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# Acute Acquired Concomitant Esotropia in Anti-GQ1b-Antibody Syndrome

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Dear Editor,

Anti-GQ1b-antibody syndrome has diverse clinical manifestations. While anti-GQ1b antibody can involve both the central and peripheral nervous systems, ophthalmoplegia with resultant diplopia (the core feature of anti-GQ1b-antibody syndrome) has mostly been ascribed to lesions of peripheral nerves.[1-3] Here, we report a patient with diplopia as a form of cerebellar esotropia (not from ocular motor nerve palsy) associated with anti-GQ1b antibody.

A 31-year-old man presented with acute horizontal binocular diplopia that was worse during distant viewing but did not change during lateral or vertical gaze. He had no associated ocular pain or headache. One week previously he had experienced watery diarrhea for 2 days after consuming raw salmon. An ocular examination showed normal visual acuity (20/16) in both eyes, but there was concomitant esotropia of 30 prism diopters during near fixation and of 40 prism diopters during distant fixation (Fig. 1A). He also showed a symmetric abduction limitation in both eyes, whereas adduction, supraduction, and infraduction were normal (Fig. 1B). Horizontal gaze-evoked nystagmus was prominent in the abducting eye, and transient rebound nystagmus was observed upon resuming the primary eye position (Fig. 1C). However, there was no vertical gaze-evoked nystagmus. Smooth pursuit was impaired in both the horizontal and vertical directions. Rightward saccades were hypermetric, and pulse-step mismatches were observed during vertical saccades (Fig. 1D and E). However, the saccade velocities were normal in both the horizontal and vertical directions during either binocular or monocular viewing (Fig. 1F and G).

The findings of video head impulse tests were positive for all six semicircular canals. Video-oculography documented normal visually enhanced vestibulo-ocular reflex (VOR) during passive whole-body rotation, but frequent catch-up saccades during cancellation of the VOR. Truncal and limb coordination was considered normal, and the findings of other neurological tests and orbit and brain MRI were normal. Nerve conduction studies in the upper and lower extremities and repetitive nerve stimulation produced no abnormal findings. The serology test was positive for anti-GQ1b-IgG antibody (optical density of 0.57 in the enzyme-linked immunosorbent assay; normal range <0.1 relative to the negative control value according to the Dong-A University Neuroimmunology Team).[4] The CSF opening pressure was 190 mm $H_2O$. There was mild CSF pleocytosis (white blood cells=13/$mm^3$, all monocytes) with no red blood cells. CSF protein was mildly elevated at 76.2 mg/dL. Serology tests for Cytomegalovirus, Epstein-Barr virus, enterovirus, herpes simplex virus, and varicella zoster virus all produced negative results.

The patient received intravenous immunoglobulin for 5 days. One month after discharge, the patient reported a slight improvement but still suffered from concomitant diplopia. Owing to ongoing discomfort, especially when working on a computer, he received a botulinum toxin injection that resulted in the complete resolution of the esotropia, saccadic dysmetria, and gaze-evoked nystagmus 3 months later.



 

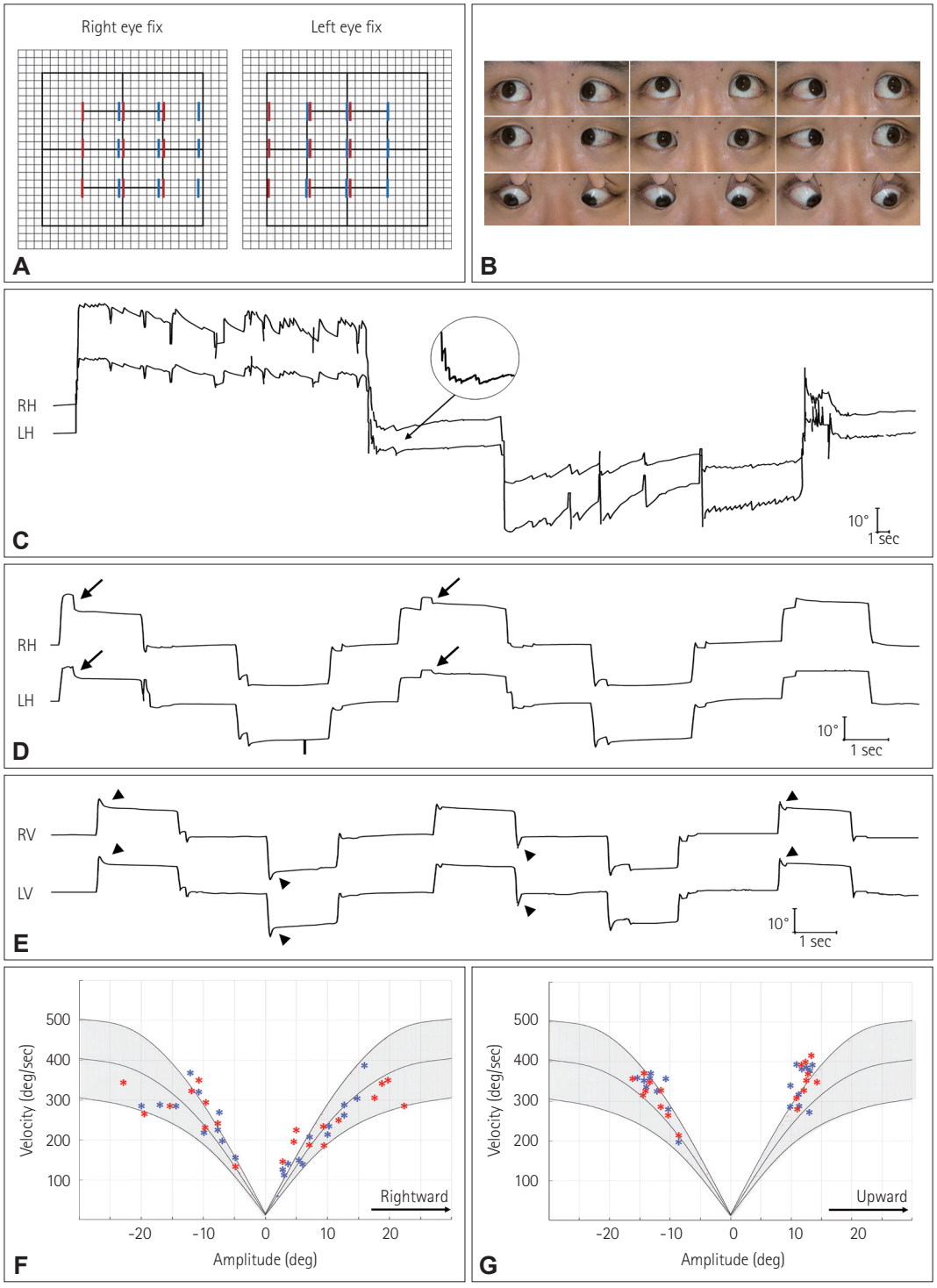


**Fig. 1.** Findings in the patient. A: The Lancaster test showed concomitant diplopia. B: Nine-gaze photography showed abduction limitation in both eyes. C–E: Video-oculography showed direction-changing gaze-evoked nystagmus during lateral gaze and rebound nystagmus upon resuming the primary eye position (C), hypermetria (arrow) for rightward saccades (D), and pulse-step mismatches (arrowheads) during vertical saccades (E), all of which indicate cerebellar dysfunction. Upward deflection indicates rightward or upward eye motion. F and G: The saccade velocities were normal in both the horizontal (F) and vertical (G) directions. Red and blue dots indicate the right and left eyes, respectively. The gray zone indicates the normal range. LH: horizontal position of the left eye, LV: vertical position of the left eye, RH: horizontal position of the right eye, RV: vertical position of the right eye.

Abducens nerve palsy is the commonest form of external ophthalmoplegia in anti-GQ1b-antibody syndrome.[5] However, the concomitant pattern of esotropia and normal saccade velocity provide evidence against abducens nerve palsy as a cause of diplopia in our patient. Acute acquired concomitant esotropia in adults, as shown in our patient, may be observed in various conditions, including age-related distance esotropia, divergence palsy, accommodative esotropia, decompensated monofixation syndrome, consecutive esotropia, sensory strabismus, and ocular myasthenia gravis. Such esotropia can also develop in lesions involving the brainstem and cerebellum.[6,7]

GQ1b gangliosides are abundant in the cerebellum as well as in the brainstem and cranial nerves.[8,9] Our patient showed acute concomitant esotropia along with signs of cerebellar dysfunction including gaze-evoked nystagmus, impaired smooth pursuit, saccadic hypermetria, and impaired cancellation of the VOR,[6] in association with serum positivity for anti-GQ1b antibody. We may therefore ascribe the concomitant esotropia observed in our patient to cerebellar dysfunction associated with anti-GQ1b antibody. The mechanism of esotropia in cerebellar dysfunction remains to be established. In monkeys, lesions in the dorsal vermis cause esophoria while those in the fastigial nucleus induce exophoria.[10] Therefore, the cerebellum appears to play a role in controlling vergence eye movement via balancing the vergence activities.[6,7,10]

In summary, our patient showed acute acquired concomitant esotropia in association with isolated cerebellar dysfunction due to positivity for anti-GQ1b antibody.

## Author Contributions

Conceptualization: Jeong-Yoon Choi. Data curation: Eunjin Kwon, Byeol-A Yoon, Hyo-Jung Kim, Jeong-Yoon Choi. Formal analysis: Eunjin Kwon, Byeol-A Yoon, Jeong-Yoon Choi, Ji-Soo Kim. Funding acquisition: Byeol-A Yoon, Jeong-Yoon Choi. Investigation: Eunjin Kwon, Jeong-Yoon Choi. Methodology: Eunjin Kwon, Byeol-A Yoon, Hee Kyung Yang, Jeong-Yoon Choi. Project administration: Jeong-Yoon Choi. Resources: Eunjin Kwon, Byeol-A Yoon, Hee Kyung Yang, Jeong-Yoon Choi. Supervision: Jeong-Yoon Choi, Ji-Soo Kim. Validation: Jeong-Yoon Choi, Hee Kyung Yang, Ji-Soo Kim. Visualization: Eunjin Kwon, Hyo-Jung Kim, Jeong-Yoon Choi. Writing—original draft: Eunjin Kwon, Jeong-Yoon Choi. Writing—review & editing: Jeong-Yoon Choi, Hee Kyung Yang, Ji-Soo Kim.

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## Conflicts of Interest

Drs. E Kwon, BA Yoon, HJ Kim, HK Yang and JY Choi report no disclosures. Dr. JS Kim serves as an associate editor of Frontiers in Neuro-otology and on the editorial boards of the Journal of Clinical Neurology, Frontiers in Neuro-ophthalmology, Journal of Neuro-ophthalmology, Journal of Vestibular Research, Journal of Neurology, and Medicine.

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This study followed the tenets of the Declaration of Helsinki and was performed according to the guidelines of Institutional Review Board of Seoul National University Bundang Hospital (B-2005-613-702).

## REFERENCES

1. Fisher M. An unusual variant of acute idiopathic polyneuritis (syndrome of ophthalmoplegia, ataxia and areflexia). *N Engl J Med* 1956;255:57-65.
2. Chiba A, Kusunoki S, Obata H, Machinami R, Kanazawa I. Serum anti-GQ1b IgG antibody is associated with ophthalmoplegia in Miller Fisher syndrome and Guillain-Barré syndrome: clinical and immunohistochemical studies. *Neurology* 1993;43:1911-1917.
3. Lee SU, Kim HJ, Choi JY, Kim JK, Kim JS. Acute vestibular syndrome associated with anti-GQ1b antibody. *Neurology* 2019;93:e1085-e1092.
4. Kim JK, Bae JS, Kim DS, Kusunoki S, Kim JE, Kim JS, et al. Prevalence of anti-ganglioside antibodies and their clinical correlates with Guillain-Barré syndrome in Korea: a nationwide multicenter study. *J Clin Neurol* 2014;10:94-100.
5. Choi KD, Choi SY, Choi JH, Kim SH, Lee SH, Jeong SH, et al. Characteristics of single ocular motor nerve palsy associated with anti-GQ1b antibody. *J Neurol* 2019;266:476-479.
6. Leigh RJ, Zee DS. *The Neurology of Eye Movements*. 5th ed. Oxford: Oxford University Press, 2015.
7. Chapelle AC, Plant GT, Kaski D. Teaching video neuroimages: cerebellar esotropia: a pitfall in ophthalmology and neurology. *Neurology* 2019;93:e114-e115.
8. Nakatani Y, Murata M, Shibata K, Nagaoka T, Utsunomiya I, Usuki S, et al. IgM anti-GQ1b monoclonal antibody inhibits voltage-dependent calcium current in cerebellar granule cells. *Exp Neurol* 2009;219:74-80.
9. Kornberg AJ, Pestronk A, Blume GM, Lopate G, Yue J, Hahn A. Selective staining of the cerebellar molecular layer by serum IgG in Miller-Fisher and related syndromes. *Neurology* 1996;47:1317-1320.
10. Takagi M, Tamargo R, Zee DS. Effects of lesions of the cerebellar oculomotor vermis on eye movements in primate: binocular control. *Prog Brain Res* 2003;142:19-33.