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Abstracts

Articles appearing in the March 2020 issue

Paraneoplastic cerebellar ataxia and antibodies to metabotropic glutamate receptor 2

Objective To report the presence of a new neuronal surface antibody against the metabotropic glutamate receptor 2 antibody (mGluR2-Ab) in 2 patients with paraneoplastic cerebellar ataxia.

Methods mGluR2-Abs were initially characterized by immunohistochemistry on the rat brain and confirmed by immunofluorescence on HEK293 cells transfected with mGluR2. Additional studies included analysis of potential cross-reactivity with other mGluRs, expression of mGluR2 in patients' tumors, and the effects of mGluR2-Abs on cultures of rat hippocampal neurons.

Results Patient 1 was a 78-year-old woman with progressive cerebellar ataxia with an initial relapsing-remitting course who developed a small-cell tumor of unknown origin. Patient 2 was a 3-year-old girl who presented a steroid-responsive acute cerebellitis preceding the diagnosis of an alveolar rhabdomyosarcoma. Patients' serum and CSF showed a characteristic immunostaining of the hippocampus and cerebellum in rat brain sections and immunolabeled the cell surface of live rat hippocampal neurons. HEK293 cells transfected with mGluR1, 2, 3, and 5 confirmed that patients' antibodies only recognized mGluR2. mGluR2-Abs were not detected in 160 controls, 120 with paraneoplastic, autoimmune, or degenerative ataxias, and 40 with autoimmune encephalitis and antibodies against mGluR5 or unknown antigens. Expression of mGluR2 in tumors was confirmed by immunohistochemistry using a commercial mGluR2-Ab. Incubation of live rat hippocampal neurons with CSF of patient 2 did not modify the density of surface mGluR2 clusters.

Conclusions mGluR2-Abs are a novel biomarker of paraneoplastic cerebellar ataxia. The potential pathogenic effect of the antibodies is not mediated by downregulation or internalization of neuronal surface mGluR2.

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Tick-borne encephalitis vaccination in multiple sclerosis: A prospective, multicenter study

Objective To assess the changes in disease activity after tick-borne encephalitis (TBE) vaccination in patients with multiple sclerosis (MS) on a variety of disease-modifying drugs and to assess the immunogenicity, safety, and clinical tolerability of the vaccine in this patient group.

Methods We conducted a prospective, multicenter, nonrandomized observational study. We enrolled 20 patients with MS receiving TBE vaccination who had been on disease-modifying treatment (DMT) for at least 6 months. Serum samples were obtained before and after 4 weeks of vaccination to determine the specific TBE antibody response. MS disease activity (Expanded Disability Status Scale and relapse rates) was evaluated for 1 year after immunization. Local and systemic adverse events were registered.

Results In 20 subjects with TBE vaccination, the annualized relapse rate decreased from 0.65 in the year before vaccination to 0.21 in the following year. Expanded Disability Status Scale remained stable during the 2-year period before vaccination and 1 year after vaccination (range: 1.50–1.97). The geometric mean titer (GMT) increased from 169 Vienna units per milliliter (VIEU/mL) to 719 VIEU/mL 4 weeks after vaccination (p = 0.001), and 77.8% had protective antibody titers after vaccination. In 9 patients treated with beta interferons, GMT increased from 181 VIEU/mL to 690 VIEU/mL (p = 0.018). Three subjects treated with glatiramer acetate developed a 2- to 9.6-fold increase. Patients treated with fingolimod developed the lowest increase in antibody titer.

Conclusions TBE vaccination showed good tolerability and was safe in patients with MS. MS disease activity was not increased, and annualized relapse rates decreased after vaccination. Vaccine response differs according to the underlying DMT.

Trial registration ClinicalTrials.gov, clinicaltrials.gov, Identifier: NCT02275741.

NPub.org/N2/9518b

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Zekeridou and V.A. Lennon. 2015; 2:e110. doi.org/10.1212/NXI.0000000000000110

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Patrick Waters, Mark Woodhall, Kevin C. O'Connor, et al. 2015;2: e89. doi.org/10.1212/NXI.0000000000000089

Does time equal vision in the acute treatment of a cohort of AQP4 and MOG optic neuritis?

Hadas Stiebel-Kalish, Mark Andrew Hellmann, Michael Mimouni, et al. 2019;6:e572. doi.org/10.1212/NXI.0000000000000572

Next-generation sequencing in neuropathologic diagnosis of infections of the nervous system

Steven L. Salzberg, Florian P. Breitwieser, Anupama Kumar, et al. 2016;3:e251. doi.org/10.1212/NXI.0000000000000251

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Alberto Vogrig, Marine Fouret, Bastien Joubert, et al. 2019;6: e604. doi.org/10.1212/NXI.0000000000000604

