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### Clinical Insights into Internuclear Ophthalmoplegia: A Case Report

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#### ABSTRACT

**Background:** Internuclear ophthalmoplegia (INO) is a rare neuro-ophthalmological disorder characterized by impaired horizontal eye movement coordination due to lesion in the medial longitudinal fasciculus. INO commonly results from demyelinating diseases, vascular lesions, or structural brain abnormalities. **Case presentation:** A 60-year-old male patient presented with diplopia for the past 4 days. He had history of hypertension and diabetes mellitus and “mild” stroke for past years. Clinical examination revealed normal primary gaze, limited medial movement of the left eye, and diplopia in all gaze positions. Hess screen examination demonstrated underaction of the left medial rectus muscle and overaction of the right lateral rectus muscle. The laboratory results an elevated blood sugar level. Brain CT scan revealed multiple infarcts in the right parietal and cerebellar lobes and left parieto-occipital lobe, with evidence of brain atrophy. The patient was diagnosed with INO. Management involved addressing the underlying systemic diseases, namely diabetes and hypertension, in collaboration with internist and neurologist. The patient also received citicoline therapy and underwent regular follow-up. In the third-month follow-up, the patient demonstrated significant improvement, with reduction in diplopia and enhancement in left eye medial movement. **Conclusion:** This case report highlights the importance of considering INO in patients presenting with diplopia and a history of vascular risk factors. Timely diagnosis and comprehensive management with regular follow-up is crucial to monitor the progress and enhance the patient's quality of life.

#### 1. Introduction

Internuclear ophthalmoplegia (INO) is a neurological disorder characterized by the inability to perform conjugate lateral gaze and ophthalmoplegia due to damage to interneurons between two cranial nerve nuclei, namely cranial nerve (CN) VI and CN III. These interneurons are known as the medial longitudinal fasciculus (MLF). The Medial Longitudinal Fasciculus carries internuclear neurons to connect nuclei in the brainstem, including the CN VI nucleus in the pons, to the contralateral subnucleus of the oculomotor nerve in the midbrain, which innervates the medial rectus muscle. INO primarily affects horizontal conjugate gaze and typically manifests as impaired ipsilateral adduction in the region of the

lesion, accompanied by contralateral abductive nystagmus.<sup>1-3</sup>

The medial longitudinal fasciculus can be damaged by various lesions (e.g., demyelination, ischemia, neoplasms, inflammation) in the pons or midbrain. The MLF is a myelinated nerve pathway that connects the ipsilateral oculomotor nucleus to the paramedian pontine reticular formation (PPRF) and the contralateral CN VI in the pons. Consequently, demyelinating lesions in the midbrain or pons often result in unilateral or bilateral INO in young patients. Approximately one-third of INO cases are caused by infarctions and are typically unilateral, more commonly observed in older individuals. Demyelination disorders contribute to one-third of

other cases and are most often bilateral, affecting younger individuals and adolescents.<sup>1,4,5</sup>

Clinical characteristics of INO typically involve partial or complete ipsilesional adduction deficit with contralateral horizontal abductive saccades, which are dissociated during attempts to gaze towards the contralateral side. Diagnosis is supported by imaging studies such as CT scans and MRI to identify existing lesions. The primary management is based on addressing the underlying disease, with the most common causes being cerebral infarctions and multiple sclerosis.<sup>1</sup> In this case report, we report a case of INO and its management.

## 2. Case Presentation

A 60-year-old male patient presented at the neuro-ophthalmology subdivision clinic with the chief complaint of double vision that had been ongoing for the past 4 days. The double vision occurs when looking with both eyes. The patient did not report any blurriness in vision. There was no history of eye pain, recurrent redness, tearing, or previous eye discharge. The patient denied any history of trauma, prior use of eyeglasses, or eye surgeries. Additionally, there were no complaints of limb weakness at the time of

presentation. The patient was referred by an ophthalmologist in a remote area with a suspicion of left eye cranial nerve III palsy.

The patient has a history of hypertension and diabetes mellitus for the past 7 years, regularly managed by an internist. The prescribed medications include bisoprolol 1x5 mg, candesartan 1x8 mg, ascardia 1x80 mg, and metformin 3x500 mg. Additionally, the patient has a history of neurologist specialist consultation one year ago, during which they presented with weakness in limb movement and were diagnosed with a "mild stroke" as per the patient's account. They received outpatient treatment at that time; however, the patient has not had a follow-up consultation since then.

On general examination, the patient presented with a blood pressure of 139/74 mmHg and was noted to have an overweight nutritional status. Ophthalmological examination revealed no visual impairment, a relatively normal anterior eye segment, mild cataracts, and no abnormalities in the posterior eye segment. The patient exhibited a relatively normal position of the eyeballs in the primary gaze. However, there was limited medial movement of the left eye.



Figure 1. Normal position in primary gaze.



Figure 2. Limitation of horizontal gaze (medial movement) in the left eye.

The Hess screen examination revealed positive diplopia. The left eye demonstrated underaction of the medial rectus muscle, while the right eye exhibited

overaction of the lateral rectus muscle. There were no abnormalities noted during the visual field examination conducted using perimetry.

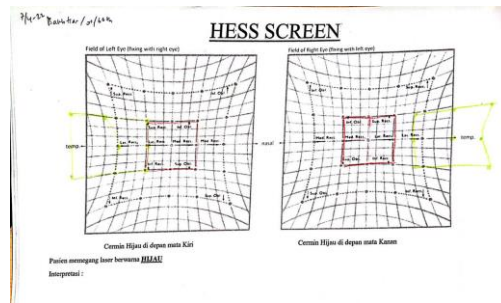


Figure 3. Hess's screen examination showed underaction of the left eye medial rectus muscle and overaction of right eye lateral rectus muscle.

Laboratory results elevated fasting blood glucose (131 mg/dL) and post-prandial blood glucose (212 mg/dL). The patient underwent their first non-contrast brain CT scan, which revealed multiple

infarctions in the right parietal and cerebellar lobes, as well as the left parieto-occipital lobe, in addition to indications of brain atrophy.

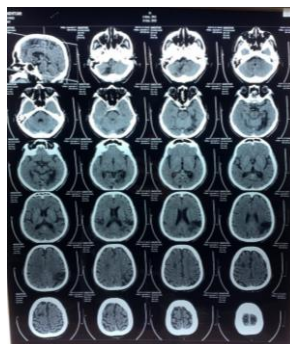


Figure 4. A non-contrast brain CT scan revealed multiple infarcts and brain atrophy.

In principle, the primary "management" in the ophthalmological aspect of INO is to identify any systemic abnormalities present in the patient with initial manifestations in the eye. Patient management is carried out comprehensively in collaboration with internists and neurologists to address the systemic disorders underlying INO in this case. Subsequently, the patient undergoes regular observation to assess clinical progress while receiving citicoline supplementation as a neuroprotective agent. In the third-month follow-up, a relative reduction in diplopia complaints was observed, along with improved medial

movement of the left eye.

### 3. Discussion

A case has been reported involving a 60-year-old male with left eye internuclear ophthalmoplegia (INO) caused by ischemia (cerebral infarction). INO occurs due to a lesion in the medial longitudinal fasciculus (MLF), which disrupts the connection between the contralateral CN VI nucleus and the ipsilateral CN III nucleus, thus affecting horizontal eye movement (Figure 5).<sup>4,6</sup>

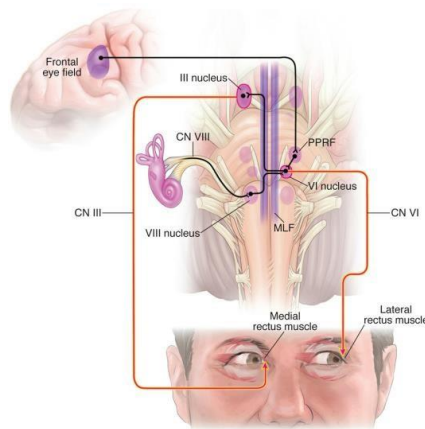


Figure 5. Horizontal eye movement physiology: INO occurs due to lesions in the MLF.<sup>7</sup>

The diagnosis of INO in this case was established through a combination of patient history, ophthalmological examination, and supportive diagnostic measures, including non-contrast brain CT scan and laboratory testing. The patient's history revealed diagnostic points such as double vision and risk factors, including advanced age, a history of stroke, diabetes mellitus, and hypertension. These complaints were corroborated by the ophthalmological examination, which indicated relatively orthophoric eye positions in the primary gaze, along with limited adduction movement in the left eye and minimal nystagmus in the right eye during abduction. The horizontal movement impairment is attributed to a lesion in the MLF, predominantly resulting from infarctions. Supportive diagnostic evaluation was conducted through a brain CT scan, which revealed multiple infarctions in the right parietal and cerebellar lobes, as well as the left parieto-occipital lobe, along with indications of brain atrophy.<sup>1,8,9</sup>

Horizontal eye movement originates from the horizontal semicircular canal, with the primary afferent fibers of the vestibular nerve (CN VIII) primarily directed toward the vestibular nucleus (CN VIII nucleus). These vestibular nuclei then send excitatory connections to the contralateral abducens nucleus (CN VI), which innervates the ipsilateral lateral rectus muscle and the contralateral CN III nucleus via the medial longitudinal fasciculus (MLF). Horizontal saccadic movement is generated in the

frontal eye field, which activates the contralateral paramedian pontine reticular formation (PPRF). Burst neurons in the PPRF stimulate the ipsilateral abducens nucleus, with the subsequent pathway mirroring the movement of the eye generated by horizontal vestibular input.<sup>7,10</sup>

The presence of a lesion in the MLF obstructs the connection between the contralateral CN VI nucleus and the ipsilateral CN III nucleus, thereby affecting horizontal eye movement (Figure 2). One of the most crucial functions of the MLF is its role in saccadic eye movements. Saccades are initiated by the Frontal Eye Field (FEF), which sends signals to the contralateral paramedian pontine reticular formation (PPRF) to generate horizontal saccadic movements and the Rostral interstitial nucleus of the medial longitudinal fasciculus (riMLF) for vertical saccades.<sup>4,10,11</sup>

The PPRF activates the ipsilateral abducens nucleus, which sends signals to the lateral rectus muscle on the same side, and through interneuron stimulation of the abducens, it reaches the contralateral medial rectus subnucleus of the oculomotor nucleus via the MLF, resulting in horizontal eye movement opposite to that initiated by the FEF. The cardinal sign of internuclear ophthalmoplegia is a slowing or impairment of adduction on the same side as the MLF lesion. This occurs because the excitatory interneuron from the abducens fails to reach the medial rectus subnucleus.<sup>4,11</sup>



#### 4. Conclusion

The significance of recognizing INO in individuals with diplopia and a background of vascular risk factors is underscored in this case report. Prompt diagnosis and a holistic approach, along with regular follow-up, are essential for tracking improvements and improving the patient's quality of life.

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