MAYO CLINIC

# Approaching Acute Vertigo With Diplopia: A Rare Skew Deviation in Vestibular Neuritis

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## Abstract

Evaluating the patient with acute constant vertigo or diplopia can be a daunting task for clinicians, who recognize that such symptoms can be the manifestation of potentially devastating disorders like stroke but may be uncomfortable eliciting and interpreting the key symptoms and subtle signs that distinguish dangerous from benign causes. We present a novel and highly instructive case of a patient with acute vertigo and binocular diplopia from a large skew deviation due to vestibular neuritis. As the case unfolds, text and video commentary guide the clinician through the important elements of the history, bedside examination, and laboratory evaluation necessary for accurate diagnosis in the acute vestibular syndrome. We demonstrate how to interpret nystagmus and properly perform the head impulse test and test of skew deviation and discuss the pitfalls of overreliance on imaging when evaluating patients with acute vertigo.


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## CASE WITH COMMENTARY

### Initial Symptoms

*A 36-year-old woman with hyperlipidemia and occasional migraines without aura but no prior dizziness, vertigo, unsteadiness, or strabismus experienced her typical migraine with nausea and osmophobia. Hours into the episode, she developed progressive dizziness and unsteadiness without directional bias, requiring assistance walking. Although the headache improved with an over-the-counter analgesic, constant vertigo and vomiting soon followed.*

Onset of vertigo during a migraine suggests a first episode of vestibular migraine as a possible etiology. Vestibular migraine is the most common cause of recurrent spontaneous (nonpositional) episodes of vertigo, and vestibular symptoms usually develop years after other migraine symptoms. Most episodes resolve within 72 hours.

### Diplopia

*The patient noted binocular vertical diplopia but no hearing loss, neck pain, dysarthria, dysphagia, facial weakness, limb incoordination, or sensory symptoms.*

Possible lesion localization in patients with vertigo involves the vestibular periphery, brain stem, and cerebellum. Diplopia, dysphagia, dysarthria, or dysmetria (the "dangerous Ds") point toward central localization, while hearing loss can have a central or peripheral cause. Patients with acute vertigo at the height of their symptoms are very distressed with nausea and vomiting and often ignore these associated symptoms. In this case, binocular vertical diplopia with an acute vestibular syndrome (AVS) is a red flag against peripheral and for central localization that requires further investigation.

### Imaging

*The patient was admitted to a local hospital after head computed tomography (CT) and head/neck CT angiography yielded normal findings in the emergency department. Head magnetic resonance imaging (MRI) with diffusion-weighted imaging (DWI), performed less than 24 hours from vertigo onset, also identified no abnormalities and no evidence of acute ischemia, demyelination, or vestibular nerve abnormality.*

Magnetic resonance imaging with DWI and apparent diffusion coefficient is the criterion standard that defines an acute stroke. However, MRI performed too early in posterior fossa ischemia occasionally fails to detect restricted diffusion. This issue is particularly important in patients with vertigo, in whom overreliance on these early studies may cause the examiner to ignore signs of central



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localization. Compelling central clinical signs (including the triad of ocular motor signs that will be described subsequently) require follow-up MRI, ideally obtained more than 48 hours after symptom onset, and careful clinical monitoring.

## Nystagmus

*Over 4 days, the patient was managed symptomatically with intravenous hydration and antiemetics. Vertigo and nausea resolved, although she could still induce brief dizziness with quick head turns. Gait and balance were improving. However, she was still squinting because of diplopia. She was discharged on day 5 with a treatment regimen of prednisone, 60 mg daily.*

*When evaluated in the otoneurology clinic the following day, results of a general neurologic examination were normal except for a moderately cautious, wide-based gait with tandem gait impairment. During Romberg testing, she listed to the left without falling. Hearing was normal to finger rub. Pupils, fundi, and extraocular range were normal. On direct examination and with video oculography during visual fixation, spontaneous right-beating nystagmus with a small torsional component (top pole of the eyes beating toward the right ear) was present in straight-ahead gaze, increased in rightward gaze, and disappeared in leftward gaze. With fixation removed, the right-beating nystagmus intensified and became present even in leftward gaze* (Supplemental Video 1, available online at http://www.mcpiqojournal.org). *Saccades were normal, without saccadic lateropulsion or gaze lateropulsion under closed eyelids (a frequent finding in lateral medullary syndrome). The right-beating nystagmus intruded into rightward and vertical smooth pursuit.*

This patient's examination revealed alterations of the vestibulospinal reflex and the vestibulo-ocular reflex (VOR). She could stand and walk but had abnormal posture with Romberg testing and a wide-based gait. Nystagmus direction may help differentiate central vs peripheral causes of vertigo. Horizontal nystagmus that changes direction with changing gaze positions, upbeat or downbeat nystagmus, and purely torsional nystagmus are associated with central lesions.[1] In this patient, the nystagmus was right-beating in straight-ahead gaze, did not change direction with lateral gaze, increased intensity with blocking fixation, and had only a mild torsional component. This nystagmus pattern is typically observed in patients with peripheral lesions but may also occur with central lesions. Therefore, additional clinical signs must be sought.

## Vestibulo-ocular Reflex Testing

*A head impulse test (HIT) revealed catch-up saccades for the left horizontal and occasionally left anterior semicircular canals* (SCCs) (Supplemental Video 2, available online at http://www.mcpiqojournal.org).

The HIT is necessary to identify the precise lesion site. The examiner rotates the patient's head quickly by a small amount toward the side to be tested, observing whether the patient can effectively use the VOR to maintain visual fixation on a target or whether a "catch-up" saccade is required to refixate the target once the head stops. A *normal* HIT result in a patient with AVS verifies the integrity of the 3-neuron VOR arc and thus suggests *central* localization, as is seen with posterior inferior cerebellar artery strokes. In contrast, lesions of the vestibular nerve or labyrinth impair the VOR and produce an *abnormal* HIT result. In this case, unidirectional horizontal nystagmus beating away from the side with an abnormal HIT result points to a peripheral vestibulopathy, most commonly vestibular neuritis (VN). However, the possibility of an anterior inferior cerebellar artery (AICA) stroke remains. The internal auditory artery, a branch of the AICA, supplies the inner ear. Accordingly, AICA infarcts may involve the labyrinth and present like an acute peripheral vestibulopathy, typically accompanied by hearing loss from cochlear infarction. Thus, the bedside examination should include assessment for acute hearing loss. So far in this case, with peripheral-appearing nystagmus and HIT result and normal hearing, the next step is to test for skew deviation.

## Skew Deviation

*The patient had a prominent leftward head tilt and right hypertropia, preferentially fixating with the left eye, as demonstrated with cover testing* (Supplemental Video 3, available online at http://www.mcpiqojournal.org). *Maddox rod testing revealed the hypertropia to be comitant,*

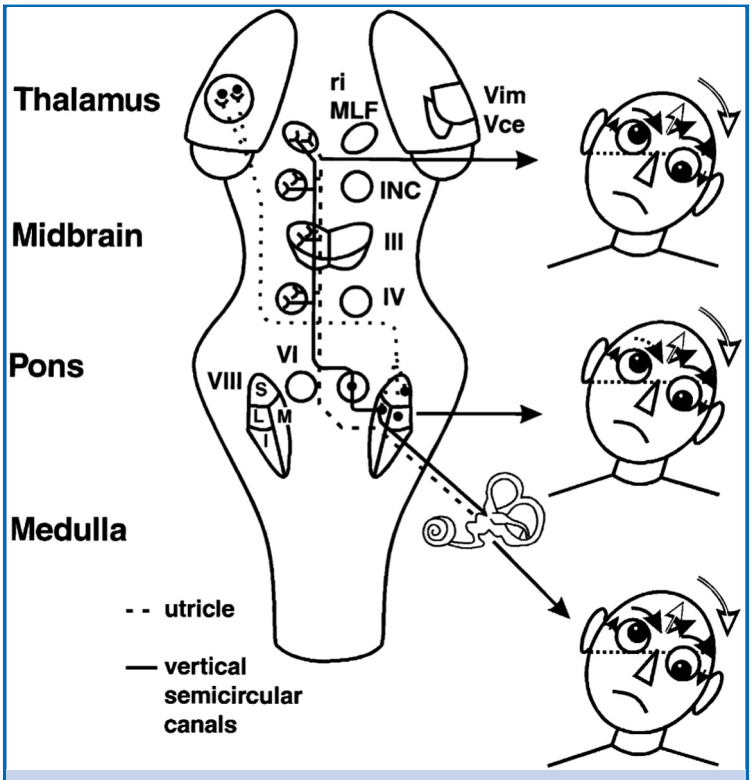


**FIGURE 1.** Ocular tilt reaction. Graviceptive pathways from the utricle and vertical semicircular canals mediating the vestibular reactions in the roll plane. The projections from the utricle and the vertical semicircular canals to the vestibular nuclei VIII and on to the ocular motor nuclei (trochlear nucleus IV, oculomotor nucleus III, abducens nucleus VI), and the supranuclear centers of the interstitial nucleus of Cajal (INC) and the rostral interstitial nucleus of the medial longitudinal fasciculus (riMLF), are shown. Ocular tilt reaction is depicted schematically on the right in relation to the level of the lesion (ie, ipsiversive with peripheral and pontomedullary lesions and contraversive with pontomesencephalic lesions). Note that lesions of the gravitational pathways above the INC will not cause ocular tilt reaction or skew. I = inferior; L = lateral; M = medial; S = superior; Vim = ventral intermediate; Vce = ventral caudalis externa. From *Surv Ophthalmol*,[2] with permission from Elsevier.

*and results of a Bielschowsky 3-step test did not suggest a trochlear nerve palsy.*

In normal individuals, tilting the head laterally activates the utricle driving the otolith-ocular reflex, a mechanism to maintain a gravitationally upright visual axis by generating a compensatory ocular counterroll in the opposite direction.[2] The resulting torsional eye movements are conjugate, whereas the vertical movements are slightly disconjugate.

Under pathologic conditions involving the peripheral labyrinth or central utricular-ocular pathways, the resulting internal misperception of verticality may produce a partial or full ocular tilt reaction (OTR) in an attempt to realign the patient with the erroneously computed vertical.[3,4] The OTR is a triad of head tilt, ocular torsion in the same direction as the head tilt, and skew deviation with the lower eye on the side of the head tilt (Figure 1). Skew is a prenuclear vertical ocular misalignment that is usually comitant (the degree of misalignment does not change in different gaze positions as it does with an extraocular muscle weakness from an acute cranial nerve palsy) and represents an "otolithic pathway" cause of diplopia. In a patient with an AVS, skew is the most likely cause of vertical diplopia.

The magnitude of skew deviation and head tilt are important. Small-amplitude skew detected by cover testing may rarely occur in VN, but a large skew deviation in a patient with AVS, such as the one seen in this patient, is much more frequent in acute stroke and represents a red flag requiring further investigation.

## Clinical Diagnosis

*Because of the large persisting skew deviation, a second head MRI was performed on day 8. The results were also normal, and acute left VN was diagnosed.*

## Vestibular Testing

*Within 2 weeks of symptom onset, diplopia, dizziness, and unsteadiness completely resolved. Quick head movements would sometimes cause the patient's vision to take a moment to catch up. Subsequent vestibular evaluation confirmed a left peripheral vestibulopathy. Warm caloric reflex testing produced 61°/s right-beating nystagmus when irrigating the right ear but no response from the left ear. Video HIT of the horizontal SCC revealed a gain of 0.87 on the right but 0.51 on the left, with overt and covert catch-up saccades (Figure 2). Gain was also reduced for the left anterior but not the posterior canal. Cervical vestibular evoked myogenic potentials (VEMPs) were normal and symmetric. Ocular VEMPs of 97 dB nHL were present bilaterally at 500 Hz, but the P1 to N1 amplitude on the left was less than half that on the right. Audiometry yielded normal results.*


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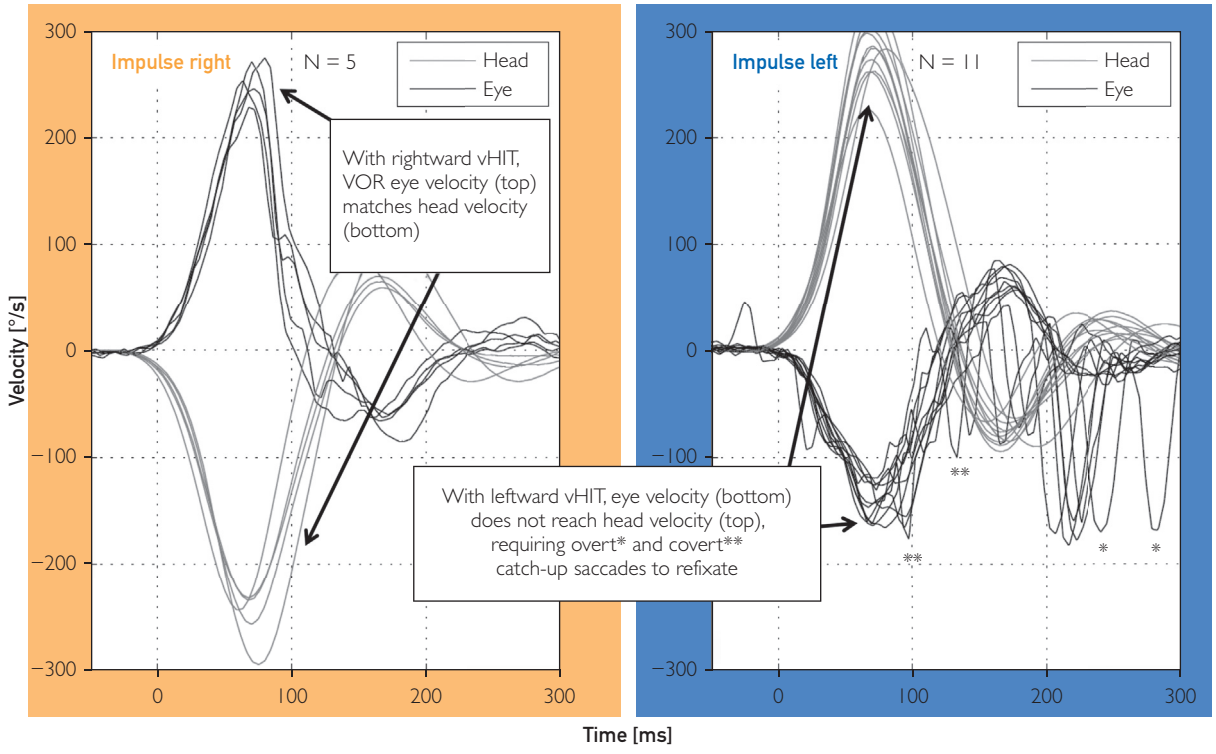


**FIGURE 2.** Video head impulse test (vHIT). Horizontal vHIT tracing using video-oculography shows abnormalities with head rotation on the left only. We compare eye velocity from several impulses to head velocity in the opposite direction over time. Overt catch-up saccades, occurring after the head stops, would be clinically evident with the bedside head impulse test without video-oculography. However, vHIT also demonstrates how catch-up saccades sometimes occur *during* the head impulse. These covert saccades are buried in the vestibulo-ocular reflex and would not be visible to the examiner without vHIT. The tracing also shows the reduced gain (ratio of eye velocity to head velocity) of the left horizontal vestibulo-ocular reflex.

From the labyrinth, the superior vestibular nerve (SVN), the most common target of VN, carries afferent fibers from the horizontal and anterior SCCs, the utricle and small portion of the saccule. The inferior vestibular nerve carries afferents from the posterior SCC and the saccule. In this case, vestibular testing with calorics and video HIT confirmed impairment of the SVN afferents, with decreased function of the horizontal and anterior canals. In contrast, the posterior canal function via the inferior vestibular nerve was spared. The role of video-oculography recording of the HIT cannot be overemphasized, as it provides both multicanal VOR assessment and quantification of VOR gain and catch-up saccades.

Results of the ocular VEMP, a test of utricular function, were abnormal on the left, while results of the cervical VEMP, a test of saccular function, were normal. Such utricular pathway dysfunction could both explain the patient's OTR and support localization to the SVN.[5] Normal audiographic results are expected in VN and argue against Ménière disease or bacterial labyrinthitis. Most strokes do not cause hearing loss, although AICA strokes may cause cochlear infarction.

## Outcome

*Examination 2 months after onset revealed steady visual fixation, although weak right-beating nystagmus was elicited by removing fixation with video-oculography and could be intensified following horizontal headshaking and with mastoid vibration. The HIT continued to show catch-up saccades for the left horizontal canal. There was a slight leftward head tilt. Alternate cover testing revealed no vertical ocular misalignment, and prism testing identified less than 1 diopter of right hyperdeviation. Gait and station*

TABLE. HINTS to INFARCT[a]

| HINTS examination component | INFARCT or central if *any* of these symptoms are present | Benign peripheral if *all* of these symptoms are present |
|---|---|---|
| **H**ead **I**mpulse | **I**mpulse **N**egative (no catch-up saccades) | Impulse positive toward lesion side, requiring catch-up saccades to refixate on target |
| **N**ystagmus characteristics | **F**ast-phase **A**lternating (direction-changing or purely vertical or torsional) | Fast phases of spontaneous nystagmus always beat away from lesion side; predominantly horizontal, with small torsional component |
| **T**est of **S**kew | **R**efixation on **C**over **T**esting (demonstrating vertical misalignment) | No skew deviation (no vertical refixation) on alternate cover testing |
| Other findings | | |
| Bedside hearing test | Acute hearing loss is a red flag for possible anterior inferior cerebellar artery stroke even when other signs point toward a peripheral cause | |
| Degree of imbalance | Severe truncal and gait ataxia (inability to sit or stand without holding on) is a red flag for a central cause | |

[a]The HINTS to INFARCT approach differentiates stroke or other potentially dangerous central causes from benign acute peripheral vestibulopathies such as vestibular neuritis. The HINTS battery should be applied to patients with an acute vestibular syndrome of acute constant dizziness, vertigo, or ataxia who lack other obvious central neurologic signs on examination. It is not to be applied to patients who experience only position-triggered vertigo or to those who are no longer symptomatic.

*were normal. Video HIT showed improved left horizontal canal gain to 0.64, but left warm caloric response was still absent.*

Normal MRIs, vestibular evaluation, and the clinical course confirmed the diagnosis of VN despite the red flag of a pronounced head tilt and large skew deviation. Through vestibular compensation, the patient's symptoms resolved except with quick head movements that challenge the high-frequency VOR. When examined long after acute vertigo has resolved, provocative maneuvers such as headshaking and vibration, with visual fixation blocked, may bring out diagnostically important nystagmus effectively suppressed with visual fixation.

## DISCUSSION

This case illustrates the frequent diagnostic challenges in patients with vertigo. The best approach starts with characterizing the vestibular syndrome by considering the timing and triggers and performing a targeted examination.[6] Although benign paroxysmal positional vertigo (BPPV) is the most common vestibular disorder, it causes brief (<1 minute) episodes of vertigo and nystagmus triggered by position changes or positional testing. In this case, spontaneous nystagmus in the upright position with constant symptoms makes BPPV highly unlikely, although the horizontal canal BPPV variant can occasionally cause "pseudospontaneous" nystagmus that should be suspected if the nystagmus reverses direction when the head is pitched forward 60 degrees. The first attack of an episodic disorder such as vestibular migraine was initially possible (and could produce nystagmus that appears central or peripheral) but became unlikely because vestibular symptoms and signs persisted for days.

In patients with AVS who lack obvious central nervous system features, a test for 3 ocular motor signs—head impulse, nystagmus, and test of skew (HINTS)—is highly sensitive for distinguishing central causes such as stroke from peripheral causes such as VN.[7,8] A normal HIT result or the presence of spontaneous nystagmus that is direction-changing, vertical, or purely torsional are unequivocal central signs. Skew deviation on cover testing is also very suggestive of a central lesion (Table). A large skew such as that detected in this case is rare in


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VN, and an OTR with prominent head tilt as seen in this patient has not previously been reported in VN nor found in a personal series of more than 100 VN patients (J.C.K., unpublished data, 2019).[7,9,10] Acute hearing loss in AVS (which this patient did not have) also appears more common with central than with peripheral causes due to AICA infarcts, making hearing assessment an important examination component.[8,11]

So far, the simple HINTS Plus battery (adding hearing assessment) appears to be superior to early MRI for detecting stroke in AVS in the hands of expert examiners.[7,12] Although this approach has been widely adopted by vestibular specialists, HINTS has not become part of the standard examination of patients with acute dizziness used by most physicians. This difference is likely due in part to physicians' generally poor understanding of the vestibular and ocular motor systems and the interpretation of their subtle examination signs.[13] Textbooks and training curricula perpetuate incorrect information. The result is that patients with acute dizziness who have benign conditions are overevaluated while those with dangerous conditions may be underevaluated. Ultimately, the likelihood of vertigo being precisely diagnosed correctly is similar to a coin flip.[14,15] Implementation of HINTS in a large multicenter clinical trial using video-oculography—guided rapid triage will provide critical answers about its potential to improve diagnosis and initial management by nonexpert clinicians and reduce unnecessary or unhelpful neuroimaging in patients with acute dizziness.[16]

## CONCLUSION

Patients with acute constant vertigo and diplopia present a diagnostic challenge that requires a careful bedside examination to distinguish benign from potentially life-threatening causes. Imaging with CT has little value, and even MRI with DWI may miss small strokes if performed too soon. When overt central neurologic signs are absent, the clinician must perform and correctly interpret results of the HIT, characterize the nystagmus, and test for skew deviation as well as assess for acute hearing loss (the HINTS Plus examination). Although this examination battery has very high sensitivity and specificity in AVS in expert hands, this case illustrates how on rare occasions a large skew deviation can result from a peripheral vestibulopathy affecting the otolith-ocular pathways. Ongoing research aims to improve diagnostic accuracy by nonexpert clinicians through both medical education and use of new technologies.

## SUPPLEMENTAL ONLINE MATERIAL

Supplemental material can be found online at http://www.mcpiqojournal.org. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.

**Abbreviations and Acronyms:** **AICA** = anterior inferior cerebellar artery; **AVS** = acute vestibular syndrome; **BPPV** = benign paroxysmal positional vertigo; **CT** = computed tomography; **DWI** = diffusion-weighted imaging; **HINTS** = head impulse, nystagmus, and test of skew; **HIT** = head impulse test; **MRI** = magnetic resonance imaging; **OTR** = ocular tilt reaction; **SCC** = semicircular canal; **SVN** = superior vestibular nerve; **VEMP** = vestibular evoked myogenic potential; **VN** = vestibular neuritis; **VOR** = vestibulo-ocular reflex

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