Abstracts

Articles appearing in the March 2020 issue

Alemtuzumab therapy changes immunoglobulin levels in the peripheral blood and CSF

Objective The use of alemtuzumab, a humanized monoclonal anti-CD52 antibody, has changed the therapy of highly active relapsing-remitting MS (RRMS). Alemtuzumab infusion depletes most lymphocytes in peripheral blood, whereas differential recovery of immune cells, probably those with a less CNS-autoreactive phenotype, is supposed to underlie its long-lasting effects. To determine whether alemtuzumab significantly reduces immunoglobulin levels in the blood and CSF of treated patients, we analyzed the blood and CSF samples of 38 patients with MS treated with alemtuzumab regarding changes in immunoglobulin levels.

Methods Blood and CSF samples of patients were collected at the beginning of alemtuzumab treatment and at 12, 24, and 36 months after the first administration of the drug. Specimens were analyzed regarding immunoglobulin concentrations in the blood and CSF.

Results We observed significant and dose-dependent reductions of immunoglobulin levels (IgG, IgM, and IgA) in serum and CSF 12 and 24 months after 2 courses of alemtuzumab. Patients with persistent or returning disease activity who were treated with a third course of alemtuzumab exhibited even further decrease in IgG levels compared with matched controls treated twice. Here, alemtuzumab-treated patients with IgG levels below the lower limits of normal were more susceptible to pneumonia, sinusitis, and otitis, whereas upper respiratory tract and urinary tract infections were not associated therewith.

Conclusions Our results suggest to monitor IgG levels for safety reasons in patients treated with alemtuzumab—in particular when additional treatment courses are required—and to consider preventive action in critical cases.

Classification of evidence This study provides Class IV evidence that for patients with RRMS alemtuzumab reduces immunoglobulin levels.

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Xenogeneic Neu5Gc and self-glycan Neu5Ac epitopes are potential immune targets in MS

Objective To explore the repertoire of glycan-specific immunoglobulin G (IgG) antibodies in treatment-naive patients with relapsing-remitting multiple sclerosis (RRMS).

Methods A systems-level approach combined with glycan array technologies was used to determine specificities and binding reactivities of glycan-specific IgGs in treatment-naive patients with RRMS compared with patients with noninflammatory and other inflammatory neurologic diseases.

Results We identified a unique signature of glycan-binding IgG in MS with high reactivities to the dietary xenoglycan N-glycolylneuraminic acid (Neu5Gc) and the self-glycan N-acetylneuraminic acid (Neu5Ac). Increased reactivities of serum IgG toward Neu5Gc and Neu5Ac were additionally observed in an independent, treatment-naive cohort of patients with RRMS.

Conclusions Patients with MS show increased IgG reactivities to structurally related xenogeneic and human neuraminic acids. The discovery of these glycan-specific epitopes as immune targets and potential biomarkers in MS merits further investigation.

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