

Clinical Reasoning: A 48-Year-Old Man Presenting With Diplopia

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Section 1

A 48-year-old man, recently diagnosed with systemic hypertension, presented with sudden-onset double vision for 4 days, which was relieved by closing one eye. On general examination, he was well-oriented in time, place, and person. His motor and sensory system examination was normal. Cranial nerves V, VII, and VIII were normal and there were no clinical signs of cerebellar dysfunction.

The ocular examination results are shown in figure 1, A and B.

Questions for Consideration:

1. What is the relevance of knowing if the diplopia was binocular or uniocular?
2. Describe the ocular examination findings in figure 1, A and B.

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Figure 1 Clinical Picture of the Patient Showing Ocular Alignment and Motility



(A) Ocular alignment. (B) Ocular motility.

Section 2

The patient in this vignette presented with binocular diplopia (relieved by closing one eye), meaning that the diplopia was related to an ocular motility issue. Unioocular diplopia (persisting after closing one eye) points towards some problem in that eye like irregular refractive media (keratoconus, lenticonus, early cataract) and the patient needs a detailed ocular examination.¹

As seen in figure 1A, there is upper eyelid retraction in both eyes (left > right) and gross anisocoria (right pupil 7 mm and

left pupil 3 mm). The right pupil did not react to direct or consensual light reactions and on attempted convergence. The left eye is grossly hypotropic by 20 prism diopters (figure 1A). There is complete upgaze palsy in both eyes, asymmetric downgaze palsy (right eye > left eye), and slight limitation of adduction in right eye (figure 1B).

In addition to the findings shown in figure 1, A and B, the patient had other oculomotor abnormalities. He was unable to converge his eyes and there was no convergence–retraction nystagmus on attempted upgaze. The doll's head maneuver failed to elicit any eye movements. There was a low-amplitude

and low-frequency horizontal jerk nystagmus, right-beating on right gaze and left-beating on left gaze. There was also downbeating nystagmus of moderate amplitude and low frequency, increasing on downgaze. It was seen more prominently in the left eye since there was complete vertical gaze palsy in the right eye. There was also a torsional component to the nystagmus to the left (video 1).

Questions for Consideration:

1. What is the importance of performing the doll's head maneuver in such cases?
2. What is this typical pattern of oculomotor abnormality called?
3. What could be the site of lesion causing these oculomotor manifestations and the possible causes?

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Section 3

While evaluating gaze palsy, one should check the doll's head maneuver to differentiate between supranuclear vs nuclear/infranuclear lesions. The doll's head maneuver involves rotating the patient's head horizontally and vertically with eyelids open, and the patient looking at a target object. This test evaluates integrity of the vestibulo-ocular reflex (VOR), which causes eye movement by stimulating the ocular motor nuclei in brainstem to reflexively stabilize the eyes without involvement of the cerebral cortex. In a patient with horizontal or vertical gaze palsy, the presence of eye movements with doll's head maneuver indicates that the nuclear and infranuclear pathways are intact and the lesion is at supranuclear level. Absence of eye movement on doll's head maneuver is suggestive of a nuclear or infranuclear lesion, as in our patient.² Since our patient has vertical gaze palsy with a negative doll's head maneuver, the site of lesion is likely to be at the thalamo-mesencephalic junction, which hosts the vertical gaze center.

Rostral interstitial nucleus of medial longitudinal fasciculus (riMLF) controls ipsilateral downward and contralateral upward gaze, hence an isolated unilateral lesion of riMLF would lead to impaired upgaze in contralateral eye and impaired

downgaze in the ipsilateral eye. Fibers controlling contralateral upward gaze cross over at the posterior commissure (PC), hence a single lesion at the PC would cause bilateral upgaze palsy. A lesion affecting the PC and riMLF on one side would result in complete vertical gaze palsy in one eye and upgaze palsy in the other eye, and this combination is called vertical one and a half syndrome.³ Our patient had a complete vertical gaze palsy in the right eye and upgaze palsy in the left eye, most likely caused by the thalamo-mesencephalic infarct affecting the PC and right-sided riMLF. The other differential diagnosis for the hypotropia in the left eye could be skew deviation in right eye with hypotropia in the left eye, but on fundus examination there was no torsion in either eye and there was no reduction in hypotropia in supine position, thus ruling out skew deviation.⁴

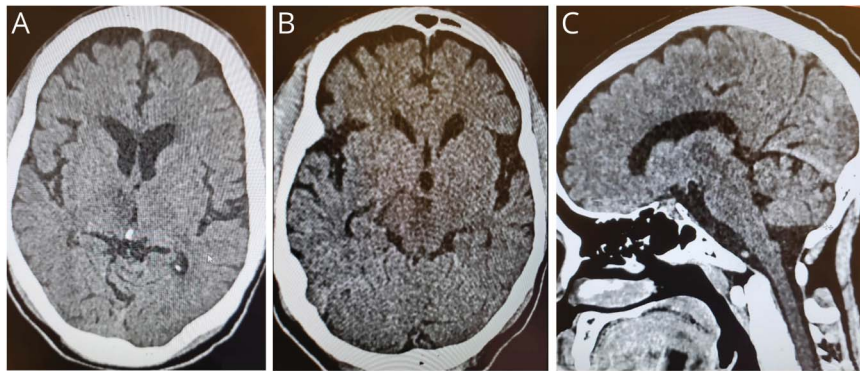
Questions for Consideration:

This patient is being managed in a resource-limited setting in sub-Saharan Africa, where only CT scan is available.

1. Can you describe the lesion seen on the CT scan of the brain in this patient?
2. Can you explain the oculomotor, eyelid, and pupillary findings based on the CT scan?

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Figure 2 CT Brain



(A) Axial section. Note hypodensity in medial part of right thalamus. (B) Axial section at the level of quadrigeminal cistern. Note the caudal extension of the infarct into the midbrain. (C) Sagittal section. Note hypodensity involving thalamus extending into rostral part of midbrain on right side.

Section 4

CT scan of the head shows a focal hypodensity in the right thalamus, suggestive of infarction, involving its medial part close to the wall of the third ventricle, as seen in axial section (figure 2A), with extension into the rostral part of the midbrain, as seen in the axial section at the level of quadrigeminal cistern (figure 2B) and also in the sagittal section (figure 2C).

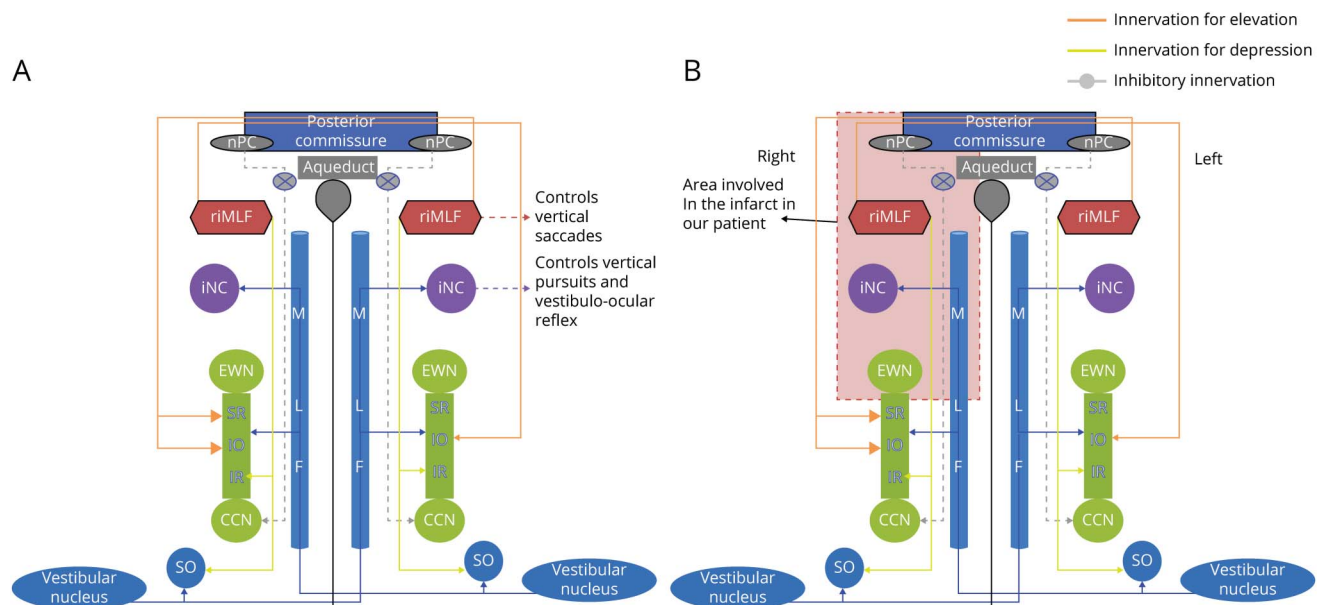
To explain all the oculomotor features of this case, a brief revision of control of vertical eye movements would help (figure 3A).⁵ The final common pathway for vertical eye movements is formed by the oculomotor nucleus complex situated in the dorsal midbrain at the level of the superior

colliculi (subnuclei of the superior rectus, inferior rectus, and inferior oblique) and trochlear nerve nuclei (supplying superior oblique muscle) situated in the dorsal midbrain at the level of the inferior colliculi. The vertical gaze center controlling the vertical eye movements is situated at the thalamomesencephalic junction and it comprises 3 principal structures: riMLF, interstitial nucleus of Cajal (INC), and PC.⁵

Table 1 summarizes details of the location, connections, functions, and clinical manifestations of lesions at these centers.

In a unilateral INC lesion associated with riMLF, torsional eye movement either does not have a fast component or is directed to the opposite side. Thus a combined involvement of

Figure 3 Schematic Diagram of Vertical Gaze Centers



(A) Vertical gaze centers, their functions, and connections. (B) Area affected by infarct in our case. CCN = central caudal nucleus; EWN = Edinger Westphal nucleus; iNC = interstitial nucleus of Cajal; IO = inferior oblique; IR = inferior rectus; nPC = nucleus of the posterior commissure; riMLF = rostral interstitial nucleus of the medial longitudinal fasciculus; SO = superior oblique; SR = superior rectus.

Table 1 Summary of Centers Controlling Vertical Gaze⁴

Structure	Location (all at the thalamo-mesencephalic junction)	Connections	Function	Lesion
riMLF	Rostral to the oculomotor nucleus and dorsomedial to the red nucleus	Supplies elevator muscles (SR and IO) on both sides, but depressor muscles (IR and SO) only on the same side	Vertical saccades	A unilateral lesion would affect the ipsilateral downward saccade
INC	Caudal to riMLF and close to the rostral end of the EWN and separated from the oculomotor nuclei by the MLF	Vestibular nuclei, ipsilateral and contralateral riMLF, and contralateral INC	Controls all vertical eye movements except saccades	Unilateral INC lesion produces an ocular tilt reaction with torsional vertical nystagmus; bilateral INC lesions affect all vertical gaze movements and may cause upbeat nystagmus
PC consists of crossing fibers intermingled with scattered cells that constitute the nPC	Rostral to the superior colliculi at the junction of the aqueduct and third ventricle	Connects INC to the oculomotor nuclei and INC on the opposite side, and fibers that connect nPC with the contralateral INC and riMLF	Involved with all vertical eye movements, especially upward eye movement	A single lesion at the PC can lead to bilateral upgaze palsy because the upgaze fibers cross at the level of the PC

Abbreviations: EWN = Edinger Westphal nucleus; IO = inferior oblique; IR = inferior rectus; INC = interstitial nucleus of Cajal; MLF = medial longitudinal fasciculus; nPC = nucleus of the posterior commissure; PC = posterior commissure; riMLF = rostral interstitial nucleus of the medial longitudinal fasciculus; SO = superior oblique; SR = superior rectus.

the riMLF and INC would lead to loss of smooth pursuits, saccades, and VOR and a vertical and torsional nystagmus with fast component to the opposite side (figure 3B).⁵

The unpaired levator palpebrae superioris (LPS) subnucleus supplies the LPS on both sides and is situated caudally in the dorsal midbrain, hence it is also called the central caudal nucleus (CCN). It is postulated to receive inhibitory inputs from the nucleus of the PC. In case of an infarct involving the PC, the inhibitory inputs to the CCN are reduced, leading to additional resting innervation going to the LPS on both sides causing bilateral upper eyelid retraction, as seen in our case.⁶ The fixed and dilated pupil can be explained by involvement

of Edinger Westphal nucleus, which is situated in close proximity to riMLF and INC.

When present, dissociated convergence (i.e., ability to converge in absence of adduction) is a useful sign to differentiate internuclear ophthalmoplegia (INO) from myasthenia gravis and oculomotor nerve palsy. Based on presence or absence of convergence, Cogan described anterior and posterior types of INO. If a patient with INO is able to converge, despite inability to adduct, the medial longitudinal fasciculus (MLF) lesion is likely to be caudal, sparing medial rectus subnucleus of oculomotor nerve, and this is called posterior INO of Cogan. A more rostral lesion at the thalamo-mesencephalic junction, where nuclei

Table 2 Summary of Clinical Manifestations and Explanation

Manifestation	Explanation
Bilateral complete upgaze palsy	Lesion at posterior commissure
Unilateral downgaze palsy on right side	Lesion at the right riMLF
Left eye hypotropia	Intact left riMLF causing unopposed downgaze movement
Downbeat torsional nystagmus with torsional component to left	Combined involvement of right riMLF and INC
Downbeat nystagmus more pronounced in left eye	Intact downgaze on left side due to intact left riMLF
Absent convergence	Involvement of convergence center situated at the tectum-pretectum level
Right INO	Involvement of riMLF at the level of rostral midbrain (as suggested by absent convergence) and involving the adjacent paramedian tracts to and from the flocculus (as suggested by the gaze-evoked nystagmus) ⁶
Bilateral eyelid retraction	Disinhibition of CCN from inhibitory impulse coming from nPC
Fixed dilated pupil in right eye	Involvement of right EWN

Abbreviations: CCN = central caudal nucleus; EWN = Edinger Westphal nucleus; INC = interstitial nucleus of Cajal; nPC = nucleus of the posterior commissure; riMLF = rostral interstitial nucleus of the medial longitudinal fasciculus.

mediating convergence reside, is likely to affect convergence and this is called as anterior INO of Cogan, as seen in our case. Thus the presence or absence of convergence helps differentiate site of lesion in INO, though this rule is not always reliable.⁷ Usually in INO there is nystagmus in the abducting eye, but our patient had right-beating nystagmus on right gaze and left-beating on left gaze. This could be a form of gaze-evoked nystagmus, which is known to be caused by lesions of the MLF involving the adjacent paramedian tracts to and from the flocculus.⁷

Based on this information and the CT scan, table 2 summaries clinical features of the patient along with possible explanations for the same.

Discussion

One limitation while managing this case is lack of availability of MRI, due to which the exact extent of infarct cannot be known. That is a limitation that we need to live with while working in low-resource settings like sub-Saharan Africa. Though the resolution of images was not comparable to MRI, it was still possible to perform neuro-radiologic correlation of complex oculomotor manifestations.

Apart from rostral midbrain, our case also had involvement of medial part of right thalamus, which can also contribute to bilateral upgaze palsy. It may be attributed to interruption of the frontobulbar fibers that decussate in the medial nucleus of the thalamus, before reaching the superior colliculus.⁸

A thalamo-mesencephalic stroke can present with oculomotor manifestations alone, as in this case. Our patient had vertical one and a half syndrome with ipsilateral internuclear ophthalmoplegia. We call it vertical one and half with horizontal half syndrome.

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Disclosure

The authors report no disclosures relevant to the manuscript. Go to [Neurology.org/N](https://www.neurology.org/N) for full disclosures.

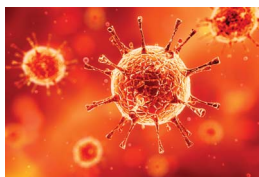
Appendix Authors

Name	Location	Contribution
Niranjan Pehere, DNB, FICO (Hon)	Liberia Eye Center, LV Prasad Eye Institute, John F. Kennedy Memorial Medical Center, Monrovia, Liberia	Conceptualization of study and study design, data collection and data analysis, drafting the manuscript, editing the manuscript
Kebede Gofer, MD	Consultant radiologist, John F. Kennedy Memorial Medical Center, Monrovia, Liberia	Data collection and data analysis, editing the manuscript

References

1. Danchavijitr C, Kennard C. Diplopia and eye movement disorders. *J Neurol Neurosurg Psychiatry* 2004;75(suppl 4):iv24–iv31.
2. Puckett E, Almarzouqi SJ, Morgan ML, Lee AG. Doll's head maneuver/phenomenon, in horizontal gaze palsy. In: Schmidt-Erfurth U, Kohner T, eds. *Encyclopedia of Ophthalmology*. Berlin: Springer; 2015.
3. Sato K, Takahashi Y, Matsumoto N, et al. Rare valiant vertical one-and-a-half syndrome without ipsilateral upward gaze palsy in a patient with thalamomesencephalic stroke. *Neurol Clin Neurosci* 2018;6:133–135.
4. Wong AM. Understanding skew deviation and a new clinical test to differentiate it from trochlear nerve palsy. *J AAPOS* 2010;14:61–67.
5. Bhidayasiri R, Plant GT, Leigh RJ. A hypothetical scheme for the brainstem control of vertical gaze. *Neurology* 2000;54:1985–1993.
6. Averbuch-Heller L. Neurology of the eyelids. *Curr Opin Ophthalmol* 1997;8:27–34.
7. Virgo JD, Plant GT. Internuclear ophthalmoplegia. *Pract Neurol* 2017;17:149–153.
8. Surapaneni K, Ferguson L, Altschuler EL. Why can't this patient look up? Bilateral vertical gaze palsy. *PM R* 2015;7:1306–1308.

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