The natural history of brainstem ocular motility disorders due to vascular pathology

F.J. Rowe
Division of Orthoptics, University of Liverpool, UK.

C.P. Noonan
Department of Ophthalmology, Warrington Hospital, UK.

ABSTRACT: Introduction/objective To perform a cross sectional study of cases of ocular motility disorders due to brainstem vascular pathology. To review the types of ocular motility disorders documented in these cases and address the natural history of recovery.
Methods Each patient underwent a full Orthoptic and Ophthalmic examination. Complete neurological workup with appropriate CT/MR brain imaging was obtained. Patients with other brainstem pathology such as multiple sclerosis, degenerative or space occupying lesions were excluded.
Results A variety of ocular motility disorders were documented. These included cranial nerve palsies, ophthalmoplegia, nystagmus and abnormalities of saccadic and smooth pursuit movements. Treatment was mostly conservative with occlusion, filters and prisms and provision of support and coping strategies. Nine of the twelve patients were managed conservatively. Two of the nine patients had a return to normal ocular motility status within a 2-month period. Three patients required active intervention (Botulinum toxin (BT) or surgery) in addition to conservative treatment.
Conclusions: 16% (2/12 patients) improved to normal ocular motility status. This occurred within 2 months of initial insult. Eight other patients (67%) had a partial recovery with symptoms relieved either by conservative methods alone or by the addition of BT or surgery.

KEYWORDS: Brainstem, Ocular motility, Vascular pathology

INTRODUCTION

Brainstem vascular accidents, result in range of ocular motility disorders dependent on the area within the brainstem affected. These range from nuclear cranial nerve palsies, gaze palsies, nystagmus and eye movement (saccadic, smooth pursuit and vergence) difficulties. The associated general signs and symptoms such as hemiplegia, tremor, central Horner's syndrome and vertigo aid the diagnosis in many cases with confirmation by neuro-imaging of the brainstem area.

Medical advances over the past decade have lead, so it seems, to an increase in the number of patients seen in our clinics with brainstem ocular motility disorders. As a result of this perceived increase, a study was undertaken to review cases with brainstem vascular pathology to document the associated ocular motility problems, treatment given and final outcome.

METHODS AND MATERIALS

For the purposes of this study patients with an acute vascular event affecting the brainstem were included. Patients with brainstem symptoms secondary to multiple sclerosis, myasthenia gravis, progressive supranuclear palsy, space occupying lesion and infectious or inflammatory conditions were excluded.

A cross section analysis was undertaken and cases were reviewed over a twelve-month period from March 2002 to March 2003. Twelve cases were identified that adhered to our inclusion criteria. A further 19 cases were excluded. Brainstem pathology was confirmed by neurological

examination involving CT but mostly MR imaging. Each patient had a full ophthalmic and orthoptic assessment.

RESULTS

Seven females and five males were reviewed with an average age at presentation of 53 years (range 25 to 78 years). There was little difference in the average age of females (51 years; range 25 to 73 years) and males (56 years; range 42 to 78 years). Vascular lesions were due to infarction in eight cases and haemorrhage in four cases.

The ocular motility disorders included double elevator palsy, internuclear ophthalmoplegia, nuclear or fascicular third nerve palsy, fascicular sixth nerve palsy, gaze palsy and abnormal movement systems of saccades and smooth pursuits. See table 1. Ocular symptoms were reported by each patient either constantly or intermittently and included binocular diplopia, oscillopsia, blurred vision and reading difficulties. There were numerous generalised symptoms including hemiplegia, seventh nerve palsy, hand tremor, and difficulties with balance and speech.

Four of the twelve patients required no treatment. One patient with a unilateral internuclear ophthalmoplegia improved spontaneously over a 6 week period. Three patients were asymptomatic due to suppression in two patients and complete ptosis in one patient. Eight patients received conservative treatment, consisting of prisms, occlusion, or Bangerter filters. Two patients received BT injection, in addition to either occlusion or prisms, one preferring multiple injections and one not benefiting from their single BT injection. One patient had surgery for a double elevator palsy which was successful. The follow-up period at the time of this cross section analysis ranged from 6 weeks to 8 years from presentation (average 2½ years).

Two patients showed no recovery in ocular motility (over a period of 2 and 3 years) although both were asymptomatic, one with the use of prisms. Two patients had full recovery of ocular motility over a period of 6 weeks and 2 months. The remaining patients showed some improvement of ocular motility ranging from minimal (three patients), partial (three patients) and good (two patients) range of eye movement. This recovery was seen over a variable time period of 6 months to 8 years. No patient was symptomatic in the primary position at follow-up due either to the use of prisms or occlusion, presence of suppression or ptosis.

DISCUSSION

The ocular motility deficits recorded in these patients were varied. Double elevator palsy is a presumed interruption of supranuclear input from the vertical upgaze areas in the midbrain (Jampel & Fells 1968, Lessel 1975. Patients typically have a hypotropia in the primary position with pseudoptosis and true ptosis. Our two patients had a complete limitation of elevation with hypotropia and pseudoptosis.

A lesion of the medial longitudinal fasciculus (MLF) will result in internuclear ophthalmoplegia (Bronstein et al. 1990) with loss/impairment of adduction of the contralateral eye due to involvement of interneurons from the ipsilateral sixth nerve nucleus to the contralateral medial rectus subnucleus. Vascular events when diffuse cause bilateral internuclear ophthalmoplegia and when more focal cause unilateral internuclear ophthalmoplegia due to the midline separation of the blood supply to the two halves of the brainstem. We reviewed two cases of internuclear ophthalmoplegia, one unilateral and one bilateral with typical characteristics of limited adduction and abducting nystagmus of the contralateral eye. Convergence was retained in both cases. A more extensive lesion of the MLF involving the ipsilateral sixth nerve nucleus will result in a one and a half syndrome with ipsilateral horizontal gaze palsy and ipsilateral loss/impairment of adduction. One of our patients was noted to have a recovering one and a half syndrome in addition to numerous other ocular motility problems.

Four of our patients had a third palsy. Two patients had a nuclear third nerve palsy, one patient had a complete left third nerve palsy and limited movement in the right eye corresponding to contralateral superior rectus involvement and the second patient had a complete right third nerve palsy with a contralateral superior division third nerve palsy. The bilateral defect is due to the anatomy of the nucleus and its fibres. The fibres for superior rectus function pass through the contralateral superior rectus subnucleus without synapse and innervate the contralateral superior rectus (Bienfang 1975). Therefore lesions in this region cause ipsilateral third nerve palsies and contralateral superior rectus weakness. Levator function is under bilateral control at the level of the third nerve nuclei due to the bilateral organisation of the caudal central subnucleus that supplies the levator muscle (Leigh & Zee 1991) and therefore can result in bilateral ptosis. Two patients had a fascicular lesion resulting in a third nerve palsy without pupil involvement but also with a vertical gaze palsy. Fascicular lesions can give additional signs such as hemiplegia, central Horner's syndrome and intention tremor, e.g. Weber's syndrome, Benedikt's syndrome and Claude's syndrome.

Gaze palsies result from involvement of the brainstem nuclei and their projections responsible for generating vertical and horizontal eye movements (Rowe 2003). Vertical gaze palsies commonly result from lesions in the brainstem as bilateral input is required to generate vertical gaze. The nuclei responsible for generating vertical gaze movements are connected via the MLF and posterior commissure and vertical gaze palsies result from lesions to the riMLF and rostral midbrain (Bender 1980, Green 1993, Lagreze 1996). Innervation is unilateral to depressor extraocular muscles but bilateral to elevator muscles. Therefore gaze palsies on elevation are more common. Upward gaze palsies were noted in four of the patients in this study. Horizontal gaze palsies result from lesions involving the sixth nerve nucleus often of a vascular pathology. Seventh nerve involvement can occur with horizontal gaze palsies or sixth nerve palsies because of its close proximity with the sixth nerve (Miller 2002). One patient had a fascicular bilateral sixth nerve palsy with unilateral seventh nerve involvement in association with the ocular motility deficit of abduction.

Disorders of saccades result in abnormalities of initiation, velocity, accuracy and inappropriate saccadic intrusions. Slow saccades may be noted with nerve palsies or drug use. Accuracy disorders may be noted with brainstem or cerebellar disease. Abnormal saccadic eye movements were noted in five patients. Normal smooth-pursuit movements may be replaced by series of small saccades termed "cog-wheeling". This was the case in one patient in this study and smooth pursuit movements were noted as abnormal and jerky in a further three patients.

Skew deviation is an acquired vertical misalignment of the visual axes caused by a disturbance of supranuclear function. (Brandt & Dieterich 1993, Keane 1975). The deviation is more common in unilateral lesions than bilateral lesions and the eye ipsilateral to the lesion is usually the hypotropic eye. Diplopia is often present but no particular extraocular muscle is involved. A comitant skew deviation was noted in one patient in this series. Nystagmus was noted in three patients and included upbeat, downbeat and gaze evoked waveforms. Gaze evoked nystagmus was more prevalent and can be seen during and following recovery of gaze palsies but also with damage to the neural integrators of horizontal and vertical gaze.

A number of our patients did not require ocular treatment due either to symmetrical involvement of eye movements or to resolution of the ocular motility defect. Of those requiring treatment, five patients had conservative options, two had BT A injections with or without prisms or occlusion and one patient had surgery with prisms to correct the small residual deviation.The indications for treatment include binocular diplopia due to strabismus, abnormal head posture for strabismus or to achieve fixation with gaze palsy, and oscillopsia. Prisms can be useful in some cases. However many are unsuccessful due to incomitance and occlusion may be required. BT is useful to ascertain the effect of weakening specific muscles before considering surgery. We had varying success with this in two cases. Surgery was undertaken successfully in one case in our study for double elevator palsy.

As regards the ocular outcome of our patients, ten patients improved of which two had full ocular motility and the remaining eight patients showing minimal, partial or good levels of improvement. Two patients showed no improvement in ocular motility although both patients were asymptomatic in primary gaze, one with the use of prisms. The time period of follow-up in this cross section analysis ranged from 6 weeks to 8 years.

The natural history of our patients could be assessed in nine of the 12 patients who required no treatment or conservative options only. Two patients had full resolution of ocular motility disturbance, one showed minimal improvement, three showed partial recovery and two showed good recovery. Evidence of improvement is encouraging and for those patients with residual binocular diplopia this could be alleviated with prisms or occlusion. In one patient the diplopia was far apart enough to be ignored without requiring prisms and in two patients suppression was demonstrated. Of the three cases that had treatment intervention, all showed improvement of a variable extent. In all patients that showed improvement the general trend was a slower recovery time for those patients with more marked abnormalities of ocular motility such as those patients with combined gaze palsies and cranial nerve palsies.

CONCLUSIONS

Of 12 patients with brainstem vascular pathology and ocular motility deficit only two showed no improvement in eye signs. The more extensive the pathology, the more significant the ocular motility disorder and the less likelihood of recovery. There was a variable time period of follow-up and recovery and some patients showed evidence of recovery (even of a minimal extent) after a period of 3-5 years. Most patients were managed appropriately with conservative means of prisms, occlusion or Bangerter filters with only three patients requiring BT or surgery. The natural history is promising and despite many patients demonstrating slow recovery, only two remained static with regard to their ocular motility status. All patients were asymptomatic in the primary position.

REFERENCES

Bender MB. 1980 Brain control of conjugate horizontal and vertical eye movements; a survey of the structural and functional correlates. *Brain*. 103: 23

Bienfang DC. 1975 Crossing axons in the third nerve nucleus. *Investigative Ophthalmology and Visual* Science. 14:927

Brandt T, Dieterich M. 1993 Skew deviation with ocular torsion : a vestibular brainstem sign of topographic diagnostic value. *Annals of Neurology*. 33: 528

Bronstein AM, Rudge P, Gresty MA, DuBoulay G, Morris J. 1990 Abnormalities of horizontal gaze. Clinical, oculographic and MRI findings. II Gaze palsy and INO. *Journal of Neurology Neurosurgery and Psychiatry*. 53: 200

Green JP, Newman NJ, Winterkorn JS. 1993 Paralysis of downgaze in two patients with clinical-radiologic correlation. *Archives of Ophthalmology*. 111: 219

Jampel RS, Fells P. 1968 Monocular elevation paresis caused by a central nervous system lesion. *Archives of Ophthalmology*. 80: 45

Keane JR. 1975 Ocular skew deviation. *Archives of Neurology*. 32: 185

Lagreze W-D, Warner JEA, Zamani AA, Gouras GK, Koralnik IJ, Bienfang DC. 1996 Mesencephalic clefts associated with eye movement disorders. *Archives of Ophthalmology*. 114: 429

Leigh RJ, Zee DS. 1991 *The neurology of eye movements*. Contemporary Neurology Series. P329

Lessel S. 1975 Supranuclear paralysis of monocular elevation. *Neurology*. 25: 1134

Miller NR, Biousse V, Hwang T, Patel S, Newman NJ, Zee DS. 2002 Isolated acquired unilateral horizontal gaze paresis from a putative lesion of the abducens nucleus. *Journal of NeuroOphthalmology*. 22: 204

Pierrot-Deseilligny C, Goasguen J. 1984 Isolated abducens nucleus damage due to histiocytosis X. Electro-oculographic analysis and physiological deductions. *Brain*. 107: 1019

Rowe FJ. 2003 Supranuclear and internuclear control of eye movements. A review. *British Orthoptic Journal*. 60: 2

Table 1 Patient Details

Case	Gender	Age at onset	Vascular pathology	Ocular motility	General signs	Symptoms	Treatment	Follow-up period	Outcome
1	Female	71	Infarct	Double elevator palsy		Diplopia	Prisms	2 years	Static
2	Female	42	Haemorrhage	Unilateral INO		Diplopia		2 months	Full improvement
3	Male	78	Infarct	Double elevator palsy		Diplopia	Prisms Surgery	3 years	Good improvement
4	Male	52	Infarct	Fixation instability, Jerky pursuits Reduced hor & vert saccades Upward gaze palsy		Blurred vision	Prisms Occlusion Filters	3 years	Static
5	Female	41	Haemorrhage	Bilateral INO		Diplopia	Prisms BT A	8 years	Minimal improvement
6	Male	42	Infarct	Complete unilateral III Upward gaze palsy	Difficulty with speech, balance, swallowing	Diplopia	Occlusion BT A	5 years	Minimal improvement
7	Female	73	Infarct	Bilateral nuclear III Spared pupils, No ptosis Reduced vert saccades	Hand tremor	Diplopia		2 years	Partial improvement
8	Male	50	Haemorrhage	Gaze evoked hor & vert nystagmus Upward gaze palsy, Cogwheeling Reduced hor & vert saccades Upbeat/downbeat nystagmus Fixation instability, Sluggish pupils	Difficulty with speech, hemiplegia	Reading difficulties Diplopia		4 years	Minimal improvement
9	Female	38	Infarct	Skew deviation, Jerky pursuits Reduced vert saccades Upbeat nystagmus Gaze evoked hor nystagmus	Dizziness Difficulty with balance Vertigo	Diplopia Blurred vision Oscillopsia	Prisms	18 months	Partial improvement
10	Female	67	Infarct	Complete unilateral III Vertical nystagmus, Jerky pursuits Reduced hor & vert saccades Reduced hor & vert gaze holding Recovering 1½ syndrome Upward gaze palsy	Dizziness Difficulty with speech and balance VII palsy	Diplopia Oscillopsia	Prisms Occlusion	6 months	Good improvement
11	Female	25	Haemorrhage	Bilateral VI	VII palsy	Diplopia	Prisms	6 weeks	Full improvement
12	Male	58	Infarct	Complete nuclear III Contralateral superior division III		Diplopia		1 year	Partial improvement