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Abstracts

Articles appearing in the March 2020 issue

Encephalitis with radial perivascular emphasis: Not necessarily associated with GFAP antibodies

Objective Autoimmune steroid-responsive meningoencephalomyelitis with linear perivascular gadolinium enhancement in brain MRI is regarded as glial fibrillary acidic protein (GFAP) astrocytopathy characterized by anti-GFAP antibodies (ABs). We questioned whether anti-GFAP ABs are necessarily associated with this syndrome.

Methods Two patients with a strikingly similar disease course suggestive of autoimmune GFAP astrocytopathy are reported. Clinical examination, MRI, laboratory, and CSF analysis were performed. Neuropathologic examination of the brain tissue was obtained from one patient. Serum and CSF were additionally tested using mouse brain slices, microglia-astrocyte cocultures, and a GFAP-specific cell-based assay

Results Both patients presented with subacute influenza-like symptoms and developed severe neurocognitive and neurologic deficits and impaired consciousness. MRIs of both patients revealed radial perivascular gadolinium enhancement extending from the lateral ventricles to the white matter suggestive of autoimmune GFAP astrocytopathy. Both patients responded well to high doses of methylprednisolone. Only one patient had anti-GFAP ABs with a typical staining pattern of astrocytes, whereas the serum and CSF of the other patient were negative and showed neither reactivity to brain tissue nor to vital or permeabilized astrocytes. Neuropathologic examination of the anti-GFAP AB-negative patient revealed infiltration of macrophages and T cells around blood vessels and activation of microglia without obvious features of clasmatodendrosis.

Conclusions The GFAP-AB negative patient had both a striking (para)clinical similarity and an immediate response to immunotherapy. This supports the hypothesis that the clinical spectrum of steroidresponsive meningoencephalomyelitis suggestive of autoimmune GFAP astrocytopathy may be broader and may comprise also seronegative cases.

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Pharmacodynamics of natalizumab-extended interval dosing in MS

Objective To determine whether the concentration and saturation of natalizumab (NTZ) administration at extended interval dosing (EID; every 5–8 weeks) over 18 months is able to be maintained in the range considered adequate to sustain the clinical efficacy of NTZ.

Methods In a cross-sectional assessment of patients with multiple sclerosis (MS) who received standard interval dosing (every 4 weeks) or EID, serum NTZ concentrations were measured using ELISA, and α_4-integrin receptor saturations were analyzed via cytometry, in blood samples obtained at trough time points.

Results Trough serum concentration was above the "therapeutic" concentration of 2.0 μg/mL in 72% of EID patients. Trough saturation was above the "therapeutic" 50% threshold in 79% of EID-treated patients. Our model predicted that at least 9 NTZ infusions/year are required to maintain adequate trough saturation and concentration levels. Higher body mass index (BMI) was a predictor of suboptimal trough saturation on EID NTZ.

Conclusions Trough α4-integrin receptor saturation >50% correlated with high clinical efficacy of NTZ in previous studies. A continual treatment with EID maintains receptor saturation and concentration that are in the "therapeutic range" for most patients. This finding provides biological plausibility for the clinical efficacy of NTZ EID. Patients with higher BMI may require closer clinical and MRI follow-up.

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