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LETTER TO THE EDITORS

# Anti-ganglioside antibody-associated acute unilateral peripheral vestibulopathy

Sun-Uk Lee[1,2] · Hyo-Jung Kim[2,3] · Jeong-Yoon Choi[1,2] · Ji-Soo Kim[1,2]

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Dear Sirs,

The causal relationship has been well established between anti-GQ1b antibody and Fisher syndrome (FS), Guillain–Barre syndrome with ophthalmoplegia, acute ophthalmoparesis without ataxia, ataxia without ophthalmoplegia, and Bickerstaff brainstem encephalitis [1–3]. However, nystagmus or abnormal eye movements are also found in more than half of those with anti-GQ1b antibody-associated diseases that cannot be classified to one of the above disorders [4]. Occasional observation of abnormal head-impulse tests (HITs) [5] and caloric paresis [6–8] in patients with anti-ganglioside antibodies suggests a peripheral vestibular involvement in the disorders associated with anti-ganglioside antibodies. We report positive anti-GQ1b and anti-GD1b antibodies in a patient with typical features of acute unilateral peripheral vestibulopathy.

A 45-year-old woman presented spontaneous vertigo for a day. She had suffered from cough and myalgia for a week before the presentation. Examination showed spontaneous nystagmus beating rightward, upward and clockwise (from the patient's perspective, Fig. 1a). The nystagmus increased during rightward gaze, and decreased during leftward gaze. HITs were positive for left anterior and horizontal canals (Fig. 1b). Bithermal caloric tests showed left canal paresis of 93% (Fig. 1c). She showed decreased ocular vestibular-evoked myogenic potentials (VEMPs) during left ear stimulation with an interaural difference at 41.7% (normal range < 21.5%). Cervical VEMPs and pure-tone audiometry were normal. Brain MRIs and MR angiography were also normal. Anti-GQ1b IgG (% ratio = 72%, normal range < 50%) and anti-GD1b IgG (% ratio > 100%, normal range < 50%) antibodies were positive, while anti-GM1 antibodies were negative (GanglioCombi ELISA, BÜHLMANN Laboratories, Switzerland). The patient was arranged for oral methylprednisolone 60 mg per day for a week, and was discharged with improvement of the vertigo 5 days later. Follow-up video-oculography 1 month later showed resolution of spontaneous nystagmus, canal paresis, and HITs along with negative conversion of serum anti-GQ1b and anti-GD1b antibodies.

Our patient with anti-ganglioside antibodies presented the features of acute unilateral peripheral vestibulopathy mimicking vestibular neuritis (VN). Previously, the authors reported nystagmus and ataxia in isolation in patients with anti-GQ1b and anti-GD1b antibodies [9]. Given the nature of the nystagmus, i.e., periodic alternating nystagmus or central positional nystagmus, nystagmus in patients with anti-ganglioside antibodies have been ascribed to dysfunction of caudal brainstem or vestibulocerebellum [10, 11]. Indeed, anti-GQ1b or anti-GD1b antibodies have been found to bind with the cerebellar granular and molecular layers, and the dentate, vestibular and olivary nuclei in humans or rats [12].

In our patient, positive HITs only for ipsilesional horizontal and anterior canals and absence of gaze-evoked nystagmus indicate involvement of the vestibular pathway distal to the vestibular nucleus [13]. Indeed, the vestibular nerve may be preferentially involved in FS [6]. The higher expression of GQ1b ganglioside in the vestibular nerve also suggests vulnerability of the vestibular nerve in anti-GQ1b antibody syndrome [14]. Even though this report on a single patient does not provide strong evidence, the causal relationship between anti-ganglioside antibodies and acute unilateral peripheral vestibulopathy may be inferred by the nearly complete absence of anti-GQ1b and anti-GD1b serum antibodies

✉ Ji-Soo Kim
jisookim@snu.ac.kr

[1] Department of Neurology, Seoul National University College of Medicine, Seoul, Republic of Korea

[2] Dizziness Center, Clinical Neuroscience Center, and Department of Neurology, Seoul National University Bundang Hospital, 173-82, Seongnam, Gyeongggi-do 13620, Republic of Korea

[3] Research Administration Team, Seoul National University Bundang Hospital, Seongnam, South Korea

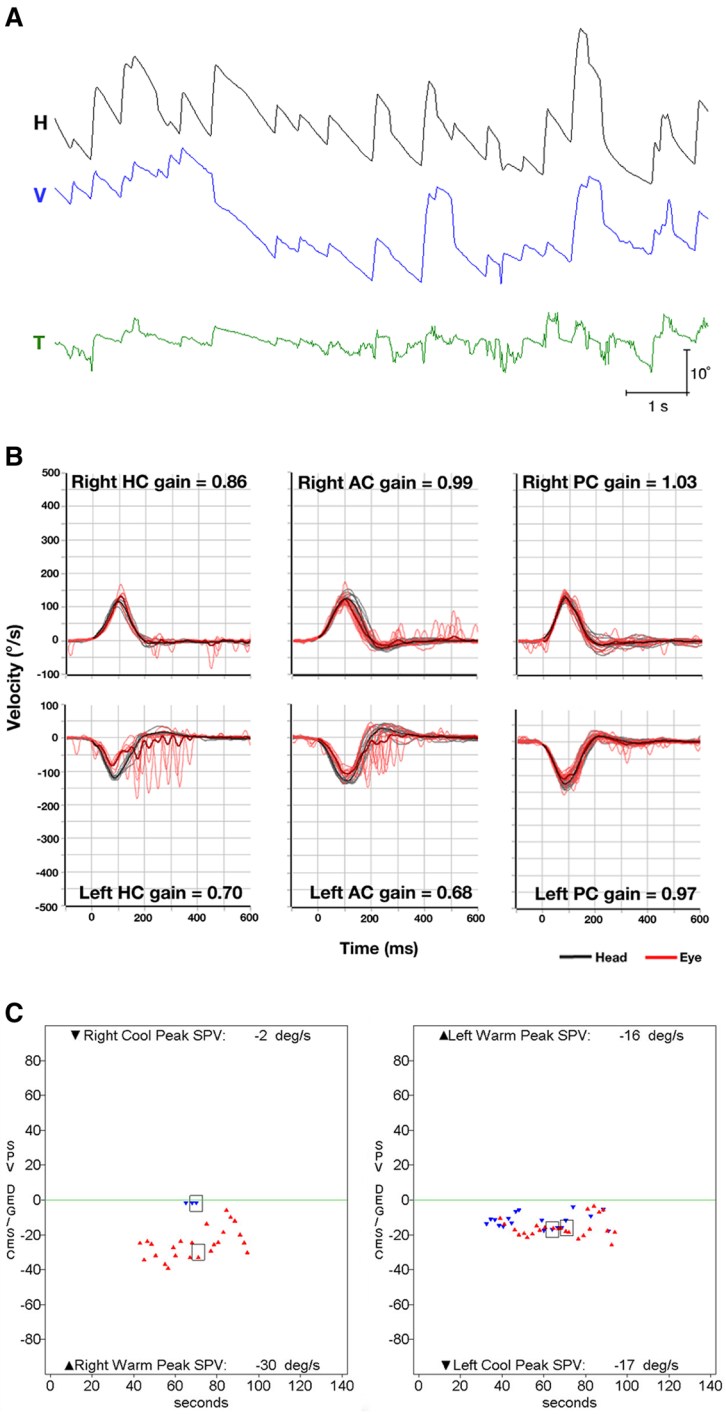


**Fig. 1** **a** Video-oculography (SLVNG, SLMED, Seoul, Republic of Korea) shows spontaneous nystagmus beating rightward, upward and clockwise (from the patient's perspective). **b** Head-impulse tests show decreased gain of the vestibulo-ocular reflex and overt saccades for left horizontal (normal gain = 0.88–1.27), and decreased gain and covert saccades for left anterior semicircular canals (normal gain = 0.75–1.29). **c** Bithermal caloric tests show left canal paresis of 93%. *H* horizontal position of the left eye, *T* torsional position, *V* vertical position

in normal population [15–17] and the negative seroconversion of antibodies after symptom resolution observed in our patient. The causal relationship between anti-ganglioside antibody and acute unilateral peripheral vestibulopathy should be validated in a large number of patients presenting acute spontaneous vertigo.

The initial presentation was typical of VN, yet showing resolution of the vestibular impairments within 1 month in our patient. Although static vestibular imbalance recovers more rapidly, dynamic asymmetry persists more than a year in more than a half of the patients with VN [18]. Indeed, the canal paresis and head-shaking nystagmus are still observed 1 month after symptom onset in nearly 90% of patients [18]. The recovery of dynamic as well as static vestibular asymmetry in our patient is consistent with the temporal profile of the resolution of ataxia and ophthalmoplegia in FS [19].

VN has been ascribed to reactivation of herpes simplex virus in the vestibular ganglion even though the

pathophysiology remains to be established [20]. The association of anti-ganglioside antibodies and acute unilateral peripheral vestibulopathy in our patient, however, suggest an additional immune-mediated mechanism in this disorder. Frequent antecedent infections in VN, likewise in anti-GQ1b antibody-related syndromes, also support this assumption [20]. Given the benign nature of acute unilateral peripheral vestibulopathy, however, routine evaluation of anti-ganglioside antibodies in this disorder should be justified by future studies involving a larger number of patients, and be validated by balancing the costs and any therapeutic gains that may be obtained with this practice. At present, the authors recommend a measurement of anti-ganglioside antibodies only in patients with fluctuating and relapsing courses of vestibulopathies of unknown etiology.

**Author contributions** SUL analyzed and interpreted the data, and wrote the manuscript. HJK and JYC analyzed and interpreted the data, and revised the manuscript. JSK designed and conceptualized the study, interpreted the data, and revised the manuscript.

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## Compliance with ethical standards

**Conflict of interest** Drs. S.U. Lee, H.J. Kim and Choi report no disclosures. 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.

**Ethical approval** 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-1810-499-101).

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