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Vertical Ophthalmoplegia Due to a Unilateral Periaqueductal Gray Matter Infarct in an Adolescent

Iván Sánchez Fernández, MD1,2, Cristina Fernández Carbonell, MD2, Marta Vázquez Ortiz, MD1,3, and Verónica González Álvarez, MD2

Abstract
Brainstem strokes affecting the periaqueductal gray matter of the midbrain can cause vertical ophthalmoplegia. Accompanying clinical features are frequently associated and reflect the involvement of other brainstem structures. We report on an adolescent presenting with vertical gaze palsy and left mydriatic pupil as the only clinical expression of a small infarct located in the left periaqueductal gray matter. Even when the lesion was strictly unilateral, vertical ophthalmoplegia affected both eyes.

Keywords
stroke, vertical ophthalmoplegia, magnetic resonance imaging

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Vertical ophthalmoplegia is frequently observed following brainstem infarcts that involve the periaqueductal gray matter of the midbrain.1-13 Even when the stroke is unilateral, vertical gaze palsy can be present on both eyes.1,3,4,6-8,10–13 Vertical ophthalmoplegia is often a part of a broader clinical picture in which associated signs and symptoms reflect the involvement of other structures in the lesion.1,2,4-7 We report on an adolescent without any vascular risk factors who suffered a small unilateral ischemic infarct with clinical expression limited to the eyes.

Case Report
A 13-year-old boy experienced, while playing soccer, sudden onset of diplopia, without headache, vomiting, or any other symptom. Personal and familial medical history were unremarkable, and a history of a significant recent trauma was absent. On physical examination a severe binocular diplopia, a severe impairment of downward gaze, a total limitation of upward gaze, and an anisocoria due to a left mydriatic pupil sluggishly reactive to light were found. Visual field examination and horizontal gaze movements were normal. The rest of the physical examination was unremarkable.

A cranial computed tomographic scan at admission (6 hours after the onset of diplopia) was normal. Despite this normal brain image, and because of the acute onset of bilateral vertical gaze palsy, a stroke affecting the structures that coordinate vertical gaze remained as the main diagnostic possibility. Therefore, a thin-slice magnetic resonance imaging (MRI) scan of the brainstem was performed 2 days after admission. It showed a left periaqueductal midbrain image consistent with an ischemic infarct (Figure 1A and 1B).

Aspirin 100 mg/day was started as secondary prophylaxis. During the following days, binocular vision, the range of vertical eye movements, left pupillary size, and reaction to light improved progressively until complete normalization 15 days after the onset of diplopia.

Regarding the etiological work-up, a cardiovascular study, including a cardiac ultrasonography scan, as well as a carotid Doppler sonography did not find any source of embolism. Cocaine and amphetamines were not detected in the urine sample collected at admission. Cervical and cranial magnetic resonance angiographic imaging performed 15 days after the onset of diplopia showed normal vessels, as well as a reduction in the size of the lesion (Figure 2). Blood cell counts and coagulation profiles (prothrombin time, partial thromboplastin time, and fibrinogen levels) were normal. Protein C and S levels, antithrombin III level, and homocysteine level were normal. Activated protein C resistance was not present. Antinuclear antibody, anticardiolipin antibody, factor V Leiden mutation,
and prothrombin gene mutation were negative. Triacylglycerol and cholesterol levels were in the normal range. Liver and thyroid function tests were normal. Vaccinations were up to date. The patient was not vaccinated against varicella, but had had an episode of chickenpox documented by his primary pediatrician at 5 years of age. There was no clinical evidence of current or recent infection, and laboratory markers of inflammation (erythrocyte sedimentation rate, and C-reactive protein) were in the normal range.

As no risk factor for recurrence was found, secondary prophylaxis was discontinued and the patient was allowed an unrestricted sport activity. After 10 months of follow-up, the patient remains asymptomatic. The etiology of the stroke remains unknown.

**Comments**

Vertical eye movement is mainly coordinated by the rostral interstitial nucleus of the median longitudinal fasciculus, and the interstitial nucleus of Cajal, located in the periaqueductal gray matter of the midbrain, close to the midline. Their specific functions and interrelationships are complex, and far beyond the scope of this report.\(^1\)\(^,\)\(^1\)\(^4\)\(^,\)\(^1\)\(^5\) Lesions to the periaqueductal gray matter limit vertical conjugate movements.\(^1\)\(^4\) As each interstitial nucleus of Cajal projects to ipsilateral ocular motorneurons and to the contralateral interstitial nucleus of Cajal by means of the posterior commissure, a unilateral lesion to the interstitial nucleus of Cajal can affect inputs to ocular motorneurons that control vertical gaze on both sides.\(^1\)\(^4\) In fact, the stroke of our patient was anatomically unilateral and restricted to the periaqueductal gray matter; nevertheless, it led to a functionally bilateral deficit. Thus, this case adds to the experimental\(^1\)\(^6\) and clinical\(^3\)\(^,\)\(^4\)\(^,\)\(^6\)\(^,\)\(^7\)\(^,\)\(^1\)\(^1\) reports in which anatomically unilateral lesions to the periaqueductal gray matter lead to functionally bilateral vertical ophthalmoplegias.

Hence, a patient presenting with bilateral vertical gaze palsy deserves a thorough study of the periaqueductal gray matter of the midbrain. Lesions limited to anatomically small, but clinically relevant, brainstem structures can be easily missed if not studied with appropriate imaging techniques. A computed

*Figure 1. Magnetic resonance imaging (MRI). A small hyperintense signal (arrow) is seen in the left periaqueductal midbrain gray matter. A, Coronal fluid-attenuated inversion recovery sequence. B, Axial T2 sequence.*

*Figure 2. Magnetic resonance imaging (MRI). Coronal fluid-attenuated inversion recovery sequence. A smaller hyperintense signal (arrow) reflects the residual lesion.*
tomography scan lacks enough resolution to detect some infarcts in the brainstem, as was the case in our patient, and in the initial computed tomographic scan in “case 1” in the series of Wall et al. Thin-slice MRI is particularly useful in such situations. Diffusion-weighted MRI has been recently advocated because infarcts in the brainstem can be missed, even when standard MRI techniques are used, as demonstrated in “case D” in the series of Seifert et al. The most common presenting symptom in vertical gaze palsy following brainstem stroke is acute or subacute onset of diplopia. Headaches or vomiting commonly accompany the onset of the infarct. The associated clinical features depend on the other structures involved in the lesion: for example, hemiparesis or ataxia reflect corticospinal tract lesion, and cerebellar involvement, respectively. Ipsilateral mydriasis is a commonly reported sign, it is attributed to a lesion to the Edinger-Westphal nucleus, located in close proximity to the interstitial nucleus of Cajal. In our patient, probably due to the location and small size of the stroke, clinical expression was restricted to bilateral vertical gaze palsy and ipsilateral mydriasis; that is, our patient adds to the uncommon cases with clinical expression restricted to the eyes.

In summary, the interest of our case lies on the following aspects: (1) our results emphasize the clinical-anatomic correlation between vertical gaze palsy and lesion to the periaqueductal gray matter of the midbrain; (2) our findings support the idea that strictly unilateral lesions affecting the periaqueductal gray matter lead to a bilateral vertical gaze palsy; (3) this study underlines the need of a very sensitive imaging technique in the diagnosis of small infarcts in the brainstem; (4) and our case adds to the infrequent brainstem infarcts with clinical expression limited to the eyes.

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Author Contributions
ISF, CFC, MVO, and VGA contributed to acquisition of clinical data. ISF, CFC, MVO participated in drafting of the manuscript (first draft). ISF and VGA supervised the study. ISF performed the revision of material for important intellectual content.

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