

Pure isolated unilateral internuclear ophthalmoplegia from ischemic origin : report of a case and literature review

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Summary

Purpose : To report a case of pure isolated unilateral internuclear ophthalmoplegia from ischemic stroke, and to review its literature.

Methods : A 55-year old man, with a history of long-standing diabetes mellitus, developed acute-onset left internuclear ophthalmoplegia. MRI revealed a small paramedian dorsal pontine infarct ventral and lateral to the aqueductus cerebri. Intracranial MR angiography was normal. A systematic search was performed of the literature from January 1980 to December 2004 by using MEDLINE and EMBASE. Case reports with or series including patients with negative MRI findings were excluded.

Results : Nine cases of pure isolated MRI-proven unilateral INO resulting from ischemic stroke including this one, have been reported. In over 75% recovery was reported.

Conclusion : Isolated unilateral internuclear ophthalmoplegia can be the sole manifestation of ischemic stroke and generally carries a good prognosis.

Introduction

Knowledge of the topographical anatomy of the ocular motor pathways is important in localizing brainstem lesions. Internuclear ophthalmoplegia (INO) is clinically characterized by adduction paresis of the eye ipsilateral to the side of the lesion and dissociated abduction nystagmus of the contralateral eye (Miller and Newman, 1998). Convergence may provide clinical indication on the topographical location of the pathological injury : lesions involving the medial longitudinal fasciculus (MLF) in the upper midbrain may be associated with loss of convergence (so-called anterior INO). The mechanism responsible for this loss of convergence is a matter of debate, but could be the result of damage of a subgroup of medial rectus motoneurons, the group C of Büttner-Ennever and Akert (1981). However despite the fact that the ipsilesional medial rectus appears weak it often can be activated during convergence, as premotor

vergence command reaches motoneurons of the medial rectus subnucleus from the rostral midbrain, and not the MLF. Alternatively, sparing of convergence might indicate involvement of the MLF at the level of the pons (often inappropriately referred to as posterior INO) (Miller and Newman, 1998). The dissociate nystagmus of the abducting eye reflects central adaptation in response to the adduction weakness (Zee *et al.*, 1987).

The MLF is not only the major route by which the neural signals for horizontal and vertical eye movements are transmitted, but also conveys the vestibulo-ocular reflexes, which join the MLF at the mid-pons. These vestibulo-ocular pathways are most likely responsible for skew deviation and torsional nystagmus observed in an extensively damaged MLF (Dehaene *et al.*, 1996 ; Tilikete and Vighetto, 2000).

INO, in association with other neurological manifestations is most commonly observed in vascular and demyelinating disease (Müri *et al.*, 1985 ; Miller and Newman, 1998 ; Leigh *et al.*, 1999 ; Moncayo and Bogousslavsky, 2003 ; Bolaños *et al.*, 2004 ; Kim, 2004). Despite the vascular anatomy and the close proximity to other eloquent brainstem structures, isolated unilateral INO of ischemic origin is rather uncommon, and accounts for approximately 12% of patients with infarcts restricted to the paramedian pons (Kataoka *et al.*, 1997). The aim of this study is to report a case of pure isolated unilateral INO from ischemic stroke, and to review its literature. A systematic search was performed of the literature from January 1980 to December 2004 by using MEDLINE and EMBASE with the following terms : internuclear ophthalmoplegia, stroke, infarction, pons, brainstem, midbrain, medial longitudinal fasciculus. In addition, the references of the articles returned from these databases were examined to collect other pertinent reports. Standard neurology and neuroophthalmology textbooks were also consulted. Case reports with or series including patients with negative MRI findings were excluded.

Case report

A 55-year-old man, with a history of long-standing diabetes mellitus, presented with sudden-onset diplopia, blurring of vision and dizziness. Neurological examination revealed normal gaze of the eyes in primary position. On attempted rightward gaze there was adduction paresis of the left eye. Right ocular movement was normal in any direction, but horizontal nystagmus appeared on rightward gaze. Convergence in both eyes was preserved. His pupils showed isocoria and responded promptly to light. Vertical eye movements (including vertical saccades and pursuit, optokinetic nystagmus and vestibulo-ocular reflexes) were normal, and no skew deviation or vertical nystagmus was observed. The rest of the neurological examination was unremarkable. His ocular symptoms were summarized as comprising a left INO. His blood pressure was 140/85 mmHg. Serum glucose level was 12.4 mmol/L and HbA1C 6.2%. Peripheral blood counts, erythrocyte sedimentation rate, serum electrolytes, creatinine, lipid profile, liver function tests, and antinuclear antibodies were normal. ECG and echocardiogram were normal. MRI revealed a small paramedian dorsal pontine vascular infarction ventral and lateral to the aqueductus cerebri (Fig.). Intracranial MR angiography was normal. The INO resolved within three months.

Discussion

INO forms part of several ischemic pontine and mesencephalic syndromes. However in the majority of these cases, particularly when related to vascular infarction, other tegmental pontine structures are involved. The pontine tegmentum is supplied at the rostral level by branches from the superior cerebellar artery and at the caudal level by branches from the anterior inferior cerebellar artery. In addition both brainstem levels receive long penetrating end-arteries of the basilar artery. The segmental distribution involvement of the paramedian small-caliber perforating end-arteries result in unilateral ischemic lesions in the brainstem, damaging the ipsilateral median tegmental pontine structures such as MLF, lemniscal or spinothalamic sensory tracts, trigeminal and facial nuclei (and/or fasciculi), and horizontal gaze centers and their connections (abducens nucleus and PPRF) (Bassetti *et al.*, 1996; Tatu *et al.*, 1996). The pathophysiological mechanism underlying ischemia in these isolated small pontine lesions is presumably based on microemboli or lipohyalinosis (Tatu *et al.*, 1996). Since MRA of the brainstem in our patient was normal either mechanism could have accounted for the patient's lesion. Furthermore, additional accompanying ipsilateral ischemic lesions – in our case ventral to the reference lesion – have been reported in 40% of patients, and often have no clinical expression (Kim, 2004).

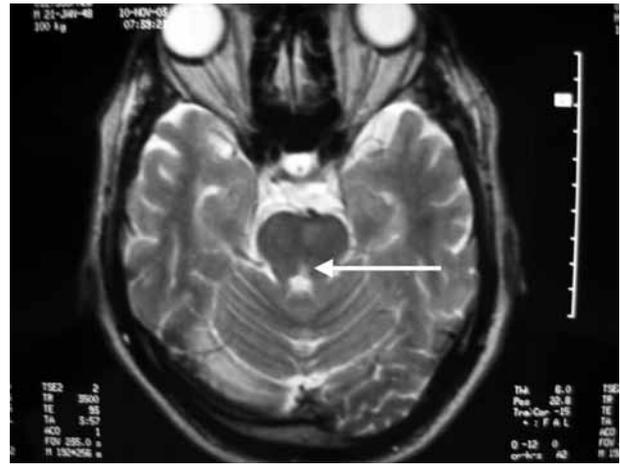


FIG. 1. — Axial brain MRI (T2-weighted image) through the upper pontine level showing a nodular region of high signal intensity just left of the midline involving the left MLF (arrow).

Although MRI has markedly improved the capacity for detecting lesions in the MLF region in patients with ischemic INO, studies indicate that only 30-52% of these ischemic lesions could be identified by this neuroimaging technique (Bolaños *et al.*, 2004; Eggenberger *et al.*, 2002; Marx *et al.*, 2002). This indicates that almost the majority of ischemic lesions are probably too small or too early to be detected. Hence the true incidence of isolated ischemic INO may be underestimated. Recently, a combination of T2- and diffusion-weighted imaging has proven to be most sensitive for the detection of brainstem infarctions (Schmidt *et al.*, 2004). Unlike in our case, more than 50% of patients present with abnormalities in the vertebrobasilar circulation that could account for the infarction (Kim, 2004). So far only 9 cases - including this one - of pure isolated MRI-proven unilateral INO resulting from ischemic stroke have been reported (Table).

Unlike, in many other reports this patient did not present in the initial stage with one-and-a-half syndrome, suggesting concomitant involvement of the PPRF (Bolaños *et al.*, 2004; Kim, 2004). Furthermore, convergence was spared clinically indicating a unilateral lesion in the pons or caudal mesencephalon.

Generally, patients with MRI proven ischemic lesions in the MLF have a smaller chance of recovery compared to MRI-negative ischemic INO. Particularly the association of ischemic INO with other neurological manifestations such as vertigo, ataxia, dysarthria and pyramidal signs carries a poor prognosis for recovery (Eggenberger *et al.*, 2002). In one study resolution of the INO was in the order of 40% (Bolaños *et al.*, 2004). In contrast, in their series of 33 patients with clinical diagnosis of suspected ischemic INO, Eggenberger *et al.* (2002) reported more optimistic values for the resolution of ischemic INO (up to 80%) with their patients becoming asymptomatic over a 2-3 month

Table

Clinical and MRI characteristics of patients presenting with pure isolated ischemic INO.

Author	Age (yr)/gender	Risk factors/ Trigger factor	INO	Location of infarction (MRI)	Recovery (duration)
Kim	67/F	DM	Lt-INO + Rt exotropia	Lt rostral pons	1 month
Kim	67/M	Smoking	Rt-INO + Lt exotropia	Rt rostral pons	7 days
Kim	45/M	Smoking	Rt-INO	Rt rostral pons	5 days
Tilikete and Vighetto	66/F	HTN/angioplasty	Rt-INO + left SD	Rt rostral pons	1 month
Tilikete and Vighetto	52/M	dyslipidemia	Rt-INO + left SD	Rt paramedian mesencephalon	7 days
Eggenberger et al.	70/F	HTN/PTCA	Lt-INO + SD	Lt dorsal pons	4 months
Schmidt et al.	65/M	none	INO (NS)	Rt midbrain tegmentum	NR
Schmidt et al.	44/M	none	INO (NS) + SD	Rt midbrain tegmentum	NR
Our patient	55/M	diabetes	Lt-INO	Lt dorsal pons	3 months

DM, diabetes mellitus ; HTN, hypertension ; INO, internuclear ophthalmoplegia ; Lt, left ; NR, not reported ; NS, not specified ; PTCA, percutaneous angioplasty ; Rt, right ; SD, skew deviation.

interval. However several limitations make the interpretation and extrapolation of their data difficult : 1) of the patients who had MRI, the majority did not have compatible MLF lesion (44%), 2) the diagnosis was retrospectively and based on records from the pre-MRI era, which may have accounted for misclassification of cases (Eggenberger *et al.*, 2002).

In conclusion, isolated unilateral INO can be the sole manifestation of ischemic stroke and generally carries a good prognosis.

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