Case Report

Wall-Eyed Monocular Internuclear Ophthalmoplegia (WEMINO) and Millard-Gubler Syndromes in a Patient with Isolated Pontine Infarction: Topographic, Oculomotor, and Radiological Analysis of Two Very Uncommon Conditions

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Keywords

WEMINO · Internuclear ophthalmoplegia · Millard-Gubler syndrome · Pontine infarction · Exotropia

Abstract

The syndromes of wall-eyed monocular internuclear ophthalmoplegia and Millard-Gubler are very rare clinical complexes commonly caused by pontine infarction, hemorrhage, or tumors that compromise the paramedian tegmentum, medial longitudinal fascicle, and the basis pontis. We present the case of a 58-year-old female with an isolated pontine infarction characterized by acute vertigo, sudden horizontal diplopia due to ipsilateral internuclear ophthalmoplegia with exotropia, facial palsy and contralateral hemiparesis. This report analyzes, theorizes, and emphasizes the correlation between these atypical neurological findings, the pontine anatomy, and magnetic resonance imaging; encouraging the clinician to make expeditious

diagnoses using the bedside skills and a high-quality oculomotor clinical examination. The phenotype and simultaneity of both syndromes makes this case a didactic exercise for the topo-diagnosis based on the neurology of eye movements, the intrinsic physiology of the pons, and the pathways that emerge or project towards it.

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Introduction

It is estimated that isolated pontine infarcts (IPI) account for 10–15% of the posterior circulation ischemic events and are more frequent than in the other brainstem structures. The anteromedial and anterolateral territories are prominently affected, and the arterial obstruction of the penetrating branches is the most frequent etiology [1, 2].

The Millard-Gubler syndrome (MGS), described in France in 1858, is a classic crossed pontine syndrome that results from damage to the ventromedial region of the pons, the corticospinal tract, the intrapontine fascicular part of the seventh cranial nerve and, occasionally, the abducens nerve fibers. Patient reports are scarce, almost always because of hemorrhagic or tumoral lesions, and rarely caused by ischemia as in our case [3–8]. The wall-eyed monocular internuclear ophthalmoplegia (WEMINO) syndrome is a rare pre-nuclear variant of internuclear ophthalmoplegia (INO) with ipsilateral exotropia and associated with an infarct of the paramedian pontine tegmentum, including the medial longitudinal fasciculus (MLF) [7, 8].

This is a unique case of IPI that simultaneously developed WEMINO and MG syndromes along with central acute vertigo. We approach and analyze the lesion from clinical, topographic, and radiological perspectives.

Case Presentation

A diabetic and hypertensive 58-year-old female presented to the outpatient clinic with a sudden and spontaneous 3-month history characterized by acute onset of vertigo, horizontal diplopia, facial weakness, hemiparesis and gait instability. Other than a general practitioner consultation, she did not get any specialized medical care on her symptoms. At the time of the first visit, all the symptoms persisted except for the vertigo followed by continuous dizziness and unsteadiness when walking. The clinical examination showed a left moderate facial paresis [9], right-sided hemiparesis and brachiorucral spasticity, hyperreflexia, Babinski sign and superficial and nociceptive hypoesthesia. Neuro-ophthalmological evaluation displayed skew deviation with left hypertropia – consistent with the alternating covert test – and left incomplete exotropia in primary position (Fig. 1). In the left eye, adduction was limited with slow, hypometric, and paretic saccades; abducting saccades were also hypometric. In the right eye, abducting saccades were hypermetric with no limitation within the range of motility. Horizontal smooth pursuit was normal. Rightwards, a dissociated nystagmus was present only in the right eye. Vertical eye movements were misaligned due to the left hypertropia with saccadic smooth pursuit in both directions (online suppl. video segments 1–2; for all online suppl. material, see www.karger.com/doi/10.1159/000501794). The horizontal clinical head impulse test showed no corrective saccades (normal) (online suppl. video segment 3). All these features integrate a left INO with homolateral exotropia (WEMINO) and a left facio-brachiorucral pontine syndrome (Millard-Gubler). In its different sequences and planes, the brain magnetic resonance imaging (MRI) showed an ischemic wedge-shaped lesion compatible with a chronic left parasagittal (paramedian) pontine infarct that extended from the facial

colliculus to the ventral pons and the medial lemniscus, involving the area of the corticospinal and corticobulbar tracts, the fasciculus of the facial nerve and, probably the superior vestibular nucleus and the central otolithic projections (Fig. 2). Brain MRI angiography was negative for stenosis or occlusion of the main arteries.

Discussion

Pontine disorders comprise a broad spectrum of clinical conditions ranging from monosymptomatic presentations to complex phenotypes. IPI represent around 15% of the acute ischemia of the vertebrobasilar territory [1]. Cohort studies do not evidence a preference between males and women [2] but emphasize that the three most relevant risk factors are hypertension, diabetes mellitus, and hypercholesterolemia [1, 2]. Although laterality is not representative in the case series, more than half of the cases in the report by Bassetti et al. [1] correspond to the left pons. Our patient was a female, hypertensive, and diabetic with a left pontine infarct. The pons is functionally and anatomically divided into a ventral portion (basis pontis) and a dorsal component (tegmentum). The first one contains the corticospinal (pyramidal) and corticobulbar (facial) tracts, connecting the cerebral cortex with the contralateral cerebellum through the middle cerebellar peduncle. The tegmentum forms the floor of the fourth ventricle and the rhomboid fossa containing ascending (e.g., medial lemniscus and spinocerebellar tract) and descending projections, and the nuclei of certain cranial nerves (V to VIII) and the critically important MLF.

For topographic analysis, we considered the pontine arterial territories and their correlation with well-defined clinical syndromes: anteromedial, anterolateral, tegmental, bilateral, and multiple pontine infarcts; together with 4 rostrocaudal levels: superior, superior medial, inferior medial, and inferior [1, 10].

In this patient, the infarct was localized in the medial inferior level, compromising the left ventromedial, ventrolateral, and tegmental, giving rise to a complex of clinical conditions usually not observed in the same patient, even 3 months after its onset (Fig. 3).

The Syndromes Developed by the Patient according to the Intrinsic Irrigation System of the Pons

Anteromedial and Anterolateral Pontine Syndromes

- Contralateral brachiorural hemiparesis (corticospinal tract)
- Contralateral hemihypesthesia (medial lemniscus)
- Ipsilateral INO (MLF)
- Skew deviation with ipsilateral hypertropia (ascending otolithic pathways in the MLF from the vestibular nuclei to the interstitial nucleus of Cajal)
- Vertical saccadic smooth pursuit (cerebellopontine projections)

Tegmental Pontine Syndrome

- Vertical saccadic smooth pursuit (cerebellopontine projections)
- Ipsilateral supranuclear facial paresis (nucleus of the facial nerve and corticobulbar tract)
- Acute vertigo (vestibular nuclei and/or cerebellopontine projections)

- Horizontal diplopia in the primary position of the gaze due to ipsilateral exotropia (possible muscle tone asymmetry between the medial and lateral recti)

The Patient Integrated Two Entities from a Classical Syndromic Description

Millard-Gubler Syndrome

- Ipsilateral supranuclear facial paresis and contralateral hemiparesis

WEMINO Syndrome

- INO with ipsilateral exotropia

With close to 20%, IPI are not that rare as they are, as we usually think them to be [1]. In this patient, the extension of the infarct from the base to the tegmentum of the pons contributed to the development of this syndromic scenario, sparing other structures of the posterior fossa. Despite the chronic stage, the clinical findings could accurately represent the localization of the deficit. The segmental distribution of the intrinsic pontine arteries showed, as described by Duvernoy [10], a predictable picture.

The MGS results from a medial and caudal pontine lesion. Augustine Millard (1855) and Adolphe Gubler (1856) proposed for the first time that facial paralysis accompanied by contralateral hemiplegia was a sign of pontine hemorrhage. They also postulated that facial weakness results from a lesion of the lower motor neuron at the level of the nucleus. Because the anatomical vicinity between the facial nerve and the VI cranial nerve nucleus, MGS is occasionally associated with abducens nerve palsy, one-and-a-half syndrome, and other neuro-ophthalmological conditions [7].

MLF lesions cause INO, affecting horizontal and vertical eye movements [11]. Our patient showed unilateral INO with contralateral dissociated nystagmus and skew deviation with homolateral hypertropia. When the lesion is unilateral, it manifests weakness as the inability or limitation to adduct the ipsilateral eye from the midline [12]. The patient complied with these features along with incomplete exotropia in the primary position on the affected side. The reason for this homolateral exotropia in a WEMINO syndrome is not clear yet. In one report, Johnston and Sharpe [13] found pontine tegmental histopathological damage that spared the oculomotor nucleus; so, we cannot completely explain this exotropia by a paresis of the third cranial nerve. One hypothesis suggests that abnormal vestibular signals that reach the medial rectus nucleus induce an asymmetry of muscle tone and the consequent ocular abduction towards the injured side [14]. Here, early vertigo might support the latter argument for an imbalance in the central vestibular tone.

A report of case series with INO in brainstem infarctions showed that 70% of the patients had exotropia, although contralateral [12]. There are two syndromes that combine an MLF lesion and contralateral exotropia; these are the pontine paralytic exotropia [12, 15] and the nonparalytic pontine exotropia [16], with the basic difference that in WEMINO syndrome the exotropia is ipsilateral to the damaged MLF [17]. There are few reports of patients with this clinical condition. Ikeda and Okamoto [17] presented a case with transient exotropia and two other cases with similar characteristics in combination with a contraversive ocular tilt reaction caused by infarction and neurocysticercosis [14, 18]. Similarly, we found a WEMINO syndrome report with skew deviation and facial paralysis also describing symptoms that were transient but with no contralateral hemiparesis [19].

Regarding the vestibulo-ocular reflex (VOR), although the leftward head impulse test could have shown an impaired left eye adduction, we considered it clinically normal (online suppl. video segment 3). Halmagyi et al. [20] proposed the contribution of the ascending tract of Dieters, which is an extra MLF pathway for the horizontal VOR might explain this. The left eye horizontal VOR gain might also be affected, but we could only measure the right eye gain (normal) because of hardware limitations.

Conclusions

From a perspective of oculomotor interest, lesions of the paramedian pontine reticular formation, MLF, and abducens nucleus, either as a whole or separately, produce syndromes that distort the conjugate horizontal eye movements with oculomotor patterns that have been extensively described and analyzed [11]. These findings allowed us to set up an adequate clinical, topographic, and radiological correlation.

The complex intrinsic structure of the brainstem implies a challenge for all clinicians, even for the experts and well-trained specialists in this field. From the descriptions of Millard and Gubler (1855–56), Foville (1858), Dejerin (1914), and many others, the clinical examination has proven to be the “*Rosetta Stone*” of the neurological topo-diagnosis. The delicate harmony between the bedside and radiological findings is essential for an accurate diagnosis, and its value should consistently be emphasized and taught.

WEMINO and MGS syndromes are rare isolated clinical entities. To the best of our knowledge, this is the first report that describes a patient with both conditions simultaneously. This concomitance is possible, and the clinician must be aware.

The lack of an expedited and specialized approach led this patient to permanent functional sequels that could be readily prevented by diagnosing her with a conscious bedside examination. In neurotology and neuro-ophthalmology, the diagnostic power of the clinical skills (e.g., oculomotor examination) is immense and irreplaceable by any technology or equipment.

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Statement of Ethics

The patient’s family provided oral informed consent for publishing this report.

Disclosure Statement

The authors have no conflicts of interest to declare.

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Author Contributions

R.C.-L. contributed to the diagnosis, physical examination and testing of the patient, reviewing and correcting the draft. C.P.-D. wrote the first draft, the additional theoretical frame and syndromic description. J.A.R.-F. analyzed, selected, and described the MRI scans. All authors read and approved the final manuscript.

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Fig. 1. **a** In the primary position, left hypertropia (skew deviation) and partial exotropia are observed. A mild left lagophthalmos is also evident. **b** Rightwards, the left eye is limited for a complete adduction. **c** Leftwards, no deficit is noticed. **d, e** Vertical misalignment is increased looking upward and downward without limitation or paresis, though.

Fig. 2. **a** T2-weighted axial MRI slice T2 showing a parasagittal hyperintense image through the pons, encompassing the topography of the facial colliculus, medial lemniscus, and the corticospinal and corticobulbar tracts. **b** T2-weighted sagittal section showing the floor of the fourth ventricle and a hyperintensity that extends from the facial colliculus (tectum) to the ventral pons. **c** T2-weighted coronal cut across the central portion of the pons. It shows areas of infarction (hyperintense image) of the left medial pontine component corresponding with the anteromedial pontine artery territory.

Fig. 3. Cross-section diagram of the middle-lower pons. The area shaded in red represents the extension of the patient's infarct. On the opposite side, the labels highlight the involved anatomical structures. Adapted with permission from Marshall Strother (user:mcstrother) and Patrick J. Lynch, medical illustrator (CC BY 3.0 <https://creativecommons.org/licenses/by/3.0/>; https://commons.wikimedia.org/wiki/File:Lower_pons_horizontal_KB.svg).