CASE REPORT

Skew Deviation and Partial Ocular Tilt Reaction Due to Intratympanic Gentamicin Injection, with Review of the Literature

Samuel M. Dresner^a, Nathan H. Kung^b, Joel R. Palko^b, Jonathan L. McJunkin^c, Joel A. Goebel^c, and Gregory P. Van Stavern^b

^aNew York Medical College, Valhalla, New York, USA; ^bDepartment of Ophthalmology and Visual Sciences, Washington University in St. Louis, St. Louis, Missouri, USA; ^cDepartment of Otolaryngology—Head and Neck Surgery, Washington University in St. Louis, St. Louis, Missouri, USA

ABSTRACT

Skew deviation is a rare side effect of intratympanic gentamicin injection for intractable Meniere's disease. When the skew deviation is accompanied by pathologic head tilt and ocular torsion, the result is an ocular tilt reaction (OTR). The authors report the case of a 56-year-old man with refractory Meniere's disease who developed binocular vertical diplopia following intratympanic gentamicin injection and was found to have skew deviation and a partial ocular tilt reaction. The authors also review the reported cases of skew deviation following intratympanic gentamicin and confirm this phenomenon, which has only rarely been reported in the literature.

ARTICLE HISTORY

Received 27 January 2017
Revised 13 February 2017
Accepted 14 February 2017

KEYWORDS

Gentamicin; ocular tilt reaction; skew deviation

Introduction

Skew deviation, a vertical misalignment of the eyes due to damage along the supranuclear pathway connecting the otolith organs to the ocular motor nuclei, is a rare side effect of intratympanic gentamicin injection for intractable Meniere's disease (MD). When the skew deviation is also accompanied by pathologic head tilt and ocular torsion, the result is an ocular tilt reaction (OTR). We report a case of gentamicin-induced skew deviation with partial OTR and summarise the existent literature on the matter.

Case report

A 56-year-old man with refractory Meniere's disease and pre-existing left sensorineural hearing loss underwent intratympanic gentamicin injection with 0.3 mL of 30 mg/mL gentamicin instilled behind the left tympanic membrane. Approximately 1 week later, he reported awakening with continuous binocular vertical diplopia, instability with head movement, and difficulty with scanning the visual environment. He was admitted to an outside hospital, where

magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) of the brain were performed, and results were normal. Video oculography was performed upon hospital discharge, which showed 6 degrees per second of rightward-beating post-headshake nystagmus, increased in rightward gaze compared with leftward gaze, and a strong ice water response in the right ear with no measurable response to ice water in the left ear, together suggesting uncompensated left unilateral peripheral vestibular dysfunction. Over the next 4 weeks, his continuous diplopia gradually resolved, only being present in far rightward gaze at the time of his referral to our clinic.

On his neuro-ophthalmic examination approximately 8 weeks after symptom onset, his acuity was 20/20 OU with normal colour perception. Pupils were 5 mm, round, and briskly reactive to light. There was no ptosis. Confrontation visual fields were normal to red cap OU. Motility was full in both eyes without spontaneous nystagmus. However, cross-cover testing showed 1–2 prism dioptres (PD) of right hyperphoria in primary gaze, which increased to 3 PD of right hypertropia in rightward gaze. Double Maddox Rod testing showed 10° of right incyclotorsion and 10° of

CONTACT Gregory P. Van Stavern, MD VanStavernG@wustl.edu Department of Ophthalmology and Visual Sciences, Washington University in St. Louis, 660 South Euclid Avenue, Campus Box 8096, Saint Louis, MO 63110, USA.

Colour versions of one or more of the figures in the article can be found online at www.tandfonline.com/ioph.

© 2017 Taylor & Francis

Figure 1. Double Maddox Rod lenses showing 10° of right incyclotorsion and 10° of left excyclotorsion.

left excyclotorsion without pathologic head tilt, suggesting skew deviation with a partial ocular tilt reaction (Figure 1). Thirty seconds of horizontal headshake while wearing Frenzel goggles showed right-beating post-headshake nystagmus. Horizontal head thrusts towards the left revealed overt refixation saccades, whereas horizontal head thrusts to the right showed a normal vestibulo-ocular reflex (VOR) response. Dynamic visual acuity testing in the horizontal plane showed impaired gaze stability during head rotation, an additional indicator of impaired VOR function. Dilated fundus examination confirmed ocular cyclotorsion but was otherwise normal.

Discussion

Meniere's disease is a chronic disorder caused by excess endolymph regulation in the labyrinth, leading to episodic attacks of vertigo, tinnitus, aural fullness,

and low- to mid-frequency sensorineural hearing loss. Intratympanic injection of gentamicin, an aminoglycoside antibiotic that destroys vestibular hair cells, is one ablative treatment option for intractable symptoms.¹

We identified three case reports in the literature^{2–4} that reported similar skew deviation following intratympanic gentamicin injection (Table 1). In these patients, the onset of symptoms post-injection averaged 4 days, with a range of 3–5 days. Our patient had onset of symptoms 8 days post-injection, a slightly longer delay between injection and onset of symptoms compared with other patients reported in the literature, a finding likely due to inter-individual pharmacokinetic variation in gentamicin absorption.⁵ Spontaneous resolution of symptoms occurred within 4 weeks of symptom onset in our patient, slightly earlier than the 6–8 weeks reported in the other cases, although our patient continued to have referable physical examination findings, including a right hyperdeviation, more pronounced on rightward gaze, with intorsion of the higher eye. The standard amounts of gentamicin used in the cases observed in the literature also suggest that skew deviation and vertical diplopia following injection may not be dose dependent.

Skew deviation is characterised by a vertical misalignment of the eyes due to damage along the supranuclear pathway connecting the otolith organs to the ocular motor nuclei.⁶ An ocular tilt reaction occurs when a skew deviation is

Table 1. Review of literature for cases of skew deviation with binocular vertical diplopia (BVD) following intratympanic gentamicin injection for Meniere's disease (MD).

Condition and treatment	Age	Gender	Symptom onset	Signs/symptoms	Resolution	Source
Left MD 4 doses of 60 mg/dL gentamicin	52	Female	4 days	Diplopia; head tilt towards left	Not reported	Acute diplopia posterior to chemical labyrinthectomy
Left MD 0.5 mL of 30 mg/mL gentamicin	79	Female	5 days	Binocular vertical diplopia (BVD); right hypertropia 3 prism dioptres (PD) in all eye positions	Spontaneous at 8-week follow-up	Binocular vertical diplopia following chemical labyrinthectomy with gentamicin
Left MD 0.5 mL of 30 mg/mL gentamicin	58	Female	3 days	BVD; 3 PD right hypertropia in primary position, decreasing to 2 PD on right gaze	Spontaneous at 8-week follow-up	Skew deviation after intratympanic gentamicin therapy
Right MD 0.5 mL of 30 mg/mL gentamicin	74	Male	4 days	BVD; 6 PD left hypertropia in primary position, decreasing to 4 PD on left gaze	Spontaneous at 6-week follow-up	
Left MD 0.3 mL of 30 mg/mL gentamicin	56	Male	8 days	BVD; 1–2 PD of right hyperphoria in primary gaze, increasing to 3 PD in right gaze	Spontaneous by 4 weeks later	Our patient

associated with pathologic head tilt and ocular cyclotorsion. These findings represent a lesion affecting inputs from the otoliths in the utricle that travel to the interstitial nucleus of Cajal in the midbrain. The ascending pathway starts in the utricle, travels along the ipsilateral vestibular nerve, then decussates in the pons, and ascends in the contralateral medial longitudinal fasciculus (MLF).⁷ An OTR can be caused by both central (e.g., midbrain, pons, or cerebellum) and peripheral lesions (e.g., otolith-utricle and vestibular nerve). Lesions occurring rostral to the point of decussation are classically associated with ipsilateral ocular hypertropia, whereas lesions occurring caudal to the point of decussation are classically associated with ipsilateral ocular hypotropia.⁷

Our patient's presentation was consistent with a left peripheral vestibulopathy induced by gentamicin injection. Although he did not have a pathologic leftward head tilt, the skew deviation with a hypertropic right eye, hypotropic left eye, incyclotorsion of the hypertropic right eye, and excyclotorsion of the hypotropic left eye support our diagnosis of a partial left ocular tilt reaction. Video-oculography corroborated our localisation and the mechanism of injury by demonstrating left unilateral peripheral vestibular dysfunction.

The HINTS (Head Impulse - Nystagmus - Test of Skew) examination, often utilised in cases of dizziness from an acute vestibular syndrome, is a three-step neuro-otologic examination evaluating for a normal head impulse test, direction changing nystagmus, or skew deviation as highly sensitive markers for acute ischaemic stroke.^{8,9} Even though our patient would have been flagged by the HINTS examination due to the presence of skew deviation, our patient was known to have a peripheral lesion, as corroborated by his mechanism of injury, peripheral pattern of nystagmus, negative MRI, and abnormal vestibulo-ocular reflex. This suggests that neuroimaging may not be required in all patients with skew deviation, particularly if known to be peripheral or provoked by gentamicin injection.

In conclusion, we confirm that skew deviation can rarely occur following gentamicin injection for Ménière's disease. In accordance with the principles of ocular innervation, the eye ipsilateral to the injected ear was hypotropic in all reported cases. Going forward, we recommend informing patients of this

potential complication of intratympanic gentamicin injection and being aware of the physical examination findings that may accompany this syndrome.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

Funding

Research was supported by DOVS Core Grant 5 P30 EY02687, Institute for Clinical and Translational Sciences grant RR023496, Biostat Core Grant U54 RR023496, an unrestricted grant from Research to Prevent Blindness, and NIH Core Vision Grant P30 EY02687.

References

- [1] Coelho DH, Lalwani AK. Medical management of Ménière's disease. *Laryngoscope* 2008;118:1099–1108.
- [2] Santos-Gorjón P, Collazo-Lorduy T, Sánchez-Terradillos E, Sánchez-Jara Sánchez-Jara Sánchez JL, Velasco-García MJ, Martín-Hernández G. Acute diplopia posterior to chemical labyrinthectomy. *Rev Soc Otorrinolaringol Castilla León Cantab La Rioja* 2012;3:83–94.
- [3] León RM, Izquierdo EL, Parra SA, Benito-León J, Nieto AA, García-Albea RE. Binocular vertical diplopia following chemical labyrinthectomy with gentamicin: a case report and review of literature. *Neurologia* 2016;31:503–505.
- [4] Ng D, Fouladvand M, Lalwani AK. Skew deviation after intratympanic gentamicin therapy. *Laryngoscope* 2011;121:492–494.
- [5] Plontke SKR, Wood AW, Salt AN. Analysis of gentamicin kinetics in fluids of the inner ear with round window administration. *Otol Neurotol* 2002;23:967–974.
- [6] Brodsky MC, Donahue SP, Vaphiades M, Brandt T. Skew deviation revisited. *Surv Ophthalmol* 2006;51:105–128.
- [7] Brandt T, Dieterich M. Vestibular syndromes in the roll plane: topographic diagnosis from brainstem to cortex. *Ann Neurol* 1994;36:337–347.
- [8] Kattah, JC, Talkad AV, Wang DZ, Hsieh YH, Newman-Toker DE. HINTS to diagnose stroke in the acute vestibular syndrome three-step bedside oculomotor examination more sensitive than early MRI diffusion-weighted imaging. *Stroke* 2009;40:3504–3510.
- [9] Newman-Toker DE, Kerber KA, Hsieh YH, Pula JH, Omron R, Saber Tehrani AS, Kattah JC. HINTS outperforms ABCD2 to screen for stroke in acute continuous vertigo and dizziness. *Acad Emerg Med* 2013;20:986–996.