Bilateral horizontal gaze palsy as an initial presentation of a clinically isolated syndrome: A case report

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Access this article online

Quick Response Code:

Website: www.saudijophthalmol.org

DOI: 10.4103/sjopt.sjopt_106_23

Abstract:

Multiple sclerosis (MS) is the most common demyelinating disease affecting the central nervous system. It has a wide range of manifestations and commonly affects the visual system. Many patients with MS report decreased vision, diplopia, nystagmus, and abnormal ocular motility. Nevertheless, bilateral horizontal gaze palsies are exceptionally rarely seen. We present the case of a 24-year-old female who came to our pediatric ophthalmology clinic complaining of bilateral horizontal gaze palsy, photophobia, and eye pain for 2 days. Although the patient had a family history of MS, there was no similar or previous complaint, with an unremarkable past medical and surgical history. During the examination, she was found to have a complete bilateral absence of horizontal saccade and pursuit, with slight limitations in vertical ones. There was no nystagmus or skew deviation, and the rest of the cranial nerves (CNs) were intact. Her ocular vital signs were normal, and her corrected visual acuity was 20/20 with full-color vision. The rest of the physical and neurological examinations were unremarkable. After referral to neurology, the magnetic resonance imaging showed multiple hyperintense lesions in deep white matter, pons, and midbrain. The correlation of imaging findings with clinical presentation confirmed the diagnosis of a clinically isolated syndrome. Extra-ocular motility (EOM) significantly improved after pulse steroid therapy and five sessions of plasma exchange, but the patient developed 35 prism diopter of acquired concomitant esotropia. She underwent a right medial rectus botulinum toxin injection which dramatically improved her condition, and became orthotropic during the last 2 months of follow-up after the injection.

Keywords:

Clinically isolated syndrome, horizontal gaze palsy, multiple sclerosis, paramedian pontine reticular formation (PPRN)

Introduction

Multiple sclerosis (MS) is a chronic immune-mediated disease affecting the central nervous system. Adults aged between 20 and 40 and women have the highest risk. It is mainly a demyelinating process of the nerve fibers in the brain, spinal cord, and optic nerve. It is diagnosed by the dissemination of lesions in time (two or more clinical events) and space (multiple lesions seen on brain and spinal imaging).[1] Clinically isolated syndrome (CIS) is the first clinical attack of MS. Furthermore, it is the first presentation in around 85% of MS patients. A 20-year follow-up showed that approximately 84% of patients with CIS would develop a second demyelinating attack and would be diagnosed with clinically definite MS. Patients diagnosed with CIS may experience four stages: CIS recovery for an uncertain period, relapsing-remitting MS, secondary progressive MS, or death.[2]

The disease presentation varies widely, and the patient may present with sensory, motor, or autonomic defects, in which ocular symptoms are common. The primary presenting ocular manifestations occur in 75% of MS patients.[3] A broad range of visual manifestations have been described in the literature, in which acute optic neuritis (ON), internuclear ophthalmoplegia (INO), and nystagmus were the most common. In general, the visual impact

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Submitted: 13-May-2023
Revised: 30-Jul-2023
Accepted: 17-Aug-2023
Published: 12-Oct-2023

How to cite this article: Alnosair G, Alanazi KA, Alhumaid FI, Alshuhayb BS. Bilateral horizontal gaze palsy as an initial presentation of a clinically isolated syndrome: A case report. Saudi J Ophthalmol 2024;38:59-63.

of MS can be divided into that affecting the afferent visual pathway (involving vision) and that affecting the efferent pathway (controlling eye movements), which is seen in between 40% and 76% of MS cases. Afferent pathway involvement includes ON (20%), retinal periphlebitis (10%), and uveitis (1%). The efferent pathway ocular motility abnormalities are divided into ocular alignment and stability disorders. The former frequently presented as diplopia and nystagmus. Ocular alignment disorders can either be paralytic or nonparalytic. Paralytic causes were mainly INO, ocular motor nuclear, and nerve palsies, while nonparalytic is mainly skew deviation causing vertical misalignment.[1]

CIS usually manifested in a young adult with signs of the optic nerve, brainstem, or spinal cord involvement. In the literature, horizontal gaze palsy due to abducens (CN VI) nucleus lesion is the most ocular motor nerve in MS, as reported in a few case reports.[4-7] However, oculomotor (CN III) involvement is less commonly reported in previous literature, and trochlear nerve involvement is rarely encountered. Isolated gaze palsies are rarely reported, commonly due to other lesions such as INO. Cases of vertical gaze palsies are rarely reported. There are few case reports of dorsal midbrain syndrome in patients with MS as a cause of upward gaze defect.[8]

In Saudi Arabia, to our knowledge, there is one study that only described the ocular manifestations of MS patients. This study showed that blurred and double vision were the most common complaints, and the most prevalent findings were optic nerve atrophy and ON. Oculomotor nerve dysfunction was observed in 3%.[9] However, none of the literature locally reported a bilateral horizontal gaze palsy as the initial presentation for MS of CIS.

Case Report

A 24-year-old female not known to have any medical illness presented to the emergency department complaining of sudden onset of horizontal gaze palsy associated with photophobia and pain in both eyes for 2 days. No history of seizure, trauma, imbalanced gait, numbness, weakness, or change in bowel habits was reported. She denied using any medications, illicit drugs, tobacco, or alcohol. Her family history is significant for one relative diagnosed with MS.

On examination, the corrected visual acuity in the clinic was 20/20, and color vision testing was 15/15 in both eyes. There were no visual field defects or scotomas, and both pupils were round, regular, and normally reacting to light and accommodation with no afferent pupillary defects. Slit-lamp examination was unremarkable in both eyes. Fundus examination showed no signs of ON in both eyes.

During the neurological examination of the extraocular movement (EOM), the patient was orthotropic in primary gaze. The examination of the monocular EOM showed a complete bilateral loss of abduction and adduction, with a slight limitation of supraduction and infraduction in both eyes [Figure 1]. Eye conversion was intact, with no nystagmus, oscillopsia, or skew deviation observed. Excluding CN VI and CN III, the rest of the sensory and motor CNs were intact.

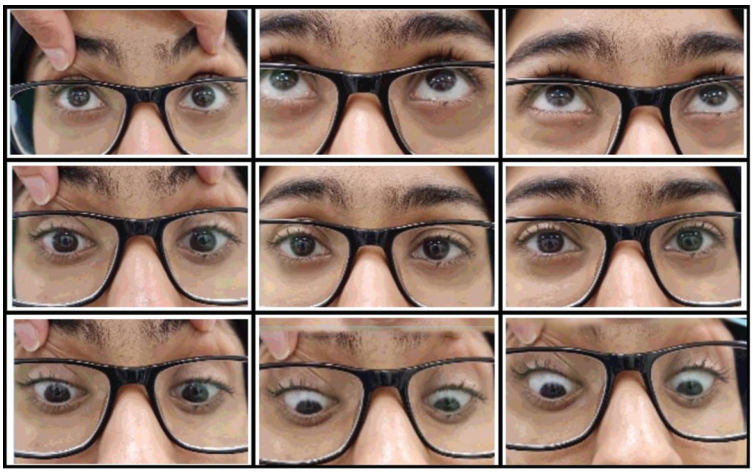
The patient was referred to the neurology department for further evaluation. Physical and neurological examinations were unremarkable; the patient was conscious, alert, and fully oriented, with normal vital signs. All the tone, power, reflexes, sensation, and coordination in the upper and lower limbs were intact. Inflammatory and autoimmune markers tests showed a positive anti-DNA, antineutrophil cytoplasmic antibodies, elevated C-reactive protein, and erythrocyte sedimentation rate. Furthermore, an urgent brain magnetic resonance imaging (MRI) showed well-defined discrete foci of hyperintense lesions of variable sizes scattered through the periventricular white matter, centrum semiovale, corona radiata, and temporal lobe white matter. Similar findings were seen within the brainstem, specifically in the dorsal pons, which explains the involvement of the paramedian pontine reticular formation (PPRF). More small scattered lesions are also seen on the left side of the midbrain, in addition to the cerebellar peduncle and left cerebellar hemisphere, which is most evident on T2-weighted images and fluid-attenuated inversion recovery (FLAIR), which is consistent with demyelination. The diagnosis of CIS was made since it was the patient's first clinical presentation. Moreover, none of the lesions showed enhancement and were considered inactive lesions [Figures 2 and 3].

There was a minimal improvement of EOM movement in adduction after intravenous pulse steroid therapy, besides other supportive measures for 5 days. The decision was to start daily plasma exchange sessions for 5 days. After completing five cycles, the horizontal gaze palsy improved significantly, and the patient's EOM was almost full without limitation. However, the patient developed comitant esotropia of 35 prism diopter (PD) at near, with, and without spectacle correction. The patient was offered to use prism glasses or receive botulinum toxin injection into the right medial rectus, which she preferred over prism use. The patient mainly used the left eye for fixation, and the esotropia was more often manifested in the right eye. Hence, the plan was to inject the right medial rectus first and then reassess later for a second injection if needed. Following up after 1 month, she significantly improved, and she was orthotropic with full correction [Figure 4], and there was no need to repeat the injection.

Discussion

Ocular motility disorders are common findings in MS and can virtually present with any pattern depending on the involved site. Some focal lesions cause abnormal motility that cannot be identified based on clinical examination alone. Some lesions result in a classic pattern, helping to point the finger toward the site of the lesion, such as INO, one-and-a-half syndrome, PPRF, and CN VI lesions.[3]

Similar to abducens nuclei lesions, PPRF lesions can result in horizontal gaze palsy, either unilateral or bilateral. The



Gaze directions		
Up Right	Up	Up Left
Right	Straight	Left
Down Right	Down	Down Left

Figure 1: The directions of gaze at the first presentation are illustrated on the right-side table. The figure shows a complete loss of right and left eye movement in straight, up, and down gaze. Also, it shows a slight limitation in vertical eye movement

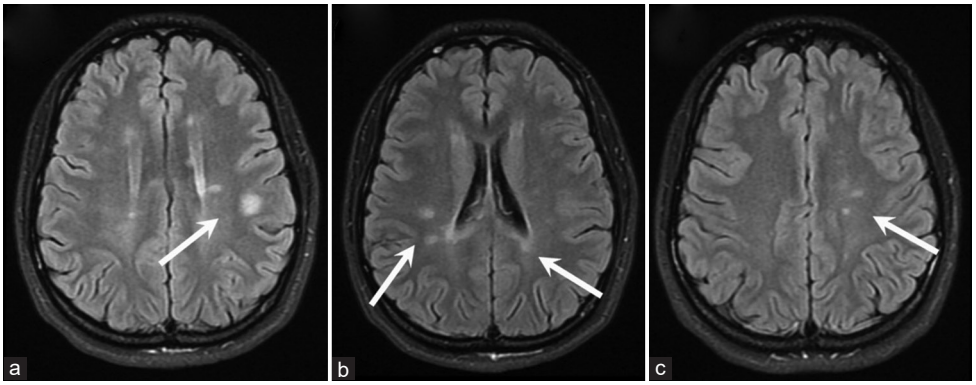


Figure 2: Multiple sections of axial T2/fluid-attenuated inversion recovery magnetic resonance imaging of the brain, showing multiple hyperintense lesions of varying sizes in the centrum semiovale (a and c), and the periventricular white matter (b)

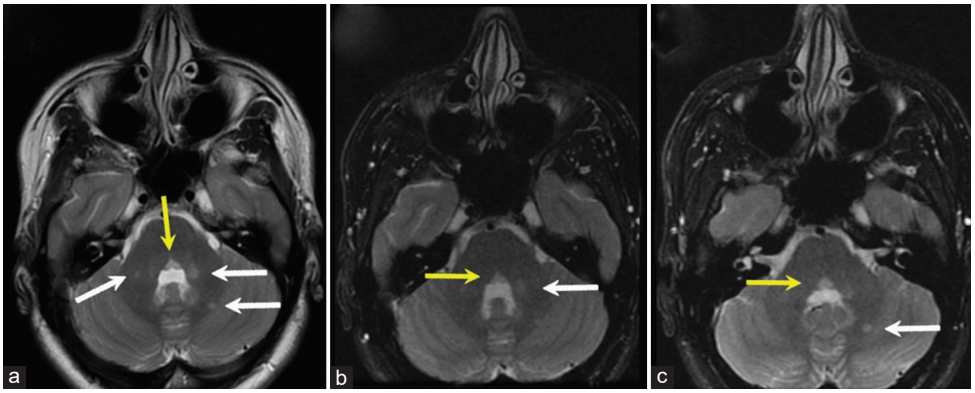
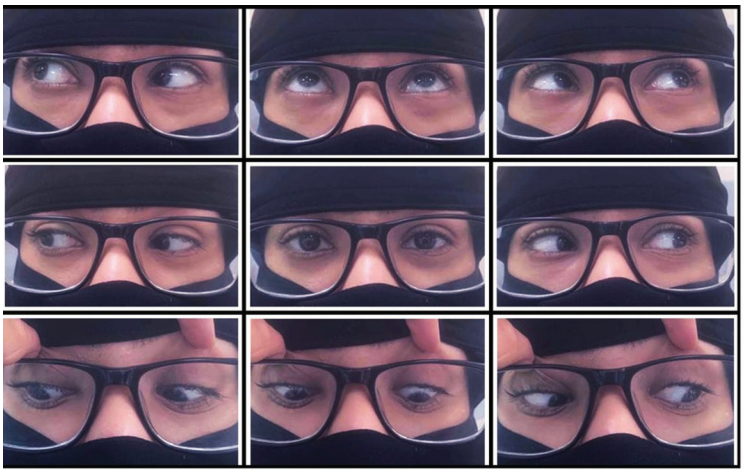


Figure 3: Axial T2-weighted magnetic resonance imaging (MRI) of the brain. (a) A hyperintense lesion in the dorsal and lateral pons (yellow arrow) and multiple hyperintense lesions of the middle cerebral peduncles (white arrows), more pronounced on the left side. The same lesions are illustrated at different levels with T2/fluid-attenuated inversion recovery MRI in photos (b and c)

PPRF is responsible for conjugate horizontal gaze and horizontal saccade. Its efferent fibers act on the ipsilateral abducens nucleus and contralateral oculomotor nucleus to simultaneously coordinate the horizontal gaze in both eyes. Damage to the PPRF can result in palsy of the ipsilateral saccade, while damage to the abducens nucleus may result in complete horizontal palsy. Moreover, the rostral part of the PPRF coordinates the vertical saccade, and lesions in that area may decrease vertical gaze velocity. Although bilateral PPRF lesions are extremely rare to encounter, there have been few reported cases in the literature, and it still should raise the suspension of pons lesions and MS.[5]



Gaze directions		
Up Right	Up	Up Left
Right	Straight	Left
Down Right	Down	Down Left

Figure 4: The nine gazes 1 month after botulinum toxoid injection. The photo shows a full recovery of extraocular motility in all directions of gaze, as illustrated in the table on the right

The patient in our case presented with a sudden onset, complete bilateral horizontal gaze palsy with vertical gaze paresis that was suddenly developed after she woke up. She had an unremarkable past medical and surgical history. There was no preceding illness or neurologic deficit. What makes this presentation unique is that, to our knowledge, there is no reported case of a similar course in a previously healthy patient. Despite the scarcity of reported cases in the literature, few cases of complete horizontal gaze palsy attributed to MS were reported. Either with a gradual onset or with a preceding primary neurological deficit.[4,6]

Hatake *et al*.[3] reported a complete bilateral horizontal palsy due to an MS case in a 30-year-old woman. Before developing the horizontal palsy, the patient had paresthesia in the left lower limb and blurry vision for 6 and 2 weeks, respectively. Similar to our patient's presentation, there was a complete bilateral horizontal gaze palsy with loss of saccade and pursuit.

MRI with T2 and FLAIR showed a hyperintense pontine lesion in the medial and lower tegmentum and a few periventricular lesions in the cerebral hemispheres. The patient received pulse steroid therapy for 3 days with partial recovery and subsequently developed left horizontal gaze nystagmus and saccade disability, which did not resolve. Besides the esotropia, we did not observe any nystagmus or loss of saccadic eye movement in our patient, which in contrast, received 1000 mg/day IV methylprednisolone for 5 days, with plasma exchange therapy for another 5 days.[4]

Milea *et al*.[10] reported two patients who presented with a similar presentation of acute bilateral gaze palsy. Both had an acute onset of bilateral impaired adduction saccade, while the abduction saccade was present with dissociated abduction nystagmus in both as well. Alongside convergence, vertical eye movement was also intact, with impaired vestibuloocular reflex. At this stage, both patients were diagnosed with bilateral INO. One week later, unexpectedly, both patients lost abduction saccade and dissociated nystagmus bilaterally, which, for an unknown reason by the author, evolved into a complete horizontal gaze palsy similar to what we present. In both cases, the MRI demonstrated a few hyperintense T2-weighted lesions in the periventricular white matter of the cerebral hemispheres and one lower pontine tegmentum lesion located at the posterior and medial sides. In our case, the diagnosis of INO was excluded due to the lack of abduction nystagmus. Furthermore, the presentation of a complete bilateral horizontal palsy was sudden, and the patient denied the presence of any residual or abnormal eye movement. Interestingly, and in both cases reported by Milea *et al*.[10] persistent bilateral limitation of abduction with horizontal diplopia was still present two months after the initial presentation. Both persisted a few weeks after the full recovery of adduction and the return of normal eye movement, which was presented in our case, and which we treated with botulinum toxoid injection with complete recovery.

Botulinum toxoid injection is considered an excellent therapeutic option in patients with acute oculomotor or abducens nerve palsies with an onset of fewer than 3 months and a horizontal deviation between 15 and 50 PD. Botulinum aims to eliminate the diplopia in the primary gaze by paralyzing the antagonistic muscle, which allows more movement and less restriction in the paretic muscle. Another vital function is to prevent antagonistic muscle contracture, which eventually if developed, will lead to muscle fibrosis and mechanical deviation.[11] We decided to give a unilateral medial rectus injection and reassess after 1 month for another possible injection on the other side. The angle of deviation was moderate (30 PD at near and 35 PD at a distance) with spectacle correction. Therefore, there was a concern about the possibility of the patient developing consecutive exotropia with bilateral medial rectus injections. In the follow-up appointment after 1 month, the patient was delighted with the result and was orthotropic with spectacle correction, with a nill angle of deviation either at near or distant.

In conclusion, early manifestations of MS encompass a wide range of common ocular and motor presentations. Isolated

horizontal gaze palsy, although rare, must be kept in mind as a possible presentation of patients suspected to have MS. A thorough evaluation and additional imaging to localize the anatomical disruption is therefore warranted to confirm the diagnosis and rule out other possible etiologies, which will eventually guide the physician to a proper management plan.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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