

How does a small area cause big syndromes? A case report of a patient with one-and-a-half syndrome and MRI review of the anatomical pathways involved in causing different pontine neuro-ophthalmological syndromes

Gonzalez-Arocha Carla, Rodriguez-Martinez Ana-Catalina, Mohamed-Noriega Jibrán*

Department of Ophthalmology, University Hospital and Faculty of Medicine, Autonomous University of Nuevo Leon (UANL), Mexico

ARTICLE INFO

Keywords:
Diplopia
Ocular motility
Stroke
Neuro-ophthalmology
One-and-a-half syndrome
Brainstem

ABSTRACT

Purpose: To describe the clinical symptoms, anatomical location of the injury and different etiologies of one-and-a-half syndrome and its variants.

Observations: A small lesion to the brainstem can cause complex syndromes that involve the disfunction of different nuclei and pathways. A 52-year-old man presented with sudden onset of diplopia characterized by horizontal gaze palsy and internuclear ophthalmoplegia (INO). With these clinical characteristics, the patient was diagnosed with the one-and-a-half syndrome. Neuroimaging revealed an acute/subacute ischemic lacunar event in the pontine tegmentum. The one-and-a-half syndrome is described as a horizontal gaze palsy in one direction (damage to the paramedian pontine reticular formation [PPRF] or the VI nerve nucleus) and an internuclear ophthalmoplegia in the other direction (damage to the medial longitudinal fasciculus). Along with the traditional description, the closed anatomical proximity with other nuclei and pathways makes possible the appearance of other more complex syndromes that have been grouped as the one-and-a-half syndrome and its variants.

Conclusions and importance: A detailed clinical neuro-ophthalmologic examination, along with a clear understanding of the neuroanatomical pathways, gives clinicians a good diagnostic opportunity to determine the precise location of injuries to the brainstem.

1. Case presentation

A 52-year-old man with diabetes mellitus type 2 and no other comorbidities presented with a three-day onset of horizontal binocular diplopia. The first examination showed in primary position of gaze an exotropia of the left eye (Fig. 1E). Ocular motility revealed limitation in adduction (Fig. 1F) and abduction (Fig. 1D) of the right eye, and limitation in adduction of the left eye (Fig. 1D). Abducting nystagmus was observed in the left eye. Pupillary reflexes were normal. The accommodative convergence was spared. Visual acuity was reduced due to diabetic retinopathy and macular edema. Neurology referral was made, and neurological examination showed left brachial and crural hemiparesis with grade 4 muscle strength. No upper motor neuron syndrome was integrated and no other positive signs were found. A gadolinium-enhanced magnetic resonance imaging (MRI) showed in the Diffusion-Weighted Imaging (DWI) sequence an acute/subacute ischemic lacunar event in the right pontine tegmentum (Fig. 1J). A one-and-a-half

syndrome with a probable ischemic etiology was diagnosed according to the representative clinical findings and brain magnetic resonance imaging. The patient was admitted and a double antiplatelet scheme (clopidogrel and acetylsalicylic acid) and atorvastatin were initiated until the patient was gradually stabilized.

2. Discussion

An important characteristic of the human visual system is its high density of photoreceptors and ganglion cells in the fovea that specializes in high-resolution spatial vision.¹ To maintain the fovea focussed on the desired objects, the central nervous system has a complex regulatory system that controls horizontal and vertical eye movements. The brainstem contains multiple nuclei and complex interconnected pathways to make the eye movements function as a unit. The paramedian pontine reticular formation (PPRF), VI nerve nucleus, and the medial longitudinal fasciculus (MLF) are essential to control the horizontal

* Corresponding author.

E-mail address: jibrán.mohamednrg@uanl.edu.mx (M.-N. Jibrán).

<https://doi.org/10.1016/j.ajoc.2021.101225>

Received 18 May 2021; Received in revised form 30 September 2021; Accepted 24 October 2021

Available online 30 October 2021

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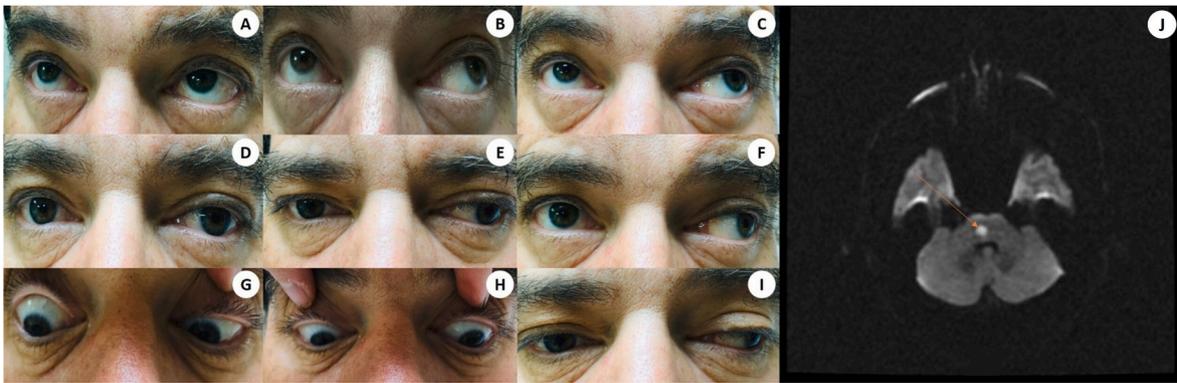


Fig. 1. Nine gaze positions and Diffusion-Weighted Imaging (DWI) sequence gadolinium-enhanced magnetic resonance imaging (MRI). Primary position with exotropia of the left eye (E), limited adduction (F), and abduction (D) of the right eye, and limited adduction of the left eye (D). The DWI sequence shows an acute/subacute ischemic lacunar event in the right pontine tegmentum (arrow) (J).

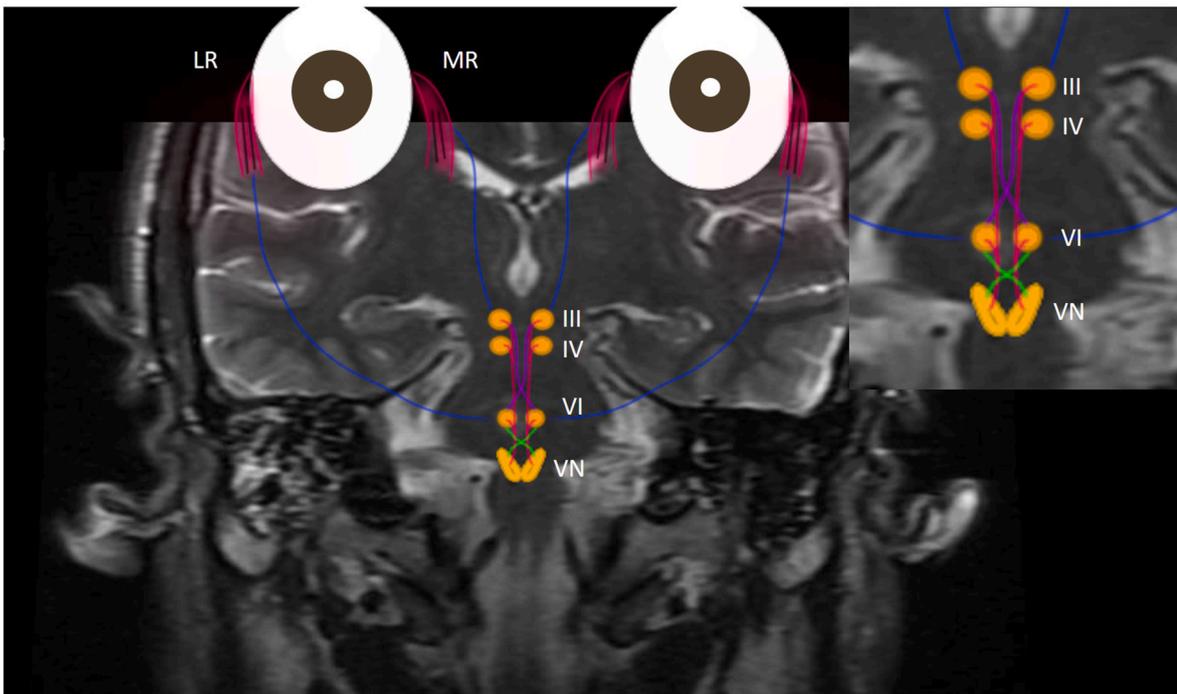


Fig. 2. Horizontal eye movements pathway. Schematic diagram of horizontal eye movements pathway in a gadolinium-enhanced brain magnetic resonance imaging (MRI) showed in T2 weighted, coronal reconstruction. MR, Medial Rectus; LR, lateral rectus, III; third cranial nerve nucleus, IV; fourth cranial nerve nucleus, VI; sixth cranial nerve nucleus, VN; vestibular nuclei.

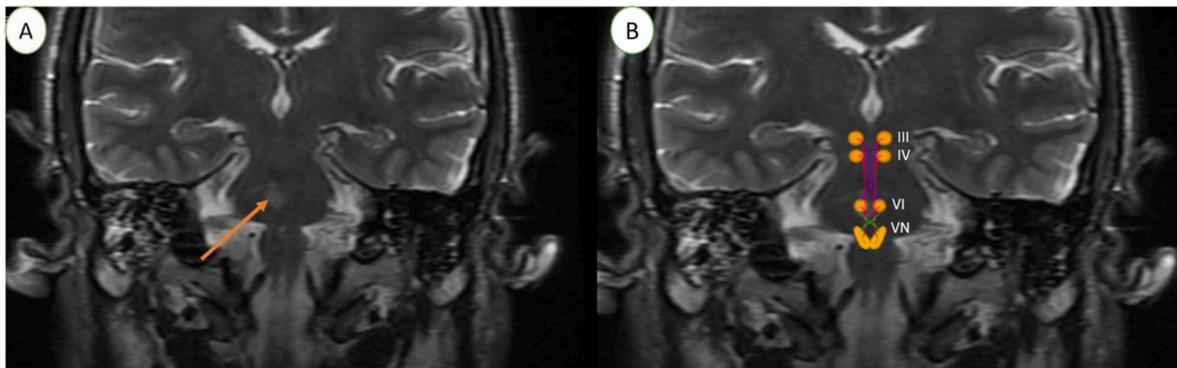


Fig. 3. Brainstem lacunar stroke. Specific location of the lacunar stroke in the right pontine tegmentum (A). Schematic diagram of the lesion in the pathway (B). III; third cranial nerve nucleus, IV; fourth cranial nerve nucleus, VI; sixth cranial nerve nucleus, VN; vestibular nuclei.

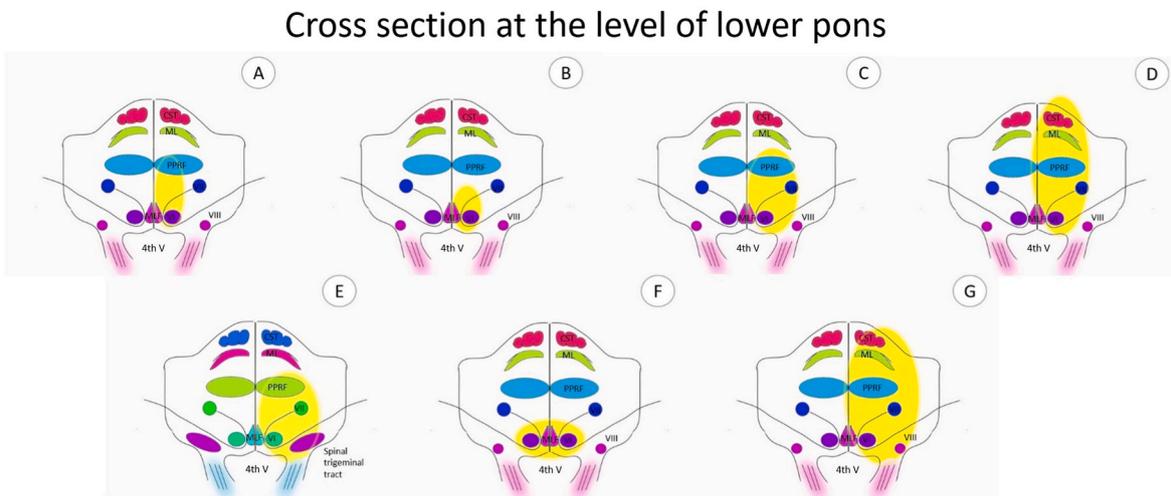


Fig. 4. One-and-a-half syndrome spectrum disorders. Schematic diagram of the lesion of one-and-a-half syndrome spectrum disorders. Cross-section at the level of lower pons. (A) and (B) One-and-a-half syndrome; (C) Eight-and-a-half syndrome; (D) Nine syndrome; (E) thirteen-and-a-half syndrome; (F) fifteen-and-a-half syndrome (G) sixteen-and-a-half syndrome. The yellow area represents the injury. ML, medial lemniscus; MLF, medial longitudinal fascicle; CST, corticospinal tract; PPRF, parapontine reticular formation. . (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Table 1

One-and-a-half syndrome spectrum disorders.

Spectrum disorder	Clinical symptoms	Damaged sites localization	Etiological factors
Eight-and-a-half syndrome ⁷⁻⁹ ($I \frac{1}{2} + VII = VIII \frac{1}{2}$)	Horizontal diplopia, unilateral facial paralysis	PPRF, Abducens nucleus, MLF, facial nerve or nucleus	Cerebrovascular disease (infarction) is the common cause Others: infection, tumor, demyelination, brain stem vasculitis
Nine syndrome ⁷ ($VIII \frac{1}{2} + \frac{1}{2}$) = 9	Horizontal diplopia, unilateral facial paralysis, contralateral hemiplegia, ataxia, hemihypesthesia	PPRF, Abducens nucleus, MLF, facial nerve or nucleus, medial lemniscus, corticospinal tract	Cerebrovascular disease (Infarction or hemorrhage) and demyelinating disease (multiple sclerosis)
Thirteen-and-a-half syndrome ⁷ ($VIII \frac{1}{2} + V = XIII \frac{1}{2}$)	Horizontal diplopia, ipsilateral facial paralysis, ipsilateral facial numbness, absent corneal sensation	PPRF, Abducens nucleus, MLF, facial nerve or nucleus, pterygopalatine trigeminal nucleus	Lymphoproliferative disease
Fifteen-and-a-half syndrome ¹⁰ ($I \frac{1}{2} + VII + VII = XV \frac{1}{2}$)	Horizontal diplopia, bilateral facial paralysis	PPRF, bilateral Abducens nucleus, MLF, bilateral facial nerve or nucleus,	Cerebrovascular disease
Sixteen-and-a-half syndrome ^{7,10} ($VIII \frac{1}{2} + VIII = XVI \frac{1}{2}$)	Horizontal diplopia, unilateral facial paralysis, ipsilateral hearing loss	PPRF, abducens nucleus, facial nerve or nucleus, corticospinal tract, cochlear nucleus	Cerebrovascular disease
Twenty-and-a-half syndrome ^{10,11} ($I \frac{1}{2} + VII + VII + V = 20 \frac{1}{2}$)	Horizontal diplopia, unilateral absence of corneal sensation and facial numbness, bilateral facial paralysis,	PPRF, bilateral Abducens nucleus, MLF, bilateral facial nerve or nucleus, trigeminal nucleus	Cerebrovascular disease
Twenty-four-and-a-half syndrome ^{10,12} ($I \frac{1}{2} + VII + VIII + VIII = 24 \frac{1}{2}$)	Horizontal diplopia, acute bilateral hearing loss, unilateral facial paralysis,	Abducens nucleus, MLF, PPRF, facial nerve, cochlear nucleus bilaterally.	Cavernoma
Vertical one-and-a-half syndrome ¹³	Vertical diplopia	Posterior commissure and decussating fibers to the oculomotor complex, rostral interstitial nucleus of MLF	Cerebrovascular disease, metastasis

PPRF; paramedian pontine reticular formation, MLF; medial longitudinal fasciculus.

movements.² The horizontal saccades originate in the frontal eye field in the frontal cortex and the PPRF acts as the brainstem generator. Horizontal conjugated eye movements are orchestrated at the abducens nucleus, located within the pons at the pontomedullary junction of the brainstem, that acts as a horizontal gaze center that collects information from the PPRF. From the VI nucleus two type of fibres arise: motor and internuclear, the motor fibres continue to the ipsilateral abducens nerve and end up in the lateral rectus muscle and the internuclear fibres connect to the contralateral medial rectus subnucleus via MLF.² Fig. 2 shows the intricate complexity of this neural pathway which can be affected by small lesions and cause different eye movement disorders. The main classes of horizontal eye movement disorders caused by brainstem lesions are: 1) lateral gaze palsy, 2) internuclear ophthalmoplegia, and 3) one-and-a-half syndrome.

The one-and-a-half syndrome, a term coined in 1966 by C. Miller Fisher,³ is a clinical disorder characterized by a horizontal gaze palsy in

one direction (damage to the VI nerve nucleus) with an internuclear ophthalmoplegia (INO) in the other direction (damage to the medial longitudinal fasciculus).² The only horizontal eye movement preserved is the abduction of the contralateral eye. Vertical eye movements are relatively preserved.¹ The case presented in this report represents the typical lesion of the tegmentum of the pons affecting the ipsilateral PPRF, the VI nerve nucleus, and the internuclear fibers of the ipsilateral MLF.²⁻⁴ Fig. 3 demonstrates the specific location of the ischemic lesion, and Fig. 4B shows the affected pathways schematically.

The most common cause of the one-and-a-half syndrome is a brainstem lacunar stroke, followed by demyelinating (multiple sclerosis), vascular anomalies, and infections such as neurocysticercosis, toxoplasmosis, and other viral encephalitis. Other uncommon causes are head trauma and brainstem tumors.^{2,4-6}

Along with the traditional description of the one-and-a-half syndrome, there are other less common syndromes in which the lesion is in

close anatomical proximity to other nuclei or pathways that produce other signs and symptoms. These group of related syndromes have been grouped as the one-and-a-half syndrome spectrum⁷ (Table 1 and Fig. 4 summarise the spectrum disorders). These spectrum syndromes have been categorized arithmetically by summation of the cranial nerves involved.⁸ Their diagnosis relies on the distinctive accompanied clinical symptoms, neuroanatomy, and imaging characteristics.⁷

The eight-and-a-half syndrome (Fig. 4C) was described by Eggenberger in 1998⁴, and it is the most common variant of this spectrum disorder.⁷⁻⁹ This includes a one-and-a-half-syndrome and ipsilateral peripheral facial paralysis (I ½ and VII = VIII ½). In this entity, the lesion is located in the ipsilateral pontine tegmentum, which includes the ipsilateral PPRF, MLF, VII nerve nucleus or nerve bundle.⁷⁻⁹ The nine syndrome (Fig. 4D) is characterized by an eight-and-a-half syndrome and contralateral hemiparesis and hemihypesthesia (VIII ½ and ½) = IX. This is due to the expansion of the pontine tegmentum lesion to the surrounding tissue.⁷ The thirteen-and-a-half syndrome (Fig. 4E) is an eight-and-a-half syndrome and ipsilateral fifth cranial nerve (VIII ½ and V = XIII ½), it is caused by a lesion affecting the pontine tegmentum and expanding to the ipsilateral trigeminal nuclei.⁷ The fifteen-and-a-half syndrome (Fig. 4F) is a one-and-a-half syndrome and bilateral damage to the seventh cranial nerve¹⁰ (I ½, VII and VII = XV ½).⁷ The sixteen-and-a-half syndrome (Fig. 4G) is an eight-and-a-half and ipsilateral damage to the cochlear nuclei (VIII ½ and VIII = XVI ½).^{7,10} The twenty-and-a-half syndrome is a one-and-a-half syndrome and bilateral

seventh and ipsilateral fifth nerve palsy (I ½, VII, VII and V = XX ½).^{10,11} The twenty-four-and-a-half syndrome is a one-and-a-half-syndrome and ipsilateral facial nerve and bilateral eighth cranial nerve palsies. (VII, I½, VIII and VIII = XXIV ½).¹¹⁻¹³ Finally, it is worth mentioning the vertical one-and-a-half syndrome, characterized by bilateral upgaze palsy and unilateral infraduction palsy. It has been reported in patients with unilateral ischemic stroke in the meso-diencephalic junction.¹³

In conclusion, a detailed clinical neuro-ophthalmic examination, along with a clear understanding of the neuroanatomical pathways, give clinicians a good diagnostic opportunity to localize precisely lesions in the brainstem.

Patient consent

Consent to publish this case report has been obtained from the patient in writing.

Declaration of competing interest

No conflict of interest exists.

Acknowledgments

None.

Appendix

Name	Location	Role	Contribution
Gonzalez-Arocha Carla	Universidad Autónoma de Nuevo León. Departamento de Oftalmología Facultad de Medicina y Hospital Universitario "Dr. José Eleuterio González"	Author	Data collection, illustration, and writing of the manuscript
Rodriguez-Martinez Ana-Catalina	Universidad Autónoma de Nuevo León. Departamento de Oftalmología Facultad de Medicina y Hospital Universitario "Dr. José Eleuterio González"	Author	Writing of the manuscript
Mohamed-Noriega Jibrán	Universidad Autónoma de Nuevo León. Departamento de Oftalmología Facultad de Medicina y Hospital Universitario "Dr. José Eleuterio González"	Author	Writing, supervising and orientation of the manuscript

Funding

Internal funding by the Department of Ophthalmology, University Hospital and Faculty of Medicine, Autonomous University of Nuevo Leon (UANL), Mexico.

Research ethics

Written consent to publish potentially identifying information, such as details or the case and photographs, was obtained from the patient(s) or their legal guardian(s).

Authorship

Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND, Drafting the work or revising it critically for important intellectual content; AND, Final approval of the version to be published; AND, Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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