LETTER TO THE EDITOR

To The Editor

A Variant of Alternating Skew Deviation in GAD65 Antibody-Associated Cerebellar Ataxia

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We report a variant of GAD65 antibody-associated skew deviation in which after a quite prolonged period of apparent stability, the direction of gaze in which it first manifested abruptly switched sides.

A 60-year-old woman reported 3 months of difficulty visually focusing and walking. Three months after those symptoms had resolved, she developed intermittent diplopia which soon persisted as constant painless binocular vertical diplopia on left lateral gaze. The initial examination showed a right head tilt, left head turn, and chin-up head position, mildly reduced right eye supraduction, left hypertropia maximal on looking to the left and up and present at distance and at near, and a mildly positive head tilt test on left head tilt. Fully 19 months later, she awoke with the previous diplopia gone but in its stead headache, vertical binocular diplopia on right gaze, vertical oscillopsia on right gaze, and gait imbalance. Examination then showed right hypertropia on right gaze, dissociated torsional jerk nystagmus on right gaze (i.e. right eye amplitude greater than left eye; nystagmus beating torsionally to the right), very small amplitude dissociated vertical nystagmus on left gaze (left eye amplitude greater than right eye), left hand incoordination, left heel-shin ataxia, gait ataxia, positive Romberg test, and inability to tandem walk.

MRI scans of the brain with contrast after the initial presentation and after the change in direction of the skew deviation were normal.

Tests for the antibodies Tr (DNER), Zic4, Hu, Yo, Ri, Ma2: Ta, CV2, amphiphysin, titin, SOX1, and recoverin were negative. Also, normal or negative were CBC, fasting glucose, hemoglobin A1C, creatinine, eGFR, TSH, thyroxine, thyroid peroxidase antibodies, parathyroid hormone, vitamins B1, B12, and E, ANA, ENA, acetylcholine receptor antibodies, gliadin IgG and IgA antibodies, transglutaminase IgA and IgG antibodies, tests for spinocerebellar ataxia types 1, 2, 3, 6, 7, 8, and 17, and oligoclonal bands.

CSF showed increased protein: 0.64 g/l (0.15–0.45 g/l).

Quantitative ELISA tests showed > 10,000 IU/ml glutamic acid decarboxylase (GAD) antibodies in serum and 196 IU/ml in CSF.

Mammography and CT scan of thorax, abdomen, and pelvis were normal.

After 6 months of intravenous immunoglobulin treatment,[1] there was resolution of the headache, diplopia, imbalance, nystagmus on left gaze, left hand incoordination, gait ataxia, positive Romberg test, and inability to tandem walk.

Cerebellar ataxia syndromes with GAD antibodies have been associated with several eye movement abnormalities, among them diplopia, alternating skew deviation, gaze-evoked nystagmus with rebound, hypermetric and hypometric saccades, saccadic pursuit, downbeat nystagmus (including one we personally saw).[2]

In an earlier report of alternating skew deviation with cerebellar-brainstem signs and anti-GAD antibodies, just 8 months elapsed between the initial vertical binocular diplopia on left gaze and vertical diplopia on right gaze plus worsening of vertical diplopia on left gaze.[3]

In our patient, 19 months elapsed before an actual switch in the direction of skew deviation occurred and torsional nystagmus was added to the picture.

This case augments the spectrum of neuro-ophthalmic presentations of GAD65 antibody-associated cerebellar syndromes.

In some patients, GAD65 autoimmunity produces a prodrome due to selective brainstem or cerebellar involvement.[4] This could provide advance warning of GAD antibody positivity, in turn allowing earlier testing, diagnosis, and treatment of GAD antibody-positive cerebellar ataxia.

Conflict of Interest

All authors have no conflicts of interest to declare.

Statement of Authorship

Conception and design (CS; AS; FT), data collection (CS; AS; FT), manuscript preparation (CS; AS; FT), critical appraisal (CS; AS; FT), review of the manuscript (CS; AS; FT).

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