

# Bilateral Internuclear Ophthalmoplegia as a First Presenting Sign of Multiple Sclerosis

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## ABSTRACT

Internuclear ophthalmoplegia is a disorder of conjugate horizontal gaze in which the affected eye shows impairment of adduction and contralateral eye abducts with nystagmus. Internuclear ophthalmoplegia is caused by disruption of the medial longitudinal fasciculus which connects the nucleus of sixth cranial nerve on one side of the pons to the medial rectus subnucleus of the third cranial nerve in the contralateral midbrain. Bilateral internuclear ophthalmoplegia due to brainstem lesions is rarely seen in clinical practice. Herein, we present a 40-year-old female who was diagnosed with multiple sclerosis after she experienced her first attack with diplopia due to bilateral internuclear ophthalmoplegia. The clinical history of the presented case revealed clearly that multiple sclerosis should be highly suspected in patients admitted to emergency rooms with diplopia, particularly in cases presenting with bilateral internuclear ophthalmoplegia. The patients with internuclear ophthalmoplegia should be searched with brain and brainstem magnetic resonance imaging.

**Keywords:** Internuclear ophthalmoplegia, diplopia, multiple sclerosis

## MULTİPL SKLEROZUN İLK BAŞVURU BULGUSU OLARAK BİLATERAL İTERNÜKLEER OFTALMOPEJİ

### ÖZET

İternükleer oftalmopleji; etkilenen taraftaki göz küresinde addüksiyon kusuru ve karşı taraf göz küresinde abdüksiyon esnasında nistagmusun olduğu bir konjüge horizontal bakış bozukluğudur. İternükleer oftalmopleji ponsun bir yarımındaki altıncı kraniyel sinir çekirdeğinin karşı taraf mezensefalondaki üçüncü kraniyel sinir alt çekirdeğiyle iletişimini sağlayan medial longitudinal fasiküldeki bozukluktan kaynaklanır. Beyinsapı lezyonlarına ikincil bilateral İternükleer oftalmopleji klinik pratikte nadir görülür. Burada, ilk atağını bilateral internükleer oftalmoplejiye bağlı diplopiyle geçirmesi sonrası multipl skleroz tanısı alan 40 yaşındaki bir kadın olgu sunmaktayız. Sunulan hastanın klinik öyküsü, acil servislere diplopi ile başvuran, özellikle bilateral internükleer oftalmoplejiyle prezente olan olgularda multipl skleroz tanısından şüphelenilmesi gerektiğini açıkça ortaya koymaktadır. İternükleer oftalmoplejili olgular beyin ve beyinsapına yönelik manyetik rezonans görüntülemeleriyle incelenmelidir.

**Anahtar sözcükler:** İternükleer oftalmopleji, diplopi, multipl skleroz

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**M**ultiple sclerosis (MS) is a common disorder of the central nervous system that is the main cause of non-traumatic disability of young adults. Although it was regarded as predominantly an autoimmune inflammatory disease in earlier reports, MS is now revealed as complex pathophysiology characterized by inflammatory demyelinating events and a significant component of neurodegeneration that manifests as neuronal and axonal loss since the early stages of the disease (1). The typical variability of phenotype and disease course observed in MS, spanning

from relapsing to primary or secondary progressive clinical scenarios, is probably due to different extent and combination of inflammatory and neurodegenerative processes involving various central nervous system areas.

Internuclear ophthalmoplegia (INO) is a disorder of conjugate horizontal gaze in which the affected eye shows impairment of adduction and contralateral eye abducts with nystagmus. INO is caused by disruption of the medial longitudinal fasciculus (MLF) which connects the nucleus of sixth cranial nerve on one side of the pons to the medial rectus subnucleus of the third cranial nerve in the contralateral midbrain. The MLF plays an integral role in the conjugate horizontal gaze and any lesion affecting this tract might result in INO. The nature of the lesion varies greatly, and includes ischaemic, autoimmune (MS), infectious, inflammatory, toxic, nutritional, traumatic and metabolic insults (2, 3).

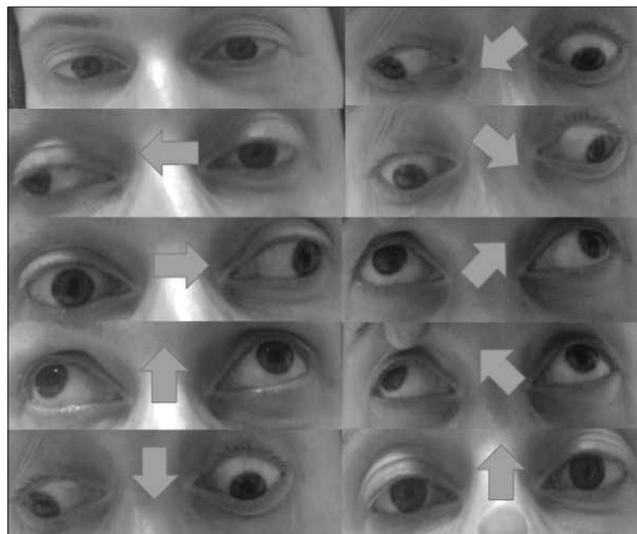
Demyelination and axonal damage of the MLF within the midline tegmentum of the pons (ventral to the fourth ventricle) or the midbrain (ventral to the cerebral aqueduct) results in INO which is the most common saccadic disorder observed in MS (1). However, bilateral INO as a presenting sign of MS is rarely seen in clinical practice. Herein, we present a female patient who was diagnosed with MS after she experienced her first attack with diplopia due to bilateral INO.

### Case report

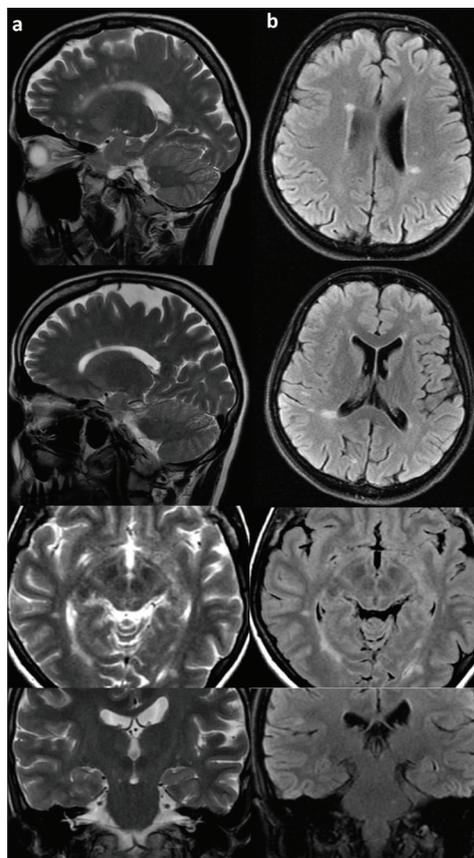
A 40-year-old right-handed woman admitted to our emergency room with the complaint of double vision for one week. She had admitted to the ER of a local hospital when her complaint had begun, and had been advised to admit to the outpatient clinic of the ophthalmology department. However, she admitted to our ER upon the progression of double vision. During the neurology consultation, she described a binocular diplopia began one week prior to admission and progressed slowly. Her diplopia was worsened on lateral gaze in either direction. In past medical history, she did not have any systemic or neurological disorder. She did not define a history of any medication, smoking or alcohol.

Neurological examination is normal except for bilateral INO. (Figure 1) The convergence reflex was also impaired. Computed tomography (CT) and diffusion-weighted magnetic resonance imaging (MRI) of the brain with apparent diffusion coefficient mapping were normal. Visual evoked potentials were normal on both sides. Multiple

demyelinating lesions were revealed on T2-weighted and Fluid Attenuation Inversion Recovery (FLAIR) sequences of the brain MRI (Figure 2). MRI showed a lesion next to the midline of the pontine tegmentum which could be



**Figure 1.** Ocular movements of the patient restricted during the adduction on horizontal gaze in both sides.



**Figure 2.** a, b. Multiple demyelinating lesions were revealed on T2-weighted (a) and Fluid Attenuation Inversion Recovery (FLAIR) sequences (b) of the brain MRI.

responsible for the bilateral INO. Cerebrospinal fluid (CSF) and serum examination for oligoclonal bands revealed that oligoclonal IgG was present in the CSF with no apparent corresponding abnormality in the serum, indicating the local intrathecal synthesis of IgG (A typical pattern for MS – Type 2).

She was introduced pulse steroid treatment (intravenous methylprednisolone, 1000 mg per day for five days). Bilateral INO did not improve after 4 weeks in her neurological examination in our outpatient clinic control visit.

## Discussion

INO is characterized by an ipsilateral slow adducting saccade, contralateral abducting nystagmus, an ipsilateral adduction deficit that is overcome with convergence and often times a skew deviation. The side of INO is named according to the side of limited adduction. Multiple sclerosis, brainstem infarctions, tumors, hemorrhages, head trauma, Arnold-Chiari malformation, infection, hydrocephalus, lupus erythematosus, and nutritional or metabolic disorders are previously reported as the etiology of INO (2, 3). Bilateral INO could be seen with a single brainstem lesion or multiple lesions affected the MLFs on both sides. Although INO is the most common saccadic disorder observed in MS, patients are uncommonly presented with bilateral INO in their first clinical attack as in our case.

Several neuro-ophthalmologic manifestations could have occurred as a consequence of relapses and/or a sign of the chronic disease phase of MS (4, 5). Optic neuritis is the classic involvement of MS in the afferent visual system which is also the most frequent relapse manifestation of the disease (5). Besides, patients with MS could also develop ocular motor disorders leading to diplopia or oscillopsia. The most common ocular motor abnormalities in patients with MS are INO, saccadic hypermetria, gaze-evoked nystagmus, and impaired vestibulo-ocular reflex suppression. The prevalence of either unilateral or bilateral INO in during the course of MS was estimated to be anywhere between 17% and 41% (6).

The bilateral INO could be rarely secondary to paralysis due to neuromuscular disorders instead of central nervous system insults named as pseudo-INO. Myasthenia graves, Miller-Fisher syndrome, Grave's ophthalmoplegia, mitochondrial disorders and oculopharyngeal muscular dystrophies were previously reported to cause pseudo-INO in the literature (7).

In conclusion, bilateral INO could be the presenting feature of the first clinical attack of MS as in our case. The ER clinicians should be aware of ocular findings occurred in MS attacks, and keep in mind that INO should be further searched with a classic brain and brainstem MRI if the CT and diffusion-weighted MRI were normal.

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