in autoimmune disorders such as drug-induced lupus, polyarteritis nodosa–like syndrome, autoimmune hepatitis, or vasculitic neuropathy. Baratta et al.⁶ report 3 patients who developed pain and weakness in the distribution of single or multiple individual nerves, with evidence of ischemic injury and vasculitis on nerve and muscle biopsy, following minocycline treatment for acne vulgaris. One of the patients, a 17-year-old woman, developed in addition to peripheral nerve involvement an acute right medial medullary ischemic stroke. Despite withdrawal of minocycline, the 3 patients required long-term immunotherapy for neurologic improvement.

Lue et al.⁷ examined peripheral inflammatory and immune mediators that could discriminate Parkinson disease without dementia (PD) from Parkinson disease with dementia (PDD). Overall, a total of 160 proteins were measured in patients' serum (52 PD and 22 PDD), identifying a 14-protein panel that when combined with age has discriminatory power in identifying PDD in patients with PD. Given that this is a discovery-based study, validation in a population-based, longitudinal study is needed.

Schubert et al.⁸ describe a remarkable case of IgG4–related hypertrophic pachymeningitis, bringing into consideration 2 thoughts: first, the possible underrecognition of this disorder among cases considered as idiopathic hypertrophic pachymeningitis; second, the importance of reaching a definite diagnosis (in this case by review of the biopsy) given that the disorder is responsive to immunotherapy.

I hope this summary of a few manuscripts will bring your interest to these and the other equally interesting articles of the February issue of *N2*.

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REFERENCES

1. Nosadini M, Alper G, Riney CJ, et al. Rituximab monitoring and redosing in pediatric neuromyelitis optica spectrum disorder. *Neurol Neuroimmunol Neuroinflamm* 2016;3:e188. doi: 10.1212/NXI.0000000000000188.
2. Schwab N, Schneider-Hohendorf T, Pignolet B, et al. Therapy with natalizumab is associated with high JCV seroconversion and rising JCV index values. *Neurol Neuroimmunol Neuroinflamm* 2016;3:e195. doi: 10.1212/NXI.0000000000000195.
3. Javed A, Reder AT. Rising JCV-Ab index during natalizumab therapy for MS: inauspicious for a highly efficacious drug. *Neurol Neuroimmunol Neuroinflamm* 2016;3:e199. doi: 10.1212/NXI.0000000000000199.
4. Zivadinov R, Cerza N, Hagemer J, et al. Humoral response to EBV is associated with cortical atrophy and lesion burden in MS patients. *Neurol Neuroimmunol Neuroinflamm* 2016;3:e190. doi: 10.1212/NXI.0000000000000190.
5. Makranz C, Qutteineh H, Bin H. Sandfly virus seroconversion associated with neurologic presentation. *Neurol Neuroimmunol Neuroinflamm* 2016;3:e184. doi: 10.1212/NXI.0000000000000184.
6. Baratta JM, Dyck PJB, Brand P, et al. Vasculitic neuropathy following exposure to minocycline. *Neurol Neuroimmunol Neuroinflamm* 2016;3:e180. doi: 10.1212/NXI.0000000000000180.
7. Lue L-F, Schmitz CT, Snyder NL, et al. Converging mediators from immune and trophic pathways to identify Parkinson disease dementia. *Neurol Neuroimmunol Neuroinflamm* 2016;3:e193. doi: 10.1212/NXI.0000000000000193.
8. Schubert RD, Wood M, Levin MH, Perry A, Gelfand JM. The severe side of the IgG4-related hypertrophic pachymeningitis disease spectrum. *Neurol Neuroimmunol Neuroinflamm* 2016;3:e197. doi: 10.1212/NXI.0000000000000197.

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