Title page

Title:

A rare cause for visual symptoms in multiple sclerosis: posterior internuclear ophthalmoplegia of Lutz, a historical misnomer.

Authors:

J.A. Nij Bijvank, MD^{1,2}, L.J. Balk, PhD¹, H.S. Tan, MD, PhD², B.M.J. Uitdehaag, MD, PhD¹, L.J. van Rijn, MD, PhD², A. Petzold, MD, PhD^{1,2,3}

¹Neurology, Neuroscience Amsterdam, VUmc MS Center, Amsterdam, The Netherlands, ²Expertise Centrum Neuro-ophthalmology, VU University Medical Center, Amsterdam, The Netherlands, ³Moorfields Eye Hospital, London, United Kingdom

Corresponding author:

J. Nij Bijvank

VU Medical Center

De Boelelaan 1118

1081 HV Amsterdam

Phone 020-4445063

E-mail j.nijbijvank@vumc.nl

Abstract:

Our 22 year old patient with multiple sclerosis had visual complaints, consisting of difficulties focusing and gaze evoked diplopia. An internuclear ophthalmoplegia (INO) was suspected and we recorded the eye movements with infrared-oculography. Based on the decreased ratio between abduction and adduction peak velocity, she was diagnosed with posterior INO of Lutz, rarely described in literature. It is defined by an abduction deficit with a prenuclear origin, but the localization and mechanism are still debated.

Keywords:

ocular motility; diplopia (double vision); multiple sclerosis; internuclear ophthalmoplegia

Text

A 22 year old female patient with an one year history of relapsing remitting multiple sclerosis (MS) complained of difficulties focusing and brief episodes of horizontal gaze evoked diplopia. Symptoms occurred intermittently in rest, and increased whilst walking or cycling in busy environments. Her past medical and family history were unremarkable and she was not taking any medication.

On examination extraocular eye movements were full and convergence was normal. There was no abducting or adducting nystagmus, and no convincingly reproducible slowing of saccades on repeated testing and no oscillopsia. The reminder of her cranial nerve examination was normal. Her vestibulo-ocular reflex was normal. The optokinetic nystagmus was not tested. We thought we had not sufficiently excluded the possibility of an internuclear ophthalmoplegia (INO) and recorded the eye movements with high-frequency infrared oculography (Eyelink 1000 plus, SR Research Ltd., Canada). The recordings of the pro-saccades (figure 1A) showed a minimal delay in peak velocity of abduction of both eyes. The versional dysconjugacy index (VDI) for peak velocity was determined, more clearly illustrating the discrepancy between ab- and adduction. The VDI is a ratio calculated by dividing the abducting eye value by the adducting eye value for every saccade, and is used for quantification of INO, in which this ratio is higher than unity [1] (figure 1B). In this case, the mean VDI to the right was 0.81, and to the left 0.73, showing a relative delay in abduction to both sides. The same pattern could be shown on repeated assessment 4 months later.

Clinically, she was diagnosed with posterior INO (pINO) of Lutz, which may contribute to the generation of her symptoms. This condition is first described by the German Ophthalmologist Anton Lutz in 1923 [2], and only a few cases of pINO in MS have ever been reported [3]. In contrast, a classical INO due to demyelination of the medial longitudinal fasciculus (MLF) can be detected by oculography in about a quarter of MS patients [4].

There is a discussion both about the anatomical location and naming of the pINO of Lutz, the latter being a misnomer. The term 'posterior' was suggested by Lutz because he assumed involvement of posterior supranuclear fibers of the pons to innervate the lateral rectus muscle [2], which has been refuted. In absence of a responsible anatomical structure, Gunther Kommerell proposed the phenotypic description 'INO of abduction' [5]. Synonymous terms used in literature are 'reverse INO' and 'pseudoabducens palsy'. The nomenclature must not be confused with Cogan's definition of an 'anterior' and 'posterior' INO caused by lesions either to the anterior midbrain or the posterior pons.

Clinically, convergence is impaired in the former and spared in the latter [6].

Three plausible mechanisms are described in literature. First, a failure to relax the medial rectus muscle due to a midbrain lesion [3,7]. Second, an interruption of the projection of internuclear neurons to the contralateral abducens nucleus via the MLF due to a midbrain lesion [8,9]. Third, lesions of the paramedian pontine reticular formation (PPRF) causing decreased activation of specific burst neurons for the abducting eye [10,11]. For the rightward pINO in our patient, revision of the MRI (figure 2) was consistent with the third option, showing a T2 hyperintense lesion in the posterior pons.

Clinically, a pINO of Lutz can be distinguished from a 6th nerve palsy, by (1) alignment of the eyes and no diplopia in primary position, (2) unrestricted abduction with pursuit eye movements, (3) preserved abduction (saccades) with caloric testing and the vestibulo-ocular reflex, and (4) possible adduction nystagmus of the contralateral eye on lateral gaze [3]. The findings in our case suggest that infrared oculography has an added value as a clinical tool for detailed investigation of this yet enigmatic sign and for unexplained visual complaints in multiple sclerosis. Prospective studies will be required to investigate the prevalence of pINO in MS.

Authors disclosures and conflicts of interest*

J.A. Nij Bijvank: reports no disclosures

L.J. Balk: the VUmc MS Centre received research support from TEVA

H.S. Tan: reports no disclosures

B.M.J Uitdehaag: has received consultancy fees from Biogen Idec, Genzyme, Merck Serono, Novartis,

Roche and Teva

L.J. van Rijn: reports no disclosures

A. Petzold: chairman of ERN-EYE neuro-ophthalmology, member of the steering committee for the OCTiMS study (Novartis), no consulting fees. Performs OCT QC for the Passos study (Novartis), receives consulting fees.

*no disclosures or conflicts of interest are related to the submitted work

Ethical standards statement

All human studies have been approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

References

- Frohman EM, Frohman TC, Zee DS, MCColl R, Galetta S (2005) The neuro-ophthalmology of multiple sclerosis. Lancet Neurol 4:111-121. doi: 10.1016/S1474-4422(05)00992-0
- Lutz A (1923) Ueber die Bahnen der Blickwendung und deren Dissoziierung. Klin Montatsble Augenheilkd 70:213-235
- Thömke F, Hopf HC (2001) Abduction paresis with rostral pontine and/or mesencephalic lesions:
 Pseudoabducens palsy and its relation to the so-called posterior internuclear ophthalmoplegia of
 Lutz. BMC Neurol 1:4. doi: 10.1186/1471-2377-1-4
- Nij Bijvank JA, Balk LJ, Tan HS, Uitdehaag VMJ, van Rijn LJ, Petzold A (2016) Prevalence of internuclear ophthalmoplegia in multiple sclerosis: a prospective infrared oculography study. Mult Scler 22(S3):88–399. doi: 10.1177/1352458516663081
- Kommerell G (1975) Internuclear Ophthalmoplegia of Abduction: Isolated Impairment of Phasic Ocular Motor Activity in Supranuclear Lesions. Arch Ophtalmol 93:531-534.
 doi:10.1001/archopht.1975.01010020547013
- 6. Cogan DG (1956) Neurology of the Ocular Muscles, 2nd edn. Charles C Thomas, Springfield
- 7. Pullicino P, Lincoff N, Truax BT (2000) Abnormal vergence with upper brainstem infarcts: pseudoabducens palsy. Neurology 55:352-358. doi: http://dx.doi.org/10.1212/WNL.55.3.352
- Rufa A, Cerase A, Annunziata P, De Santi L, Buccoliero R, Monti L, Federico A (2010) Transient supranuclear paresis of the abduction in viral encephalitis of the brainstem. Neurol Sci 31:653-655. doi: 10.1007/s10072-010-0339-9
- Remler B, Leigh RJ (2008) Posterior internuclear ophthalmoplegia of Lutz revisited: report of a
 case associated with a midbrain lesion. In: Leigh RJ, Devereaux MW (ed) Advances in
 understanding mechanisms and treatment of infantile forms of nystagmus. Oxford University
 Press, New York, pp 156-161

- 10. Zhou W, King WM (1998) Premotor commands encode monocular eye movements. Nature 393:692-695. doi: 10.1038/31489
- 11. King WM (2011) Binocular coordination of eye movements Hering's Law of equal innervation or uniocular control? Eur J Neurosci 33:2139-2146. doi: 10.1111/j.1460-9568.2011.07695.x

Figure captions

- Fig. 1 Saccadic movements of our patient with posterior INO of Lutz to both sides.
- a. Recording of eye position with infrared oculography. Left graph shows a saccade to the right, indicated by upward deflection of the traces, the right graph a saccade to the left, indicated by downward trace deflection. During the saccades, there is slowing of the abducting movements (arrows)
- b. Schematic diagram of the saccadic movements of typical binocular INO (left) versus binocular posterior INO (right), nystagmus of the contralateral eye can be present (black arrows)

Fig. 2 Magnetic resonance imaging of the lesion.

Brain magnetic resonance imaging revealed a T2 hyperintense lesion (arrow) in the posterior pons which involves part of the paramedian pontine reticular formation (PPRF), the medial longitudinal fasciculus (MLF), and right nucleus prepositus hypoglossi (NPH). There was a leftward gaze deviation during MR imaging which was not due to a horizontal gaze palsy