Internuclear Ophthalmoplegia as a Presenting Neuro-Ophthalmic Manifestation in a Case of Multiple Sclerosis

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Abstract

Multiple Sclerosis is a disease which has well documented neuro-ophthalmic manifestations of optic neuritis and internuclear ophthalmoplegia. Optic neuritis is characterised by subacute painful visual loss, reduced colour vision, contrast sensitivity and visual field loss. A case history of multiple sclerosis in a 25 year old female is presented. The presenting symptoms were blurred vision and dizziness on laevoversion and tingling in the left foot. Examination of ocular movements demonstrated limitation of right adduction and left abduction nystagmus with diplopia on laevoversion, consistent with unilateral right internuclear ophthalmoplegia. Although a diagnosis of optic neuritis was eventually made, this was not consistent with the presenting symptoms. This case highlights the importance of a full orthoptic investigation of neuro–ophthalmic patients.

Key Words:
multiple sclerosis, internuclear ophthalmoplegia, optic neuritis, orthoptic investigation.

Multiple Sclerosis

Multiple sclerosis (MS) is the most common idiopathic inflammatory disease of the central nervous system [1]. According to Weinshenker [1], MS 'begins as a relapsing–remitting disease and evolves secondarily into a progressive neurological illness in 60% of patients'. Optic neuritis and eye movement control defects, particularly internuclear ophthalmoplegia are common in MS [2].

Optic Neuritis

Optic Neuritis is a frequent forerunner of MS and is characterised according to Warner and Lessells [2], by 'subacute painful visual loss, with disproportionate loss of colour and contrast sensitivity, central or caecocentral scotoma, and an afferent pupillary defect'.

These "classic" visual field defects have been challenged by the recent Optic Neuritis Treatment Trial conducted in the USA, which reported that only 8% of patients showed central or caecocentral scotomas [3].

Arcuate, altitudinal or nasal step defects were found in 20%, and diffuse (nonfocal) depressions were present in 48% of patients.

Abnormalities in contrast sensitivity in patients with optic neuritis in the Treatment Trial, were reported to be as high as 98% [3].

Beck et al [4] state that even when visual acuity returns to normal, abnormalities of other visual functions such as visual field, colour vision and contrast sensitivity defects persist.

Internuclear Ophthalmoplegia

Patients with internuclear ophthalmoplegia (INO) are usually asymptomatic and rarely complain of diplopia. Symptoms of oscillopsia and a sudden onset of heteronymous diplopia on side gaze are reported by some patients [5,6,7].

Internuclear ophthalmoplegia may be unilateral or bilateral, more commonly reported to be bilateral and is characterised by the presence of several features:

1. limitation of adduction of one eye (on the side of the lesion) or of both eyes;

2. jerky horizontal nystagmus of the contralateral eye or eyes on abduction, with the fast phase in the direction of gaze.

Duane [5] reports that nystagmus of much smaller amplitude is is always present in the paretic adducting eye, but may require oculography for detection.

3. retention of convergence in most cases [5,6,8,9].

In addition, bilateral INO is often associated with gaze evoked vertical nystagmus and impaired vertical pursuit [6,7]. The ocular movement abnormalities seen in INO are present regardless of the stimuli, be it for smooth pursuit, saccadic or vestibulo-ocular reflex movement.

Brainstem Control of Ocular Movement

Excitatory impulses from the horizontal gaze centre within the paramedian pontine reticular formation (PPRF) of the pons, synapse in the ipsilateral abducens (VI) cranial nerve nucleus. Internuclear axons then cross and ascend via the contralateral medial longitudinal fasciculus (MLF) to the oculomotor (III) cranial nerve nucleus at the level of the midbrain [5,6]. The MLF axons convey saccadic, vestibulo-ocular and pursuit signals in this manner [5] (see Figure 1).

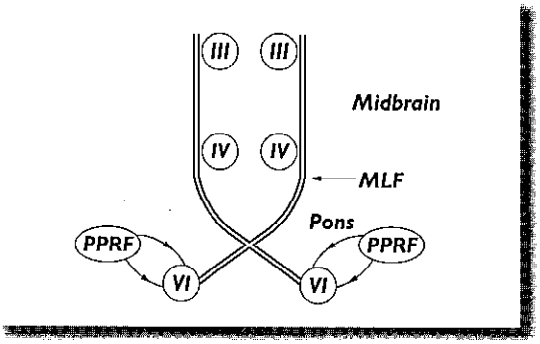

Figure 1
Schemmatic representation of brainstem ocular control.

Unilateral interruption of the MLF between the mid-pons and the III cranial nerve nucleus, disconnects the ipsilateral medial rectus subnucleus, resulting in failure of adduction during horizontal gaze. However, the same medial rectus subnucleus usually functions for convergence. Under the constraints of Herring's Law of equal innervation, excessive signals are supplied to the contralateral lateral rectus yoke muscle, which is the probable cause of the dissociated nystagmus seen in INO [6,9].

According to Duane [6], any process that structurally or functionally interrupts conduction in the MLF may potentially result in an INO.

Case History

The following case highlights the importance of ocular motility assessment in combination with other ophthalmic investigations.

MN a 25 year old Asian female lawyer presented complaining of a two week history of slightly blurred left vision on laevoversion and dizziness on laevoversion. In addition, she reported a tingling sensation in the left foot. These symptoms had increased in severity during this period.

Initial ophthalmic assessment showed:

- Visual acuity (uncorrected):
  Right: 6/12 +2 Left: 6/12 −1
  ph: 6/6 −2 6/9 +2
- Visual fields:
  Full on confrontation.
- Anterior segments, media and fundi were all within normal limits. A mild degree of bilateral myopia was diagnosed.
- Intraocular pressures were 12mmHg right, 16mmHg left.
- Some colour desaturation was reported by the patient.
- There was no evidence of relative afferent pupillary defect (RAPD).

A Bjerrum visual field test was requested on the following day and the result showed a slight enlargement of the blindspot superiorly and temporally on the right and a moderate enlargement of the blindspot inferiorly on the left.

Contrast sensitivity and colour vision testing were requested at a fortnightly follow up visit.

Contrast Sensitivity

Contrast sensitivity was assessed using the Pelli-Robson Chart. The Pelli-Robson Chart is quick and easy to administer. It is most appropriate as a screening device for contrast sensitivity but must be recognised as not being designed to be sensitive to retinal image quality [10].

Contrast sensitivity expresses the ability of the visual system to detect spatial contrast, and thus is really a measure of visual sensitivity [10,11]. The Pelli-Robson Chart uses letters of constant size (low spatial frequency), rather than gratings that decrease in size. Hence the test gives a single measure of contrast sensitivity (known as peak contrast sensitivity) rather than a contrast sensitivity function curve. The test uses Sloan letters which appear in triplets on the chart, each triplet having letters of the same contrast. The lowest contrast 'triplet' in which two out of three letters are named correctly is recorded.

The contrast threshold is recorded as the log of the reciprocal of contrast sensitivity [10].

Normal standards are 1.80 log units or above for a person younger than fifty years and 1.65 log units or above for a person older than fifty years [10].

- The Pelli-Robson Chart log unit scores for MN were:
  Right: 1.80 – normal
  Left: 1.50 – reduced

Colour Vision

Colour vision was tested using the Roth 28 Hue Test. This test is based on the Farnsworth Munsell 100 Hue. This test is sensitive to acquired dischromatopsia and may detect congenital colour vision abnormalities [12]. For this case it was the test of choice as it is easy to perform and relatively quick.

- Results: (see Figures 2a & 2b)
  Right: Few errors, indicating a mild acquired colour vision defect.
  Left: Many errors, but no axonal pattern, indicating a significant acquired colour vision deficit.

Orthoptic Assessment

- Cover Test:
  Near and distance–exophoria with good recovery.
- Stereoacuity (Titmus):
  100 secs of arc
- Ocular Movements:
  Marked limitation of right adduction on laevoversion with left abducting nystagmus with blurred vision on left gaze and vague diplopia (see Figure 3).
- Convergence:
  Intact with a near point of 5cms
- Goldmann visual fields :
  Right: Depressed field superiorly
  Left: Significant enlargement of the blindspot.

MN was referred to a neuro-ophthalmologist who diagnosed an internuclear ophthalmoplegia and left optic neuritis consistent with a demyelinating condition.

Neuro–ophthalmological investigation included Magnetic Resonance Imaging (MRI) and VERs. The MRI showed multiple areas of unidentified bright objects (UBOs) and the VERs showed the central field response as being delayed from the left eye and absent from the right eye.

The diagnosis of MS was made.

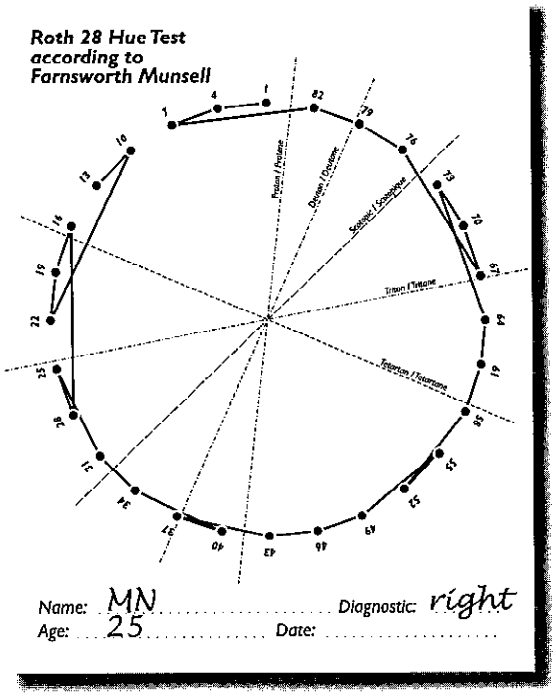

Figure 2a

Roth 28 Hue Test Right Eye

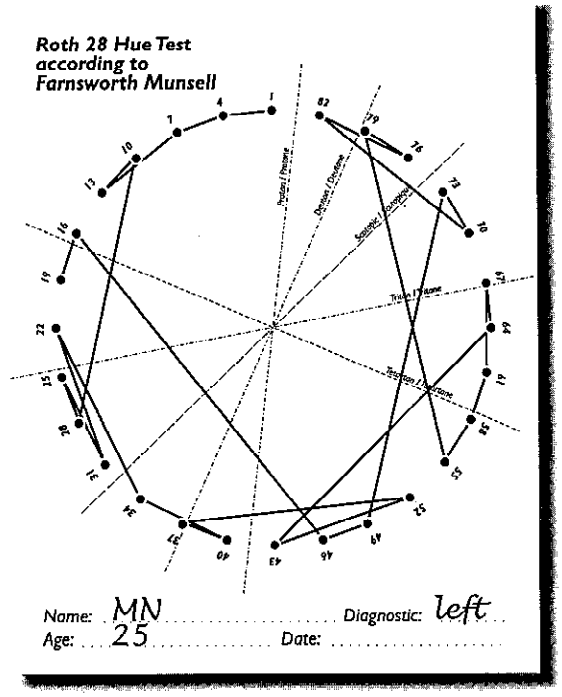

Figure 2b

Roth 28 Hue Test Left Eye

MN was administered with 500mg of intravenous methyl prednisolone for 4 consecutive days and with oral prednisone 75mg per day for 7 days.

MN was asymptomatic for 24 hours after the onset of treatment and on subsequent visits continues to be symptom free.

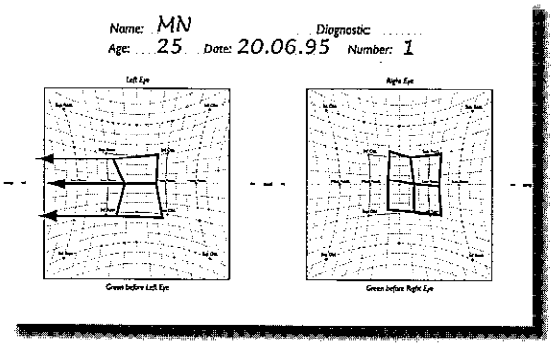

Figure 3

Hess Chart showing limitation of adduction Right Eye

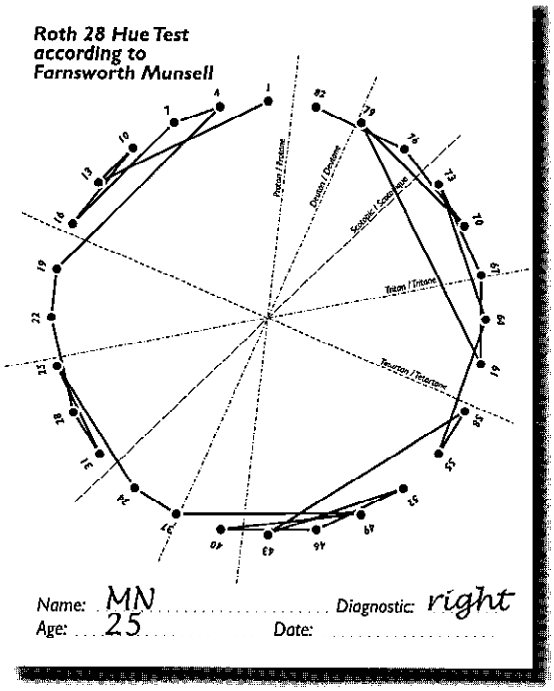

Figure 4a

Roth 28 Hue Test Right Eye

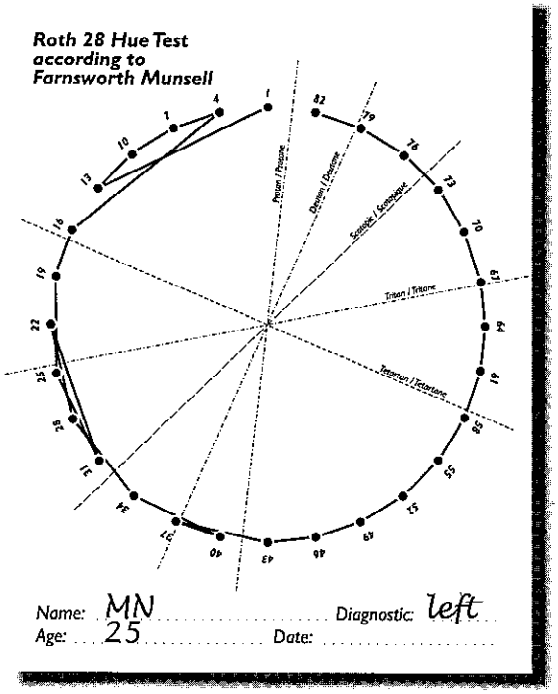

Figure 4b

Roth 28 Hue Test Left Eye

The patient is to be followed up by the neuro-ophthalmologist and to have repeat MRI scans.

1st Follow–Up Orthoptic Assessment; 17 Days Later

- Cover test–near and distance:
  Small exophoria with rapid recovery
- Convergence:
  7cm left eye failed with diplopia
- Ocular Movements:
  No limitation of movement
- Contrast sensitivity: Pelli-Robson Chart
  Right 1.65 log units
  Left 1.50 log units
- Colour vision with the
  Roth 28 Hue Test (see Figures 4a & 4b):
  Right: multiple errors indicating a deterioration in colour discrimination.
  Left: minimal errors, showing a marked improvement in colour discrimination.

2nd Follow–Up Orthoptic Assessment; 1 Month Later

- Visual Acuity (uncorrected):
  R 6/18 L 6/18
  ph 6/6 pt ph 6/12
- Ocular Movements : no limitation of movement. Normal horizontal and vertical saccades.
- Contrast sensitivity scores were unchanged from the previous assessment.
  Pelli-Robson Chart
  Right 1.65 log units
  Left 1.50 log units

Colour vision with Roth 28 Hue Test Right and left showed an increased error pattern indicating a further deterioration in colour discrimination(see Figures 5a & 5b).

Goldmann visual fields showed bilateral enlargement of the blind spots.

Discussion

Review of the current literature suggests that the patient who may ultimately be assigned a diagnosis of MS, presents because of loss of vision which may vary in severity from a slight deficit in the field of vision to complete loss of light perception [4].

Although the diagnosis of MS was eventually made in this patient, she did not present with the classical symptoms associated with

optic neuritis, (ie sudden loss of vision associated with pain on eye movements and a relative afferent pupillary defect) [13]. MN presented complaining of symptoms related to the INO. Symptoms of blurred vision on laevoversion and dizziness on laevoversion prompted MN to seek medical investigation.

Examination of ocular movements revealed a right INO which was an obvious clinical sign in this patient. Although the INO was easily recognised in MN, Muri and Weinburg [9] showed that the disjunction of horizontal saccades has proved to be a most sensitive diagnostic criterion of INO. In their study of 34 patients with MS, mild forms of INO (internuclear ophthamoparesis) were diagnosed with slowing of adduction saccades as the only clinical sign that could be detected. Duane [6] states that assessment of OKN may also disclose a subtle form of INO. This relies on demonstration of impairment of innervation of the medial rectus compared with its yoke and contralateral lateral rectus during horizontal saccades. Therefore, as clinicians it is essential that we routinely include saccadic eye movement testing in addition to assessment of versions so as to ensure that subtle signs of INO are detected.

The reduction of visual acuity at the initial and subsequent visits was only minimal in MN, however, this reduction in vision may have been complicated by the fact that MN had mild uncorrected myopia. The abnormalities in the visual fields, contrast sensitivity and colour vision present at the initial visit were the clinical indicators which led to a subsequent diagnosis of left optic neuritis.

Fleischman et al [14] and Saunders et al [15] state that these functions of vision are 'more sensitive indicators of optic nerve function than is visual acuity'.

At the follow up visits there was no evidence of the INO and the optic neuritis was thought to have resolved. However, the visual field, contrast sensitivity and colour vision results continued to show abnormalities. These findings are consistent with those reported by Beck et al [4] who state that, 'most patients have lasting symptoms of impairment of visual function and even when visual acuity returns to normal, abnormalities are common in other aspects of visual function such as visual field, colour vision and contrast sensitivity'.

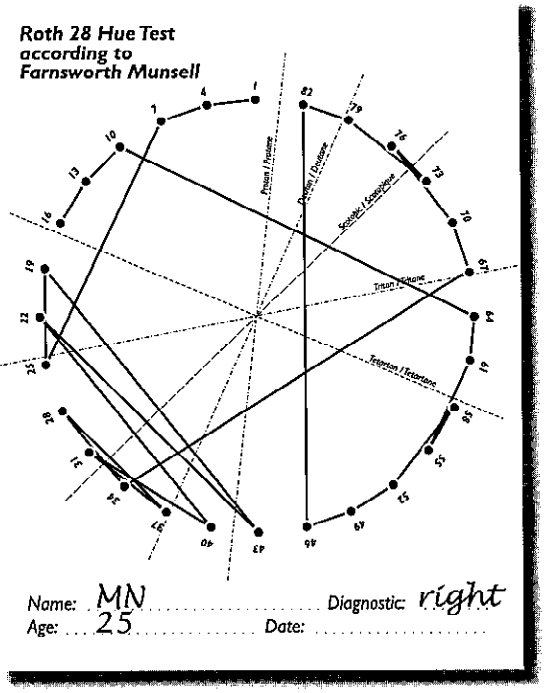

Figure 5a

Roth 28 Hue Test Right Eye

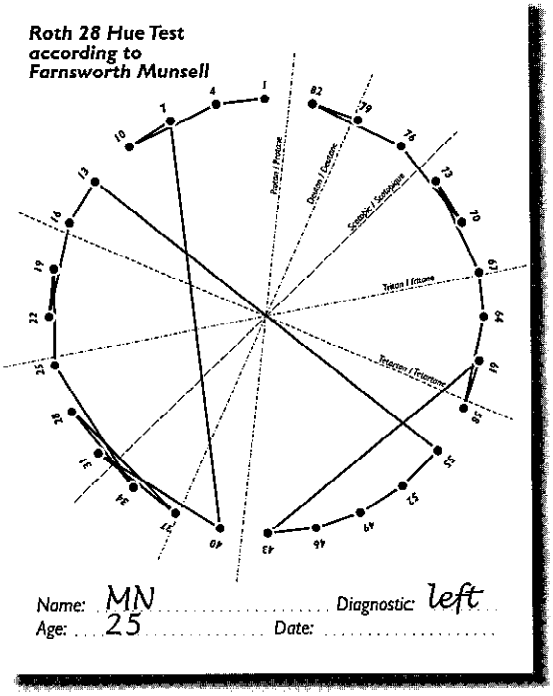

Figure 5b

Roth 28 Hue Test Left Eye

The defect in the visual field and colour vision present in the fellow (right) eye in MN at the initial assessment has increased in severity at subsequent testing along with a slight reduction in contrast sensitivity. Beck et al [16] looked at the abnormalities in the fellow eye and reported that 'abnormalities were found on measurement of visual acuity in 13.8%, contrast sensitivity in 15.4%, colour vision approximately 21% and visual fields in approximately 48% of patients'. However, they also stated that ' the majority of the fellow eye deficits resolved over several months' [16]. These

authors also reported, that the improvement of many of the visual deficits indicates that visual abnormalities detected in the fellow eye at the onset of unilateral optic neuritis may not represent pre-existing optic nerve demyelination, but rather acute loss concomitant with the symptomatic involvement of the fellow eye [16].

In a patient who presents with an attack of optic neuritis or INO which are indicative of demyelinating disease, MRI scanning is essential. The MRI clearly identifies areas of focal high white signal aberration, often reffered to as UBOs in periventricular cerebral regions [3]. The Optic Neuritis Treatment Trial, a multi-centre study conducted in the USA showed that MRI was the strongest predictor of the development of MS. Patients found to have two or more periventricular cerebral signal abnormalities had a 36% chance of developing MS after 2 years; patients with scans showing one signal abnormality had a 17% chance of developing MS; and those whose scans lacked these abnormalities had only a 3% chance [3]. The diagnosis of a demyelinating disease was confirmed in the case of MN following MRI which showed 'multiple UBOs'.

Corticosteroids have been widely used in the treatment of optic neuritis, however no properly controlled studies had ever evaluated the treatment. The Optic Neuritis Treatment Trial, (ONTT) was conducted to investigate the value of corticosteroids as treatment for optic neuritis.

The research consisted of three groups:

1. the oral prednisone
2. intravenous methylprednisolone followed by oral prednisone and
3. placebo.

The most significant conclusions to be drawn from the ONTT are:

1. That treatment with intravenous methylprednisolone followed by oral prednisone has no effect on visual function at least 1 year post treatment, but it reduced by more than 50% the 2 year rate of developing MS. This protective effect which began to wane at 2 years, was especially evident in those patients whose MRI scans manifested multiple signal abnormalities typical of MS.
2. Treatment with oral prednisone alone had no affect on visual recovery, and in fact increased the number of recurrences of optic neurtis [3].

Conclusion

This case history demonstrates the need to heed the patient's reported symptoms and the importance of a full orthoptic assessment in combination with ophthalmic investigation. Ocular motility assessment provided the diagnosis of the right INO which was causing the principal presenting symptoms. Having made the diagnosis of INO, the results of contrast sensitivity, visual field and colour vision testing aided a diagnosis of left optic neuritis. The clinical picture now more complete, prompted MRI which provided evidence of demyelinating disease and the requirement of intravenous corticosteroid treatment.

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