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Phosphodiesterase 10A IgG

A novel biomarker of paraneoplastic neurologic autoimmunity

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Study objective and summary result

This study aimed to describe a novel antiphosphodiesterase 10A (PDE10A) autoantibody that serves as a biomarker for paraneoplastic neurologic autoimmunity. PDE10A autoimmunity is likely rare and the majority of patients presented with movement disorders.

What is known and what this paper adds

Various autoimmune movement disorders have been described in a paraneoplastic context. This investigation reports a novel biomarker for autoimmune movement disorders that expands the spectrum of diagnosable paraneoplastic CNS disorders.

Participants and setting

The investigators examined the cases of 7 patients (4 men; median age, 70 years; age range, 66–76 years) for whom sera or CSF underwent testing at the Mayo Clinic Neuroimmunology Laboratory (Rochester, MN) and yielded a distinctive immunoglobulin G (IgG) staining pattern predominantly of the basal ganglia when applied to murine brain tissue. Five patients were retrospectively identified in the Mayo Clinic Neuroimmunology Laboratory database, and 2 were prospectively identified.

Design, size, and duration

The patients' clinical data were extracted from electronic files (n = 1) or provided by referring physicians (n = 6). Immunoprecipitation of pig basal ganglia extractions with the patients' autoantibodies and mass spectrometry were used to identify the antigen. The specificity was confirmed with antigen-specific recombinant western blotting, cell-based immunofluorescence assays, and immune absorption experiments.

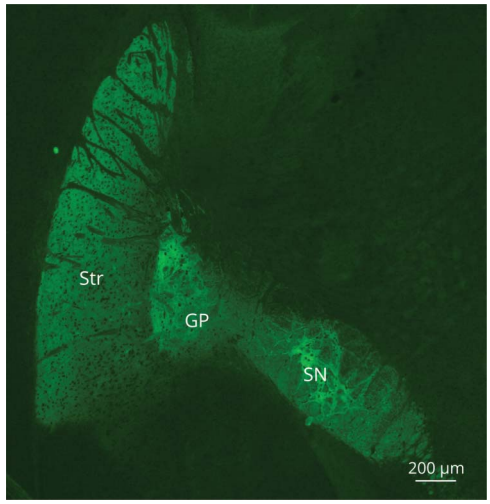
Primary outcome measures

Identification of the antigen of interest and the patients' clinical presentation.

Main results and the role of chance

PDE10A was identified as the antigen of interest. Four patients had documented movement disorders, and 6 had cancer. Two patients developed hyperkinetic movement disorders during treatment with immune checkpoint inhibitors for their cancer. MRI assessments with fluid-attenuated inversion-recovery and T2-weighted sequences revealed basal ganglia hyperintensities in these 2 patients and CSF-restricted oligoclonal bands were present.

Figure Indirect immunofluorescence assay performed on murine tissue with patient serum demonstrates synaptic staining of the basal ganglia



Bias, confounding, and other reasons for caution

A small group of patients were assessed in this study and limited clinical data were available for 5 patients.

Generalizability to other populations

The rarity of this disorder may limit the generalizability of the results.

Study funding/potential competing interests

This study was supported by the Center for Individualized Medicine, Mayo Clinic. Some authors report having filed patent applications related to anti-PDE10A autoimmunity, having licensing and patent interests in anti–aquaporin-4 autoimmunity in the context of neuromyelitis optica, receiving research support from various healthcare companies, and consulting for various healthcare companies. Go to Neurology.org/N for full disclosures.

A draft of the short-form article was written by M. Dalefield, a writer with Editage, a division of Cactus Communications. The authors of the full-length article and the journal editors edited and approved the final version.

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