Clinical Reasoning:

A 55-year-old woman with vertigo

A dizzying conundrum

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SECTION 1

A 55-year-old woman presented to the emergency department complaining of dizziness. Several hours earlier she abruptly felt “the room spinning and moving back and forth.” Simultaneously, she experienced nausea, vomiting, and gait unsteadiness. The dizziness exacerbated with head movement. She denied head or neck pain, photophobia,

phonophobia, auditory symptoms, weakness, numbness, diplopia, dysarthria, dysphonia, dysphagia, history of recent illness, prior dizziness, or headache. Medical history included hyperlipidemia and hypertension.

Question for consideration:

1. What is the differential diagnosis for acute vertigo?

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SECTION 2

To determine the cause of acute vertigo, it is important to know whether it is transient (seconds to minutes) or prolonged (hours to days); a single episode of vertigo or a recurrence; if it is positionally provoked (e.g., benign paroxysmal positional vertigo); and if there are any accompanying symptoms or signs. The most common causes of acute prolonged vertigo include a peripheral vestibulopathy, Ménière syndrome, migrainous vertigo, or brainstem or cerebellar ischemia.¹ This discussion is limited to the distinction between a peripheral vestibulopathy and ischemia.

The acute vestibular syndrome (AVS) develops over seconds to hours and is characterized by vertigo, nausea, vomiting, gait instability, head motion intolerance, and nystagmus.^{2–4} It is caused by either an acute peripheral vestibulopathy (APV) or brainstem/cerebellar ischemia, and similarities in presentation often make the distinction a diagnostic challenge. Transient ischemic attacks can cause acute vertigo with rapid resolution but vertigo resulting from a

stroke, like an APV, may last days to weeks. Vertigo caused by ischemia is almost always accompanied by other neurologic symptoms and signs but may occur in isolation.^{2–5}

An APV is characterized by acute prolonged vertigo, oscillopsia (the visual illusion of movement of a stationary object due to spontaneous nystagmus), unilateral canal paresis with a positive head impulse test (HIT), nausea, vomiting, exacerbation of vertigo with head movement, and imbalance.^{2–4} Depending on the presence or absence of auditory symptoms, an APV is further classified as either labyrinthitis or vestibular neuritis, respectively. Vertigo is maximal within minutes to hours and can persist for days to weeks. There may be a viral prodrome or a history of brief vertiginous attacks in the days prior to the onset of prolonged vertigo.¹

Questions for consideration:

1. What is the pathophysiology of nystagmus?
2. How is the vestibular system assessed on physical examination?

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SECTION 3

In an acute destructive lesion affecting 1 labyrinth, such as an APV, symptoms result from ipsilesional afferent hypoactivity and relative contralesional hyperactivity from the vestibulocochlear nerve. During a normal head turn to the left, there is left-greater-than-right asymmetry in afferent vestibular signals and the eyes drift to the right to maintain stable vision (i.e., vestibulo-ocular reflex or VOR).⁶ A right APV is perceived as a leftward head turn even though the head is still. As a result, the eyes continuously drift to the right (slow phase of nystagmus), and a position reset mechanism (fast phase) quickly brings the eyes back to the left (to midline) (figure 1).⁶ The nystagmus is of larger amplitude when gazing in the direction of the fast phase (i.e., Alexander law). The horizontal component of peripheral vestibular nystagmus is inhibited with fixation (there is a poor torsional fixation mechanism),⁷ which does not occur with central causes of vestibular nystagmus.

Since the intensity of peripheral nystagmus is influenced by fixation, observation under various conditions can help distinguish central vs peripheral causes of vertigo as peripheral nystagmus inhibits with fixation, and conversely, increases with fixation removed. Occlusive funduscopy is performed by visualizing the optic disc with an ophthalmoscope and then covering the patient's viewing eye, thus removing fixation, which enhances peripheral nystagmus but has no effect on central nystagmus.⁷

Similarly, the penlight cover test involves having the patient fixate on a penlight, and then covering 1 eye, thus removing fixation as the uncovered eye continues to view only the bright penlight.⁸ Having the patient view a featureless scene such as a piece of white paper has a similar effect: since there is no feature available for foveation, fixation is suppressed.⁷

Dynamic assessment of the vestibular system includes the HIT, which tests angular VOR function (figure 2).⁹ Although a peripheral pattern of nystagmus with an abnormal HIT implies labyrinthine or vestibular nerve dysfunction, it is important to recognize that the etiology may be ischemia. The vascular supply to the inner ear is via the internal auditory artery, so a "peripheral" lesion can be from infarction.¹⁰

Another important sign to look for in the AVS is a skew deviation, which is a nonparalytic preocular vertical ocular misalignment due to an imbalance of utricular inputs to the ocular motor system. It is often accompanied by features of the ocular tilt reaction (OTR), which includes the triad of skew deviation, head tilt, and ocular counterroll.¹¹ A skew deviation is best demonstrated during alternate cover testing demonstrating vertical correction of the uncovered eye to maintain fixation, or subjectively with Maddox rod testing. A skew deviation and a fourth nerve palsy may present similarly (figure 3). A skew deviation occurs most

Figure 1 Pathophysiology of peripheral nystagmus in an acute peripheral vestibulopathy

Nystagmus from an acute peripheral vestibulopathy (APV) is mixed horizontal-torsional, indicating a lesion of the entire vestibular nerve or all semicircular canals within one labyrinth. Stimulation of individual canals move the eyes in distinct planes (i.e., horizontal, vertical, or torsional). In a right APV, the direction of nystagmus is determined by the intact left labyrinth: the 2 oppositely oriented left anterior and posterior canals cancel out vertical movement, leaving only a slight torsional component contributed from each, while the horizontal vector is attributable to the unopposed left horizontal canal.⁷ This generates a slow (pathologic) phase (in red) toward the affected ear with a fast (position reset) phase (in black) away from the affected ear. Nystagmus is named for the direction of the fast phase. The nystagmus is present in primary position and beats in the same direction (unidirectional) with gaze to either side. LAC = left anterior semicircular canal; LHC = left horizontal semicircular canal; LPC = left posterior semicircular canal; RAC = right anterior semicircular canal; RHC = right horizontal semicircular canal; RPC = right posterior semicircular canal. Redrawn and modified from Leigh RJ, Zee DS. *The Neurology of Eye Movements* (Contemporary Neurology Series), 4th ed. New York: Oxford University Press, Inc.; 2006: figure 2-2. By permission of Oxford University Press, Inc.

(A) Normally, during a quick 20 ° head turn to the right, the patient will be able to maintain fixation on the examiner's nose (i.e., the target). (B) With a right peripheral vestibulopathy, when the head is turned quickly to the right, the line of sight moves with the head due to a hypoactive VOR, necessitating a compensatory catch-up saccade to the left to refixate on the examiner's nose. Reprinted from: Edlow JA, Newman-Toker DE, Savitz SI. Diagnosis and initial management of cerebellar infarction. *Lancet Neurol* 2008;7:951–964. With permission from Elsevier.

commonly with brainstem or cerebellar lesions, but also may be seen with a lesion anywhere from the utricle to the interstitial nucleus of Cajal in the rostral midbrain.¹¹

Other signs of central localization of acute vertigo include direction-changing (i.e., gaze-evoked or bidirectional) nystagmus, pure horizontal, torsional, or vertical nystagmus, impaired or asymmetric smooth pursuit, inability to suppress the VOR (combined eye-head tracking of moving targets), dysmetric saccades, and associated brainstem and long tract signs.^{1,7}

In our patient, blood pressure was 143/79 mm Hg and general medical examination including otoscopy were normal. In primary gaze there was left-beating horizontal-torsional jerk nystagmus that intensified with left gaze, and lessened but remained left-beating in right gaze (video, first half, on the *Neurology*® Web site at www.neurology.org). The nystagmus intensified with removal of fixation during occlusive funduscopy and the penlight cover test. The HIT was normal to the left but abnormal to the right (video, second half), demonstrating a catch-up saccade, confirming a hypoac-

Figure 3 Distinguishing a fourth nerve palsy from skew deviation with Maddox rod testing

(A) Left fourth nerve palsy compared with (B) skew deviation. By convention, the Maddox rod is placed over the right eye. In both (A) and (B) there is a vertical misalignment in primary gaze with the left eye higher than the right (i.e., left hypertropia). A left fourth nerve palsy is diagnosed in (A) by demonstrating greater vertical separation between the light and the horizontal line (i.e., greater degree of left hypertropia) in contralateral gaze (with the paretic eye adducted), downgaze, and ipsilateral head tilt (not shown). A left hypertropia caused by a skew deviation in (B) is typically comitant, meaning the degree of vertical misalignment is consistent in all directions of gaze. In contrast to the head tilt seen in a fourth nerve palsy, which is compensatory (i.e., a contralateral head tilt minimizes ocular misalignment due to impaired intorsion of the affected eye), the head tilt in the OTR occurs in the same direction as the cyclotorsion (ocular counterroll).¹¹ Reprinted from: Kheradmand A, Bronstein A, Zee DS. Clinical bedside examination. In: Eggers SD, Zee DS, eds. *Vertigo and Imbalance: Clinical Neurophysiology of the Vestibular System: Handbook of Clinical Neurophysiology*. New York: Oxford University Press, Inc.; 2012: figure 2 (in press 2012). By permission of Oxford University Press, Inc.

tive right VOR. Suppression of the VOR, smooth pursuit, and saccadic eye movements were normal. There was no vertical misalignment. When testing tandem gait, there were multiple side-steps to the right, and she could not maintain balance with Romberg testing. The remainder of the neurologic examination was normal.

Questions for consideration:

1. What are the most common manifestations of cerebellar ischemia?
2. What are the 3 most important bedside ocular motor tests to differentiate a stroke from an APV?
3. How has the examination narrowed the differential diagnosis in this patient?

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Table Distinguishing peripheral vs central localization in the acute vestibular syndrome

Clinical sign	Peripheral	Central	Comments
Nystagmus	Unidirectional; mixed horizontal-torsional; obeys Alexander's law; slow phase with constant velocity; more intense when lying with affected ear down	May change direction; pure horizontal, torsional, or vertical; slow phase with constant, increasing or decreasing velocity	Peripheral nystagmus suppresses with fixation and increases with fixation removed, while central nystagmus is poorly suppressed by fixation ^{4,7}
Head impulse test (horizontal)	Abnormal	Typically normal	Lesions of the vestibular nucleus, root entry zone of 8th cranial nerve, or caudal cerebellum may cause an abnormal head impulse test ¹²
Skew deviation	Absent	May be present	Rarely, a small skew may be apparent from a utricular lesion, but a large skew with diplopia suggests central localization ¹
Associated symptoms or signs	Hearing loss or tinnitus, minor gait instability, and veering toward the side of the lesion	Headache or neck pain (particularly concerning if abrupt onset, prolonged, or severe), weakness, numbness, diplopia, dysarthria, dysphonia, dysphagia, Horner sign, drop attack (abrupt fall with preserved level of consciousness), incoordination, marked gait instability, and lateropulsion	A central lesion presents uncommonly as isolated vertigo

SECTION 4

In a series of 66 patients with isolated cerebellar infarctions, vertigo and lateropulsion (defined as an irresistible sensation of falling to one side) were the most common symptoms.⁵ Although vertigo and lateropulsion can each occur in isolation with a cerebellar stroke, other signs and symptoms are typically present, including limb ataxia, nausea/vomiting, truncal ataxia, dysarthria, nystagmus, headache, confusion, or somnolence.^{3,5}

A stroke in the posterior inferior cerebellar artery territory can cause a “pseudovestibular neuritis” manifesting as isolated vertigo without auditory or other symptoms, but typically has a normal HIT.³ A superior cerebellar artery stroke can cause a “pseudointoxication” picture because of gait or truncal ataxia with dysarthria, or “pseudogastroenteritis” with nausea and vomiting.

The internal auditory artery (IAA) is an end artery from the anterior inferior cerebellar artery (AICA) that supplies the vestibulocochlear nerve, cochlea, and vestibular labyrinth. Due to a paucity of collaterals, the IAA is vulnerable to ischemia. A labyrinthine infarction usually presents with sudden loss of hearing and vertigo accompanied by other AICA-territory signs (e.g., cerebellar, lateral pontine, or midbasilar syndromes).^{2,3} However, isolated labyrinthine ischemia may herald AICA infarction.^{2,10} In a series of 82 patients with AICA strokes, 80 had acute prolonged vertigo and vestibular dysfunction of peripheral, central, or combined origin; 35 had acute prolonged vertigo with audiovestibular loss; 24 had acute prolonged vertigo without audiovestibular loss, while a selective loss of vestibular

lar (4) or cochlear (3) function was much less common.¹⁰ AICA strokes have also been referred to as “pseudolabyrinthitis.”³

In patients presenting with the acute vestibular syndrome, the combination of direction-changing nystagmus, skew deviation, and a normal HIT were more sensitive in detecting stroke than MRI (table).⁴ A normal HIT strongly indicates a central process, but an abnormal HIT is a less reliable indicator of a peripheral lesion because of APV mimics (i.e., ischemia of the vestibular nucleus, root entry zone of the eighth cranial nerve, or caudal cerebellum may cause an abnormal HIT).^{12–14} In addition to the findings on bedside examination, vertigo due to cerebrovascular disease should be considered if any of the following factors are present: stroke risk factors, risk of vertebral artery dissection, abrupt onset, inability to ambulate, paucity of nausea and vomiting with marked gait instability or severe nausea and vomiting with little gait instability, or other accompanying central neurologic symptoms and signs.³

Our patient had a right APV without auditory symptoms, and was diagnosed with vestibular neuritis. Prior to evaluation by the authors and within 24 hours of symptom onset, a brain MRI was found to be normal. Although brainstem/cerebellar infarctions may be missed acutely on MRI, the positive HIT, unidirectional nystagmus, and absent skew deviation all pointed away from a central process, and therefore an MRI was arguably unnecessary.⁴ Her symptoms improved significantly over several days with only antiemetics, and vestibular rehabilitation was recommended.

AUTHOR CONTRIBUTIONS

Daniel R. Gold, DO: conceptualization, drafting, and revising the manuscript. Stephen G. Reich, MD: drafting and revising the manuscript.

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DISCLOSURE

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