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

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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 dysfunction 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...
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.
movements. The horizontal saccades originate 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. Figure 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, 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). The only horizontal eye movement preserved is the abduction of the contralateral eye. Vertical eye movements are relatively preserved. The case presented in this report represents the typical lesion of the tegmentum of the pons affecting the ipsilateral MLF, the VI nerve nucleus, and the internuclear fibers of the ipsilateral MLF. Figure 3 demonstrates the specific location of the ischemic lesion, and Figure 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.

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 categorized arithmetically by summation of the cranial nerves involved. Their diagnosis relies on the distinctive accompanied clinical symptoms, neuroanatomy, and imaging characteristics.

The eight-and-a-half syndrome (Fig. 4C) was described by Eggensberger in 1998 and it is the most common variant of this spectrum disorder. This includes a one-and-a-half syndrome and ipsilateral peripheral facial paralysis (1½ 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. The nine syndrome (Fig. 4D) is characterized by an eight-and-a-half syndrome and contralateral hemiparesis and hemihyposthesia (VIII ½ and ⅞) = IX. This is due to the expansion of the pontine tegmentum lesion to the surrounding tissue. The thirteen-and-a-half syndrome (Fig. 4E) is an eight-and-a-half syndrome and ipsilateral fifth cranial nerve (VIII ½ and V = XV ½), it is caused by a lesion affecting the pontine tegmentum and expanding to the ipsilateral trigeminal nuclei. The fifteen-and-a-half syndrome (Fig. 4F) is a one-and-a-half syndrome and bilateral damage to the seventh cranial nerve (V ⅞ and VII and VII = XV ⅞). The sixteen-and-a-half syndrome (Fig. 4G) is an eight-and-a-half and ipsilateral damage to the cochlear nuclei (VIII ⅛ and VIII = XVI ⅛). The twenty-and-a-half syndrome is a one-and-a-half syndrome and bilateral seventh and ipsilateral fifth nerve palsy (I ⅛, VII, VII and V = XX ⅛).

The twenty-four-and-a-half syndrome is a one-and-a-half syndrome and ipsilateral facial nerve and bilateral eight cranial nerve palsies (VII, I ⅞, VIII and VIII = XXIV ⅞). 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.

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.

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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     | Universidad Autónoma de Nuevo León. Departamento de Oftalmología Facultad de Medicina y Hospital Universitario “Dr. José Eleuterio González” | Author        | Writing of the manuscript                        |
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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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