# Unilateral Internuclear Ophthalmoplegia with Secondary Deviation


***ABSTRACT***

***Introduction***

*Internuclear ophthalmoplegia (INO) is a disorder of eye movement characterized by adduction limitation combined with contralateral dissociated abduction nystagmus.*

***Objective***

*To report unilateral INO with secondary deviation.*

***Case Report***

*This is a case of a 60 year old man with double vision since 1 month ago. No history of redness, trauma, or strabismus. Patient had a history of hypertension, dyslipidemia, vertigo and cigarette consumption. No history of weakness of the extremities, tinnitus and headache. He had exotrophia with adduction limitation of the right eye and nystagmus in the left eye when he looked to the left side. Magnetic resonance imaging (MRI) showed infarct lesion on the pons. MRI with contrast enhancements examination showed no intracranial hemmorhage, space occupying lesion or neoplasma. Patient was diagnosed by unilateral INO with secondary deviation, myopic astigmat simple on both eyes, hypertension grade II, dyslipidemia. Patient got artificial tears eyedrop, neuroprotector, anti-hypertension, lipid lowering agent and thrombolytic agent.*

***Conclusion***

*Internuclear ophthalmoplegia is one medial longitudinal fasciculus (MLF) related syndrome that represents a useful model by which to objectively characterize a distinctive neurologic syndrome and its corresponding disability, with associated imaging measures of brain tissue injury.*


## I. Introduction

Internuclear ophthalmoplegia (INO) is a disorder of eye movements, characterized by adduction limitation combined with contralateral dissociated abduction nystagmus. Lesions of the MLF produce INO, when the lesion is unilateral, the INO is characterized by weakness of adduction ipsilateral to the side of the lesion. This weakness can vary from a complete loss of adduction beyond the midline to a mild decrease in the velocity of adduction without any limitation in range of motion.[1,2]

The most common causes of INO are multiple sclerosis and brainstem infarction. Other causes include head trauma, brainstem and fourth ventricular tumors, Arnold-Chiari malformation, infection, hydrocephalus, and lupus erythematosus. Internuclear ophthalmoplegia is clinically characterized by total or partial failure to adduct one eye in lateral gaze and a monocular nystagmus of the abducting eye. It may be unilateral and bilateral. The method of choice for

diagnostic imaging of MLF lesion in patients with INO is magnetic resonance imaging (MRI).[2,3]

This case report would like to present unilateral INO with secondary deviation in patient with systemic disease.

## II. Case Report

A 60 year old man came to Cicendo Eye Hospital with suddenly developed double vision since 1 month before admission. There was no history of trauma, fever, cold, malaise, convulsion, and loss of consciousness. He has never felt any headache or pain on eye movement as well as history of diabetes mellitus. Patient has a history of hypertension, dyslipidemia, vertigo and cigarette consumption.

General examination revealed hypertension grade II. Ophthalmology examination showed best corrected visual acuity on the right eye was using C-3.25x70$^0$ became 1.0, and on the left eye using C-2,50x70$^0$ became 1.0. He had adduction paresis on his right eye, and left gaze-evoked nystagmus on his left eye. vertical eye movement was unaffected but convergence was affected. The anterior segments of both eyes were within normal limit and there were no found relative afferent pupillary defect (RAPD). The intraocular pressure was within normal limit. The funduscopy were within normal limit in both eyes. Confrontation test showed no visual field defect in four quadrant. Color vision test using Ishihara showed 34/34 on both eyes, central visual field testing using Amsler grid showed no scotoma or metamorphopsia on both eyes and contrast sensitivity test using LEA number showed 1.25% on both eyes. Humphrey 30-2 visual field test on the right eye was low reliability with mean deviation (MD) -3.37 dB P<2%, and on the left eye was low reliability with MD -3.48 dB P<2%, arcuata visual field defect in inferonasal. Neurologic examination was within normal limit. Blood laboratory showed HbA1c 6.9% (2.00-6.00); low density lipoprotein (LDL) cholesterol 106 mg/dL (<100).

Patient was diagnosed as unilateral INO on the right eye with secondary deviation, simple myopic astigmatism on both eyes, dyslipidemia and hypertension grade II. He was given citicholine 500 mg twice a day,

acetylsalicylic tablet 80 mg once a day, artificial tears eye drop 4 times a day, and the patient was consulted to the internist for regulating his blood pressure, prevent the risk factors include high blood cholesterol level and stop cigarette smoking, lack of physical activity, and unhealthy diet.

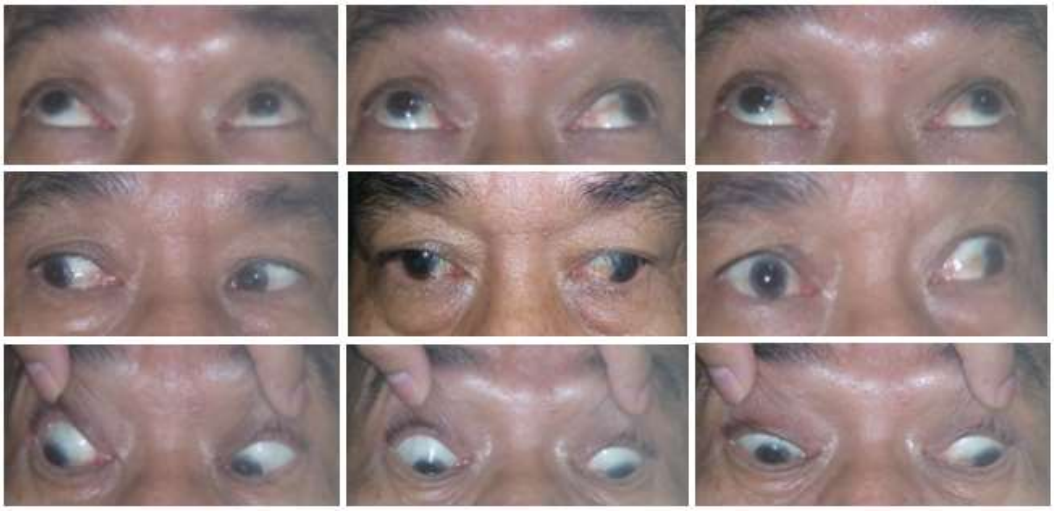

**Figure 2.1** Extraocular movements in 9 cardinal gazes. There was exotrophia in primary position and the right eye showed INO with incomplete adduction. The deviation is greater when the right eye as fixating eye.

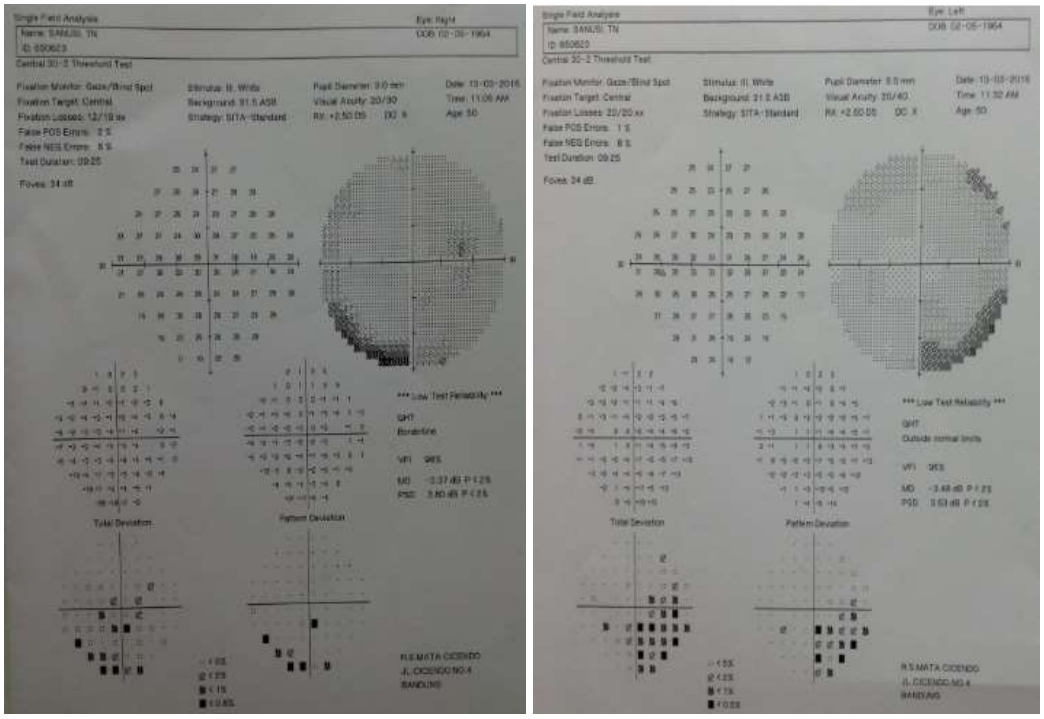

**Figure 2.2**. Humphrey 30-2 visual field test showed low reliability on both eyes with arcuata defect in the left eye.

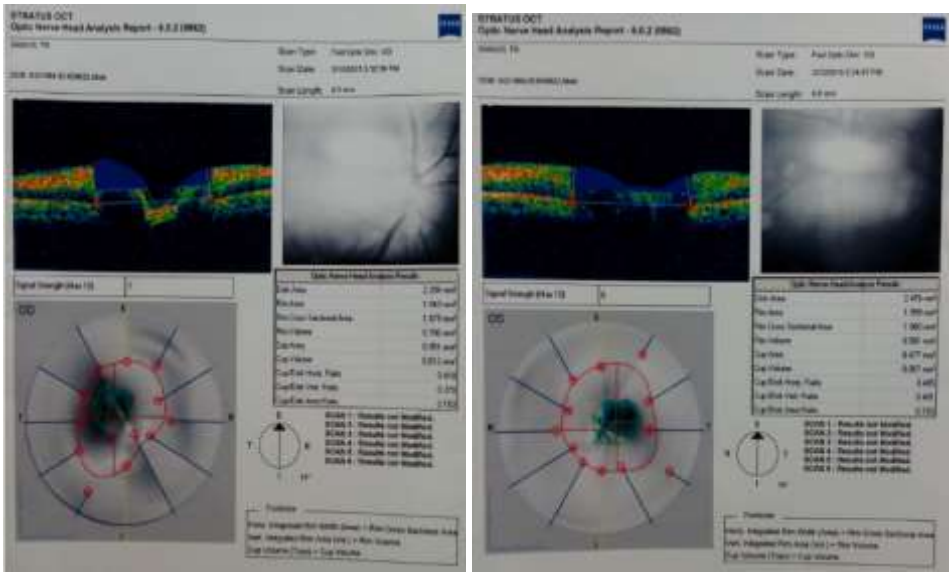

**Figure 2.3** OCT of both eyes showed optic nerve head analysis revealed normal cup to disc ratio.

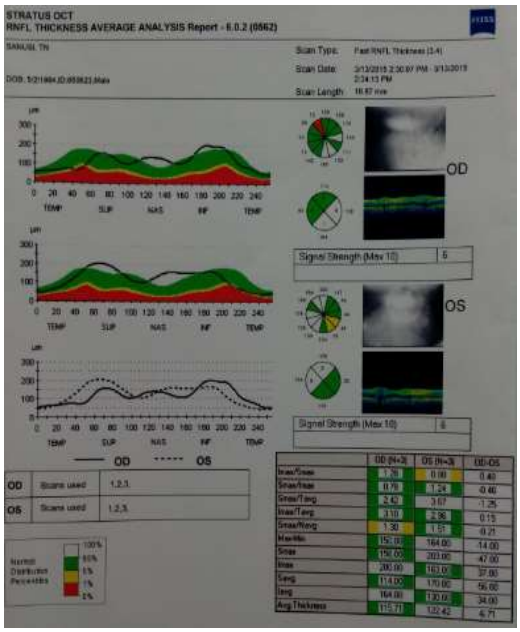


**Figure 2.4** Retinal nerve fiber layer thickness analysis showed slighty swelling in inferior and nasal quadrant of the right eye and superior and nasal quadrant of the left eye.

Magnetic resonance imaging brain showed infarct in the pons. MRI with contrast enhancements examination showed no intracranial hemorrhage, space occupying lesion or neoplasma, aneurism or vascular malformation. Patient reported that double vision was remained.

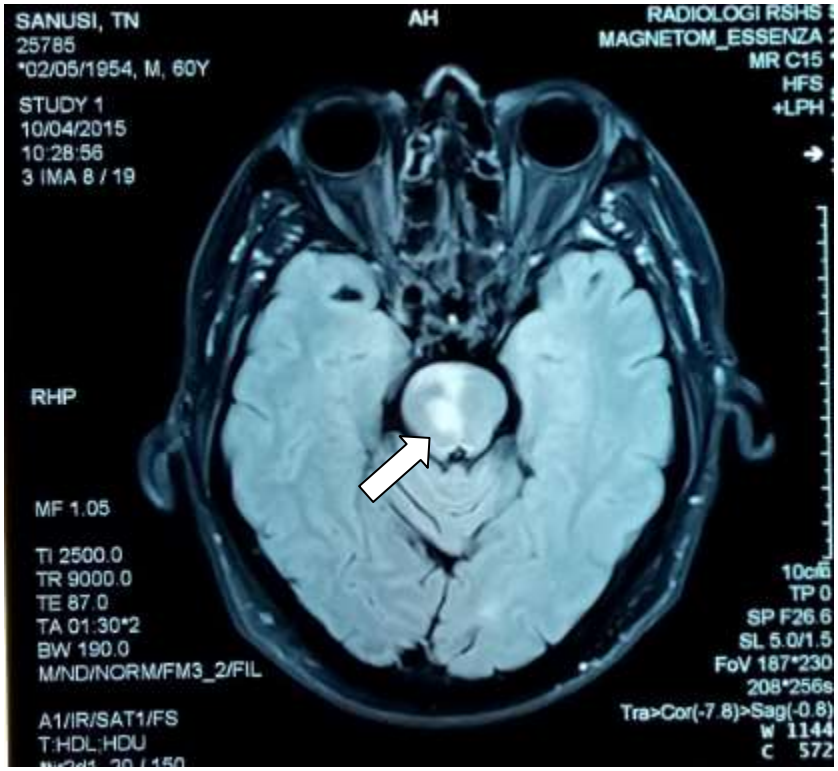


**Figure 2.5** Axial MRI of the brain showed infarct in the pons.

## III. Discussion

Internuclear lesion is one that disrupts the MLF, a bundle of fibers that connect the sixth nerve nucleus on one side of the pons to the medial rectus subnucleus (of the third nerve) on the contralateral side of the midbrain. This type of lesion produces an INO. Lesions that damage the MLF may also damage the abducens nucleus, fascicle, or both on either side of the brainstem. Lesions that damage the MLF on one side and the ipsilateral abducens nucleus produce the one-and-a-half syndrome, whereas lesions that damage the ipsilateral abducens fascicle produce horizontal ophthalmoplegia in the ipsilateral eye from the combination of an INO and an abducens nerve palsy. Lesions that damage the MLF on one side and the paramedian pontine reticular formation (PPRF) or abducens nucleus on the opposite side produce a horizontal gaze palsy toward the damage PPRF or abducens nucleus. In such cases, the INO cannot be diagnosed because of the overriding horizontal gaze palsy. Damage to the MLF on one side and the contralateral abducens nerve fascicle will produce abduction weakness of the contralateral eye combined with adduction weakness of the ipsilateral eye. In

this setting, there will be a "pseudo-horizontal gaze palsy" on attempted horizontal gaze away from the side of MLF lesion. The diagnosis may be suspected in a patient who appears to have a horizontal gaze that is asymmetric, with one eye (usually the adducting eye) being much more limited than the other.[1,2,3]

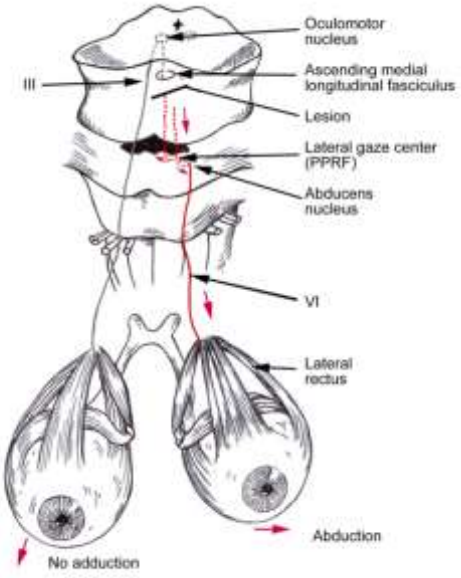


**Figure 3.1** Lesion of the medial longitudinal fasciculus resulting in internuclear ophthalmolpegia.
Source:Kaye[4]

Patients was diagnosed with unilateral INO with secondary deviation. The cardinal feature of a unilateral INO is slowed adducting saccadic velocity in one eye. This limitation is usually associated with nystagmus of the abducting eye. The eye with the slowed adduction may have limited or a full range of adducting movement. When the lesion is unilateral, the INO is characterized by weakness of adduction ispilateral to the side of the lesion. This weakness may vary from a complete loss of adduction beyond the midline to a mild decrease in the velocity or acceleration of adduction without any limitation in range of motion. Convergence may be spared or disrupted. By convention, the INO is named for the side of limited adduction. That is, right INO is one that limits adduction of the right eye secondary to a lesion of the MLF on the right side of the brainstem.[2,3]

The patient in this case showed adduction paresis on his right eye, and we also observed gaze-evoked nystagmus of the abducting eye, with convergence disruption.

Patient with a manifest deviation of one eye (heterotropia) will fixate a target only with one eye at a time. During viewing with that eye, the visual axis with the opposite (nonfixing) eye will be deviated a certain amount from the target. Patient with a comitant strabismus have the same amount deviation of the nonfixing eye regardless o the eye that is fixing or the field of the gaze. Most patient with incomitant (and especially paralytic) strabismus tend to fix with the nonparetic eye if visual acuity is equal in two eyes. The deviation of the nonfixing eye is called the primary deviation. When the patient is forced to fix the same target with the paretic eye is called the secondary deviation. The secondary deviation is always greater than the primary position.[2]

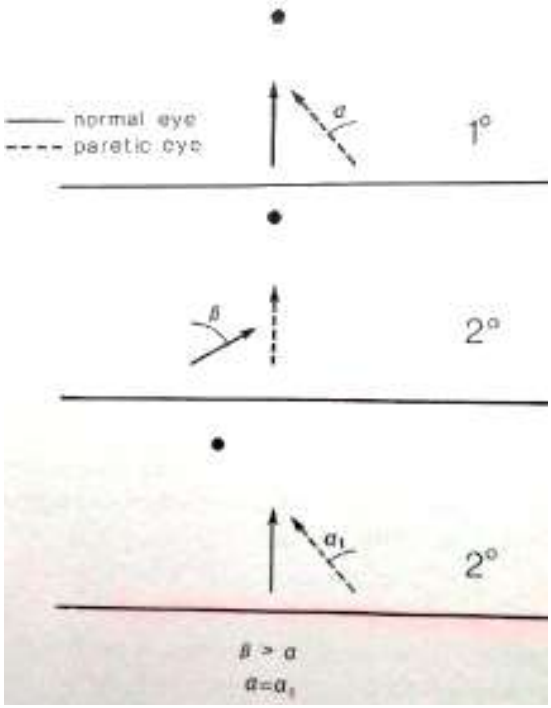


**Figure 3.2** The principle of primary and secondary deviations. α= the primary position, β=the secondary position. $\alpha_1$=the paretic eye were fixing on an object in the oppposite direction.
Source : Miller NR, et al[2]

Fixating eye in this patient was alternating but patient was prefer to use the right eye (the paretic eye), so when the patient used the right right eye as the fixating eye made greater deviation than if the left eye as the fixating eye. Abnormal eye movements may occur because of inability to maintain fixation, loss of the normal inhibitory influences on the eye movement control system, or loss of the normally symmetric input from one of the vestibular pathways to the ocular motor nuclei. The second cardinal of INO is nystagmus on abduction in contralateral eye. This nystagmus consists of a centripetal (inward) drift, followed by a corrective saccade that may hypermetric, hypometric or orhometric. It is presents nearly all patients with INO. The cause of abduction nystagmus must relate either to lesions outside the MLF or to an adaptive response to the initial adduction weakness. Gaze evoked nystagmus develops because of an inability to maintain fixation in eccentric gaze. The eyes drift back to the midline due to the elastic properties of the orbit, and a corrective saccade is generated to reposition the eyes on the eccentric target, the fast phase is always in the direction of gaze in bilateral INO and is often caused by a midbrain lesion near the third nuclei.[4,5]

The most sensitive sign is slowed adducting saccades due to damage on the MLF, as we can see in this patients. Saccades are quick, simultaneous movements of both eyes in the same direction. Saccades can be tested by having patient rapidly shift gaze between two targets, which are held to the left and right of the patient. The slowed adducting saccades is appreciated as a lag in the adducting eye compared to the abducting eye in reaching the saccadic endpoint during repetitive gaze shifts initiated by eye fields in the frontal and parietal lobes of the brain, saccades serve as a mechanism for fixation, rapid eye movement and the fast phase of optokinetic nystagmus. The horizontal saccade pathway involves axons that travel from cell bodies in the PPRF to the contralateral third nerve nucleus via the MLF.[3,5]

The fibers subserving horizontal gaze in the MLF each carry commands for all types of conjugate eye movements. Thus, vestibular slow phases, pursuit, and optokinetic following movements and saccades and quick phases of nystagmus are all affected by the MLF lesion, when patients with INO are able to

convergence, despite absence of voluntary adduction, a caudal lesion with preservation of the medial rectus subdivision of the oculomotor nuclear complex can be assumed. Patients with INO and intact convergence were said to have a posterior INO by Cogan. Although the presence of intact convergence is important in such cases, the absences of convergence in the setting of an INO does not necessarily imply a rostral lesion involving the medial rectus nuclear subdivision. Some patients are not able to produce a strong convergence effort, and the vertical disparity that occurs when a unilateral INO is associated with a skew deviation also may interfere with convergence effort.[3,5] This patient showed absence convergence. The patients came to neuro-ophthalmology unit with complaint of double vision. Diplopia can occur due to extraocular muscle paralysis.

Abnormality of pupillary reactivity also known as Marcus Gunn pupil or RAPD, is the hallmark sign of impaired optic nerve conduction. An RAPD may result from any lesion that decreases the ganglion cell input to the optic nerve. The degree of the RAPD relates to the number of fibers affected. Impaired conduction of the light stimulus along one optic thus produces decreased stimulus to papillary constriction in both pupils. The RAPD derived from the disparity between the direct and consensual light responses in the affected pupil.[2,6,7] In this patient there was no RAPD.

The etiology of INO includes multiple sclerosis (MS), tumor, infection, hydrocephalus, trauma, nutritional or metabolic disorders, vascular diseases, myasthenia gravis can produce pseudo-INO, usually with lacks the vertical gaze-evoked nystagmus of a true INO and is often accompanied by myasthenia eyelid signs.[2,6]

The study by Keane et al about unsual causes of INO, 410 cases of INO, 157 (38%) were caused by infarction (from cardiac emboli in 5 cases), 139 (34%) were caused by MS, and 114 (28%) were due to unusual causes (trauma, infection, herniation, tumor, brainstem hemorrhages, vasculitis). Infarction was considered definite in 133 of 157 patients, and MS was considered definite in 99 of 139 cases.

Unilateral INO occurred in 136 infarcts (87%), 38 MS cases (27%), and 48 unusual cases (42%). Blunt head injury was the cause of INO in 16 patients.[6]

Patient in this case was diagnosed by unilateral INO. Unilateral INO is usually related to an infarct of the brainstem in the older age group. In adolescents and younger adults, bilateral INO is typically caused by demyelination. In older adults, microvascular disease is the most common cause. The study by Kim et al about INO as an isolated or predominant clinical manifestation showed twenty-four presented with INO, whereas six initially presented with one-and-a-half syndrome that changed into INO. Dorsal brainstem infarcts responsible for the INO were located in the caudal pons in 4, rostral pons in 8, rostral pons and isthmus in 2, isthmus area in 14, isthmus and midbrain in 1, and midbrain in 1 patient. The pathogenesis is heterogeneous, including distal occlusion of small penetrating arteries, atheromatous branch occlusion from the basilar artery (BA), superior cerebellar artery (SCA), or posterior cerebral artery (PCA), or major BA occlusion.[7,8]

Patient in this case had a history of vertigo, but no vomiting. Vertigo, nausea, and vomiting, and abnormal oculomotor signs, such as nystagmus, lateral gaze abnormalities, diplopia, pupillary changes, represent involvement of the vestibular system. In general, stroke occur because of ischemic events (80-85% of patients) or hemorrhage (15-20% of patients). A number of risk factors are associated with stroke, such as increasing age, family history, race, prior history of stroke, hypertension, coronary artery disease, diabetes mellitus, cigarette smoking, heart disease, obesity, physical inactivity.[8,9] The risk factor that we found in this patient are hypertension, dyslipidemia, cigarette smoking and physical inactivity.

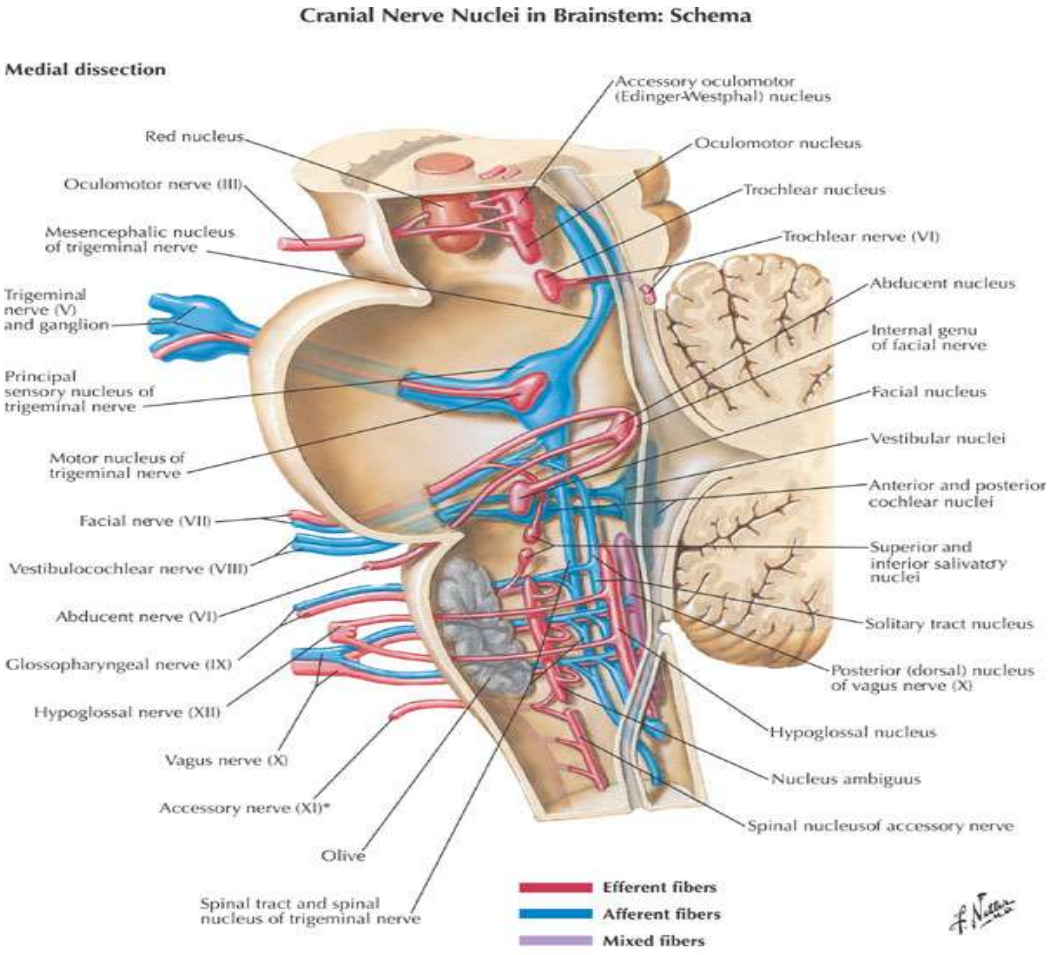


**Figure 3.3** Anatomy of Brainstem
Source:Kaye[4]

Isolated facial nerve palsy usually manifests as Bell's palsy, Bell's palsy appeared less likely because of the acuity of his presentation, encephalopathy-like imaging, and hypertension. The case report by Agarwal et al about pontine stroke presenting as isolated facial nerve palsy mimicking Bell's palsy, showed unusual case is one in which the patient appeared to have Bell's palsy but turned out to have a pontine infarct. The facial nerve has a predominant motor component which supplies all muscles concerned with unilateral facial expression. Anatomic knowledge is crucial for clinical localization. Bell's palsy accounts for around 72% of facial palsies. Other causes such as tumors and pontine infarcts can also

present as facial palsy. Isolated dorsal infarct presenting as isolated facial palsy is very rare. Case report by Agarwal emphasizes that isolated facial palsy should not always be attributed to Bell's palsy. It can be a presentation of a rare dorsal pontine infarct.[9]

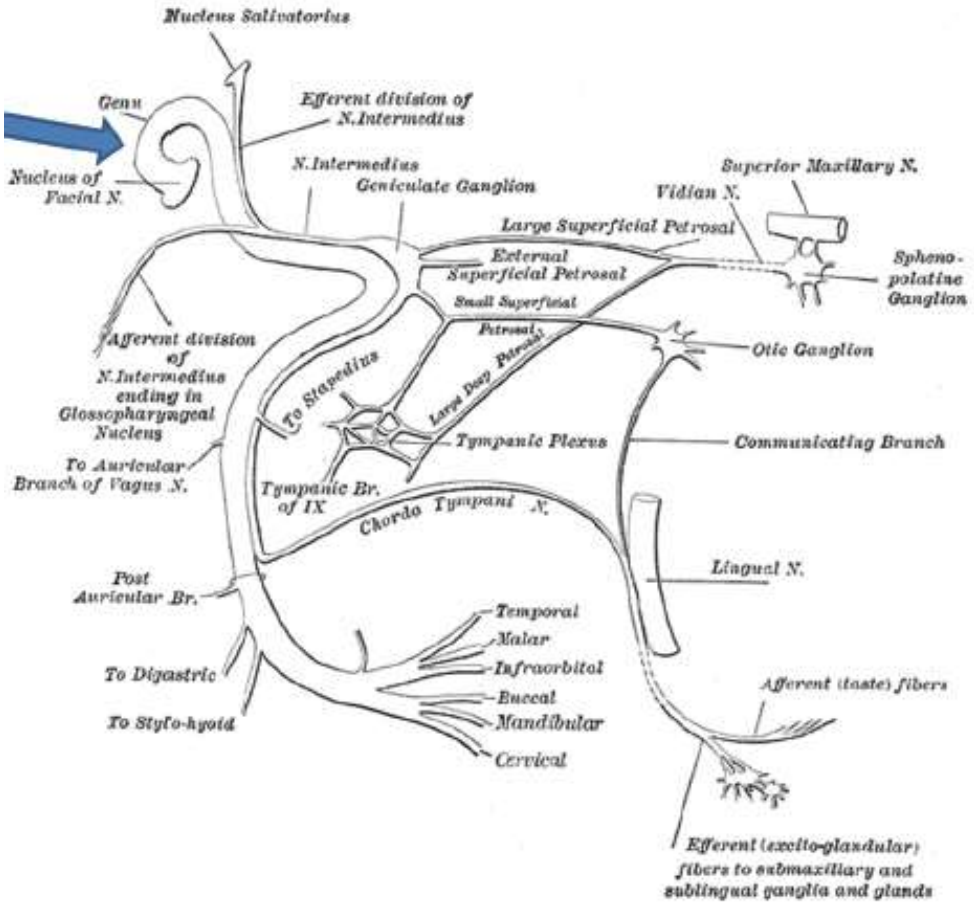


**Figure 3.3** The facial motor nucleus is located in the lower third of the pons. The nerve roots, after arising from the motor nucleus, pass around the abducens nerve nucleus as they emerge from the brainstem
Source:Agarwal[9]

When patient reports binocular double vision, anatomic localization is again critical, and the pattern of misalignment becomes all important, both Computed Tomography (CT) and MRI may provide the necessary information regarding the extraocular muscles. MRI is more sensitive to the various changes associated with inflammation or infiltration, but CT well delineates the size of the extraocular muscles, particularly on direct coronal image.[10]

The MRI findings in this case was infarct in the pons. The study that was performed by Eggenberger et al about the prognosis of ischemic INO showed that thirty three patients with ischemic-related INO, when performed magnetic resonance imaging (MRI) demonstrated the causative infarct in only 52% of cases, the presence of an MRI-demonstrable lesion was not significantly associated with prognosis for resolution, MRI has limited yield in demonstrating the causative infarct.[10,11]

MRI diffusion-weighted imaging (DWI) has been shown to have an advantage over CT in the detection of acute ischemic stroke, but even DWI can lead to false negative diagnoses within the first 24 hours after presentation. Such false-negative findings are more common in strokes involving the posterior circulation, including the brainstem. In a study of 139 stroke patients, Oppenheim et al found that 5.8% patients had negative MRI findings within the first 24 hours after presentation. Repeat MRI performed after 24 hours of onset maybe helpful in detecting such lesions which are initially negative on MRI.[10,11]

Patients treated with 1000mg/day citicoline. Citicoline, an intermediate in the biosynthesis of phosphatidylcholine (PtdCho), has shown beneficial effects in various CNS injury models and neurodegenerative diseases. Citicoline as a neuroprotective studies in transient cerebral ischemia suggest that citicoline might enhance reconstruction (synthesis) of PtdCho and sphingomyelin, but could inhibit the destructive processes (activation of phospholipases). In radiological assessments, it was shown that citicoline was able to induce a reduction in infarct volume in some patients.[11,12]

The prognosis of quo ad vitam is dubia because patient have hypertension, dyslipidemia and cigarette consumption; quo ad bonam is dubia because MRI brain finding showed infarct. The patient got treatment neuroprotector, anti-hypertension, antithrombolytic, lipid lowering agent and stop smoking. The study by Kim et al showed thirty patients presenting with INO without (n = 12) or with (n = 18) minimal other neurologic signs were studied. The INO eventually disappeared in all patients, tending to last longer ($p = 0.05$) when it was associated with other neurologic signs. The study by Eric et al 78.8% demonstrated

resolution of diplopia in primary position with an average time to resolution of 2.25 months. The presence of associated neurologic symptoms (vertigo, ataxia, dysarthria, facial palsy, pyramidal tract signs) correlated with a worse prognosis for resolution of diplopia. Similar to ischemic ocular motor palsies, most ischemic-based INO become asymptomatic in primary position over 2 to 3 months. The presence of associated features correlated with persistent diplopia.[7,10]

## IV. Conclusion

Internuclear ophthalmoplegia is one MLF-related syndrome that represents a useful model by which to objectively characterize a distinctive neurologic syndrome and its corresponding disability, with associated imaging measures of brain tissue injury. INO is a disorder of eye movements, characterized by adduction impairment combined with contralateral dissociated abduction nystagmus. The functional prognosis of these patient is dubia and quo ad functionam is dubia.

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