Wall-eyed bilateral internuclear ophthalmoplegia (WEBINO) in a pediatric patient with Systemic Lupus Erythematosus.

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Background: *Wall-eyed bilateral internuclear ophthalmoplegia (WEBINO) is presented by a lesion of the pontine tegment (includes paramedian pontine area, medial longitudinal fascicle and nuclei of the abducens). It presents bilateral limitation in adduction and exotropia in the position of the primary gaze, abducting eye nystagmus and inability to converge.* ***Case report:*** *We present the case of a 14-year-old patient with a history of Systemic Lupus Erythematosus who debuted with sudden onset horizontal diplopia. WEBINO's diagnosis was clinical and associated with findings of ponto-mesencephalic ischemic injury in magnetic resonance imaging and magnetic resonance angiography. Treatment with Methylprednisolone was administered and she presented gradual resolution of the symptoms, however, one week later she died of systemic cryptococcosis.* ***Conclusions:*** *Making the WEBINO diagnosis is challenging due to its rarity and the precision of its neuroanatomical location. A detailed examination should be performed to define the probable cause and establish the appropriate treatment that favors the neurological prognosis.*

Keywords: *WEBINO, internuclear ophthalmoplegia, dyplopia, vasculitis, Systemic Lupus Erythematosus, exotropia.*

Introduction

Internuclear ophthalmoplegia (INO) appears in various commitments of the brain stem involving the premotor centers of horizontal gaze (lower part of the bridge and upper part of the medulla) and vertical (rostral part of the midbrain). Ophthalmic symptoms allow pathology to be differentiated into unilateral or bilateral.

Wall-eyed bilateral internuclear ophthalmoplegia (WEBINO) is due to a lesion of the pontine tegment: paramedian pontine area, medial longitudinal fasciculus (MLF) on both sides and nuclei of the abducens. It has bilateral limitation in ocular adduction, exotropia in primary gaze, abducting eye nystagmus and inability to converge[1] .

There are disorders associated with this syndrome that vary according to age. In older adults, ischemia can be found in the distribution of the pontine paramedian penetrating arteries arising from the basilar artery, as well as pontine hemorrhagic lesions secondary to hypertension. In younger adults, other conside-

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rations are multiple sclerosis (MS), vasculitis, cavernous angiomas, trauma and opportunistic infections. Pontine gliomas and medulloblastomas are common causes in children.

Alterations of the corpus callosum, hippocampal atrophy and white matter damage due to different immunological mechanisms such as vasculopathy, presence of autoantibodies, choroid plexus dysfunction, proinflammatory processes, neuroendocrine immune effects, direct damage to the central nervous system (CNS) and also by non-immunological mechanisms have been described in patients with Systemic Lupus Erythematosus (SLE)[2].

Vasculitis in SLE[3] is a process where multiple mononuclear cells accumulate around the blood vessels, proliferative changes of the intima are generated and vascular hyalinization occurs, causing alterations in the blood-brain barrier which allows the passage of autoantibodies to the CNS or generates small ischemias due to luminal occlusion[4] .

The clinical diagnosis of WEBINO must be accompanied by imaging studies such as magnetic resonance imaging (MRI), magnetic resonance angiography (MRA) and intra-arterial digital subtraction angiography (IADSA), depending on the cause.

Carrying out a correct diagnosis to promptly initiate specific treatment according to the etiology favorably modifies the neurological prognosis.

Pediatric reports of this syndrome are sparse, so this case represents special interest since it also corresponds to the group of related atypical etiologies.

Case report

A 14-year-old female patient with a 4-year history of SLE with skin, immune and joint compromise, membranous nephropathy and secondary arterial hypertension. She had suffered multiple relapses due to poor adherence to treatment with Prednisone, Azathioprine and Mycophenolate, which she voluntarily abandoned for 8 months, prior to admission.

He consulted for exacerbated 2-day course of chest pain. She was hospitalized in an Intensive Care Unit due to a hypertensive emergency with a compromised renal and cardiac, requiring infusion of Labetalol and immunosuppressive therapy.

During his hospitalization, he presented severe multi-system compromise for SLE with chronic renal failure that required the start of peritoneal dialysis, hypertensive cardiomyopathy, anemia with multiple transfusion requirements, hypogammaglobulinemia, thrombotic microangiopathy treated with hemodialysis and plasmapheresis, in addition to multiple secondary infectious complications.

After 5 months of hospitalization, the patient suddenly debuted with bilateral horizontal diplopia, oscillopsia and alteration of the primary gaze. Physical examination revealed preserved superior functions, light-reactive 2-mm pupils, adduction paresis along with abduction nystagmus in both eyes and alternating exotropia in primary gaze (Figure 1).

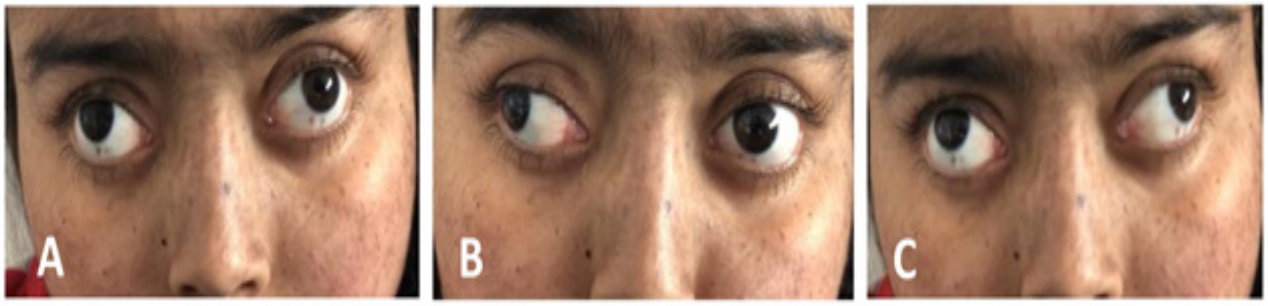
Simple cerebral MRI was performed, which showed cortical atrophy, hyperintensity in the periventricular white matter and focus of restriction on diffusion in the medial dorsal mesencephalic region with involvement of the MLF corresponding to paramedian midbrain infarction (Figure 2). In addition, other lesions with alteration of the diffusion in the corpus callosum and the left paracentral lobule were evident (Figure 3). Demyelinating disease in the brain stem was ruled out because the lesions described restricted diffusion.

Cerebral MRA in the arterial and venous phase reported an irregular course of terminations in the anterior and middle territory, possibly in relation to vasculitis, without clear differentiation for this type of study.

An intermittent eye patch was placed and he received 5 days of treatment with pulses of Methylprednisolone 30 mg/kg/day on suspicion of lacunar ischemic events secondary to vasculitis, presenting clinical improvement and resolving the alteration of eye movements. Subsequently, prophylactic anticoagulation with low molecular weight heparin was started to decrease the risk of new infarctions.

At 2 weeks after the onset of the symptoms, the patient presented clinical deterioration due to fever associated with nausea, confusion and drowsiness that progressed towards compromise of the respiratory pattern, requiring orotra-

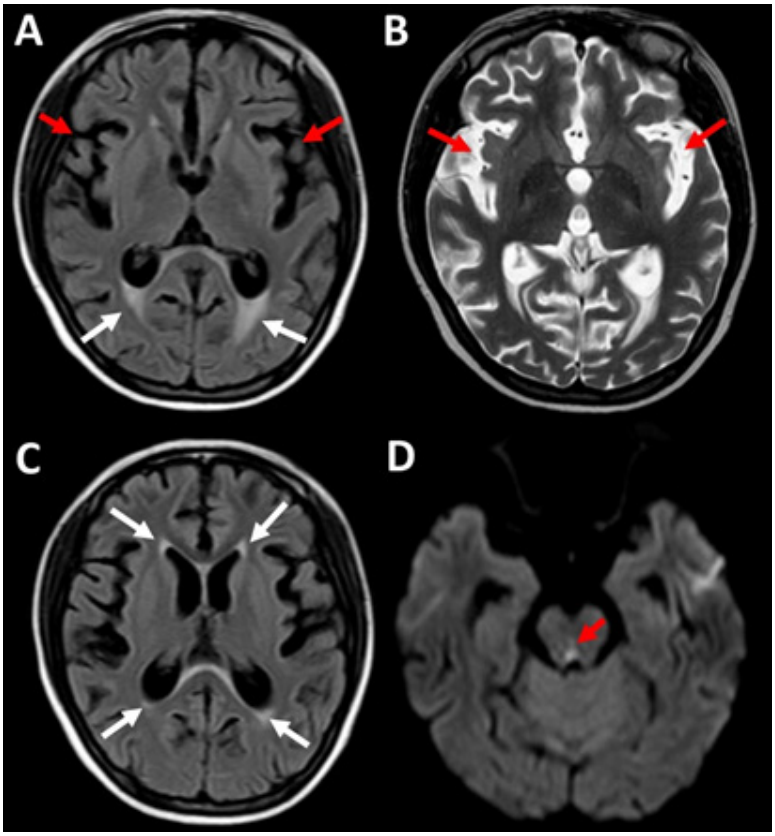
Figure 1. Wall-eyed bilateral internuclear ophthalmoplegia (WEBINO). Eye movements of a 14-year-old woman with Systemic Lupus Erythematosus, high blood pressure, and kidney failure presenting with bilateral horizontal diplopia.



This is the result of the bilateral affection of the medial longitudinal fasciculus, in the case of this patient, due to a paramedian mesencephalic ischemic episode.

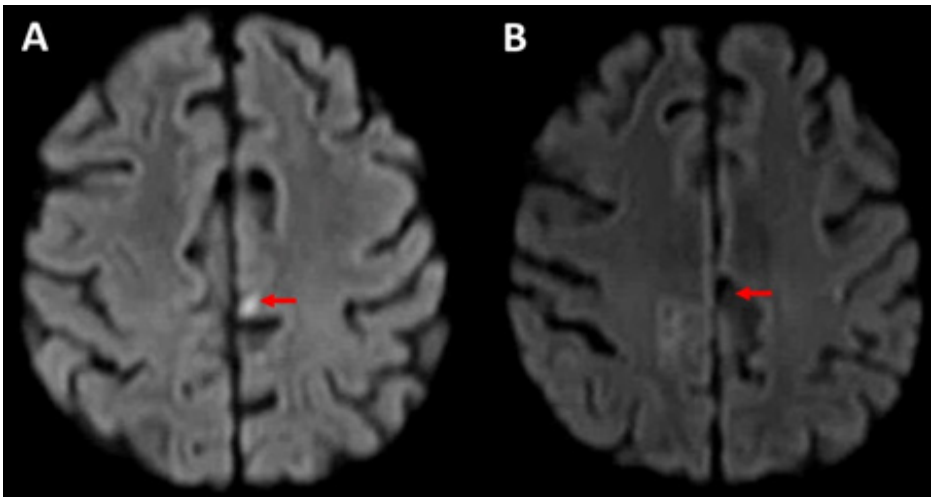
A. Primary gaze. Bilateral limitation of adduction. Exotropia. Inability to converge.
B. When trying to look to the right, the left eye does not cross the midline.
C. In the gaze to the left, the right eye does not cross the midline either.

Figure 2. Brain MRI simple sequence T1 (A), T2 (B), Flair (C), Diffusion (D).



A. Sequence T1: cortical atrophy described in a patient with SLE (red arrows). Posterior periventricular white matter hyperintensities (white arrows).
B. Sequence T2: cortical atrophy described in a patient with SLE (red arrows).
C. Sequence FLAIR: Periventricular white matter hyperintensities (white arrows). Possible loss of volume of the brain parenchyma that conditions ventriculomegaly.
D. Sequence DWI: diffusion restriction focus at the level of the lower midbrain in its right posterior portion at the pontomesencephalic junction (red arrow).

Figure 3. Diffusion alteration in the left paracentral lobule.



Focus of diffusion restriction due to cytotoxic edema in the left paracentral lobule.

A. Sequence DWI: hyperintense signal demostrating acute microinfarct (red arrow).
B. Sequence ADC: hypointense signal demostrating acute microinfarct (red arrow).

cheal intubation with sedation and relaxation as measures of neuroprotection.

Cerebrospinal fluid and peritoneal fluid analyzes were performed with the presence of encapsulated yeasts compatible with Cryptococcus neoformans and treatment with Amphotericin B was started. However she evolved unfavorably and died due to the development of this serious opportunistic infection secondary to the state of immunosuppression and complications of your underlying disease.

Discussion

WEBINO is a syndrome caused by an injury that bilaterally affects the MLF and the fibers of the VI cranial nerve in its emergence from both subnuclei of the internal rectus, from which exotropia and the inability to converge are derived.

The most frequent causes are ischemic and demyelinating, such as MS with involvement of the brain stem[5] . Other causes include vasculitis (SLE)[6] , Arnold Chiari malformation and endocranial hypertension[7] . Infectious etiologies such as meningeal tuberculosis, meningovascular syphilis[8] , hydrocephalus due to meningeal cryptococcosis[9] , traumatic brain injury and neurodegenerative disorders (progressive supranuclear palsy)[10] have also been described.

We propose that WEBINO in this case was due to vasculitis as a complication of SLE, but not attributable to acquired cryptococcosis given the state of immunosuppression. This is supported by the clinical findings associated with the study of abnormal neuroimaging with paramedian midbrain infarction and a favorable response to established management.

Frequent findings of MRI in SLE are cerebral atrophy that occurs in 8.7-32% of cases, loss of volume of the corpus callosum and periventricular dilation[11] . In patients with SLE and OIN the most commonly found findings are hyperintense lesions, large or small, in subcortical areas and in the periventricular white matter[12] , as occurred in the present case.

Due to the patient's outcome, it was not possible to perform IADSA, the study of choice to confirm vasculitis.

Treatment should focus on solving the cause. Diplopia that persists after management of any underlying condition can be treated with surgery or botulinum toxin. In patients with SLE and cerebrovascular disease, anticoagulation or antiaggregation should be defined in the presence of antiphospholipid antibodies[13]. In the case of vasculitis, treatment is based on glucocorticoids associated or not with Cyclophosphamide[14] .

The prognosis is variable and depends on the

etiology of the syndrome. A retrospective study of patients with SLE and INO reported that after receiving initial steroid management at high doses for 3 days followed by a maintenance dose, 75% of cases resolved ophthalmoplegia[15] as our patient.

Making the diagnosis of bilateral ophthalmoplegia is challenging due to its rarity and the precision of its neuroanatomical location. The clinical history and the detailed physical examination together with the imaging studies will allow to discern between the most probable etiologies and to initiate a timely treatment that resolves the cause and improves the specific clinical prognosis.

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