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CASE SERIES

Causes and outcomes for patients presenting with diplopia to an eye casualty department

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Abstract

Purpose **To evaluate the causes and outcomes for patients presenting with diplopia to an eye casualty department.**

Methods **Patients presenting with diplopia as a principal symptom, who were referred to the Orthoptic Department from Moorfields Eye Casualty over a 12-month period, were retrospectively investigated.**

Results **One hundred and seventy-one patients were identified with complete records in 165 cases. There were 99 men and 66 women with an age range of 5–88 years. Monocular diplopia accounted for 19 cases (11.5%), whereas 146 patients (88.5%) had binocular diplopia. Cranial nerve palsies were the most common cause of binocular diplopia accounting for 98 (67%) of cases. Isolated sixth nerve palsy was the largest diagnostic group ($n = 45$). Microvascular disease (hypertension or diabetes mellitus, or both) was present in 59% of patients with cranial nerve palsies, and of this group, 87% resolved spontaneously by 5 months rising to 95% by 12 months.**

Conclusion **Patients with clinically isolated single cranial nerve palsies associated with diabetes or hypertension are likely to recover spontaneously within 5 months and initially require observation only. However, patients with unexplained binocular diplopia and those who progress or fail to recover should be investigated to establish the underlying aetiology and managed as appropriate.**

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Introduction

Diplopia, visual confusion, and vestibular ocular reflex disturbance may all accompany acute onset of ophthalmoplegia. Collectively, these symptoms may be referred to as diplopia, which is a common presenting complaint to the ophthalmologist and a distressing symptom for the patient. Despite its clinical importance, there are surprisingly few published studies on the incidence of the different causes and natural history of diplopia of acute onset. Previous studies have examined the causes of diplopia for patients presenting initially to an eye casualty department, but have not assessed the outcomes for these patients.[1] Other studies have looked at both causes and outcomes of diplopia, but only in selected patient populations. These have included a paralytic squint clinic,[2] a general ophthalmic outpatient clinic,[3] and in an orthoptic department.[4] Trimble and Kelly[5] examined the causes and outcomes for patients presenting with diplopia to an eye emergency department but excluded patients with monocular diplopia and had relatively few patients with complete follow-up. Rush and Younge[6] studied the causes and outcomes for third, fourth, and sixth cranial nerve palsies in a larger cohort of one thousand patients but did not look at other causes of diplopia and their patient group is not representative of the totality of cases presenting to eye casualty departments with diplopia. Many patients with acute onset diplopia regard their problem as primarily an ocular one and as a result will initially present to an eye casualty department. At Moorfields Eye Hospital, the casualty department provides a twenty-four-hour emergency service that includes General Practioner and Optometrist referrals as well as self-referrals. Fifteen years ago, Morris[1] examined the causes but not the

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outcomes of double vision presenting to the same eye casualty department. In this study, we retrospectively examined both the causes and outcomes for patients who presented with diplopia to Moorfields Eye Casualty over a 12-month period.

Materials and methods

Patients who present to Moorfields Eye Casualty Department with diplopia are routinely referred to the Orthoptic clinic for further assessment. In this retrospective study, we reviewed the case notes of all such patients over a 12-month period from January 2002 to December 2002. This included patients with diplopia as a presenting symptom from any cause including those with a history of trauma. In this group, 57% were self-referrals, 24% came via their general practitioner, and 19% from an optometrist. All patients were examined by an ophthalmologist and by an orthoptist and were referred as appropriate to a specialist ophthalmic or neuro-ophthalmic clinic. There was a minimum follow-up period of 12 months in all cases (range 12–36 months). Patients with congenital fourth nerve palsies were diagnosed based on the clinical history, an increased vertical fusion range, and the absence of torsional diplopia. Following detailed clinical assessment, a number of patients were subsequently referred for further neurological investigations and management. For the purpose of this study, recovery meant that the patient was orthotropic and could maintain binocular single vision (BSV) for near and distance without adopting an abnormal head posture. Twelve patients who failed to return for follow-up appointments and in whom the clinical outcome was unknown were contacted either by telephone or letter to establish the outcome.

Results

In all, 171 patients were referred from Moorfields Eye Casualty to The Orthoptic Department between January and December 2002. Of these, complete case notes were available in 165 cases. There were 99 males and 66 females with an age range of 5–88 years with 71.5% between 40 and 80 years of age. The duration of symptoms of diplopia before presentation ranged from 1 to 270 days with a mean of 19 and a median of 7 days. There were 19 patients with monocular diplopia, all of whom had identifiable causes for their symptoms which are summarised in Table 1. Of these, four patients had monocular diplopia from extraocular optical causes, whereas 14 patients had monocular diplopia owing to a variety of ocular abnormalities of the lids, cornea, lens, and retina, and in one patient following a migraine episode.

Table 1 Causes of monocular diplopia

Cause	*Number of patients*
Optical	
Bifocal segment incorrect	1
Incorrect refraction	3
Lid	
Ectropion	2
Entropion	2
Cornea	
Abrasion	2
Corneal epithelial dystrophy	1
Herpes simplex keratitis	1
Lens	
Cataract	2
Retina	
Epiretinal membrane	2
Choroidal neovascular membrane	1
Macular oedema	1
Other	
Migraine	1

There were 146 patients with binocular diplopia. Cranial nerve palsies were the single biggest group accounting for 98 cases in total (67%) and the causes are summarised in Table 2. Of this group, 45 patients had isolated sixth nerve palsy and one had bilateral sixth, 37 had isolated fourth nerve palsy, 12 had a third nerve palsy, and two patients had combined fourth and sixth nerve palsies. The pupil was not involved in any of the 12 cases of third nerve palsy. The largest subgroup of patients with cranial nerve palsies comprised those with presumed microvascular disease owing to hypertension or diabetes accounting for 58 out of 98 patients (59%). Of these, 49 patients had hypertension, 26 diabetes mellitus, and 15 patients had both.

Forty patients had cranial nerve palsies from a variety of causes other than microvascular disease and the causes are listed in Table 2. Trauma and decompensated congenital fourth nerve palsies were most common with a wide variety of other cause found, including, myasthenia gravis, herpes zoster infection, migraine, multiple sclerosis, neurosarcoidosis, and Miller Fisher syndrome. One patient aged 10 presented with isolated sixth nerve palsy and was subsequently diagnosed with a malignant astrocytoma and died 12 months later.

Forty-eight patients had binocular diplopia from causes other than cranial nerve palsies and the results are summarised in Table 3. The largest group of these

Table 2 Cranial nerve paralysis as a cause of binocular diplopia

Cause	*Number of cases for each affected cranial nerve*			
	III	*IV*	*VI*	*IV and VI*
Hypertension	8	15	26	—
Diabetes	4	10	12	—
Trauma	—	6	1	—
Congenital	—	6	—	—
Herpes zoster	1	1	2	1
Myasthenia gravis	1	—	1	—
Migraine	—	1	2	1
Sinusitis	1	—	—	—
Demyelination	—	—	2	—
Miller Fisher syndrome	—	—	1	—
Neurosarcoid	—	—	1	—
Malignancy	—	—	1	—
Blocked VP shunt	—	—	1	—
Unknown	2	6	6	—

One patient had bilateral sixth nerve palsy owing to raised intracranial pressure from a blocked VP shunt. Fifteen patients had coexistent hypertension and diabetes mellitus.

Table 3 Causes of binocular diplopia excluding cranial nerve palsies

Cause	*Number of patients*
Trauma	
Soft tissue	9
Orbital floor fracture	7
Muscular/neuromuscular junction	
Thyroid	7
Myasthenia gravis	4
Myositis	2
Superior oblique myokymia	2
Previous surgery	1
Orbital	
Metastases	1
Cellulitis	1
Dacryoadenitis	1
Decompensating phoria	
Esophoria	1
Exophoria	2
Hyperphoria	1
Brainstem lesion	
Internuclear ophthalmoplegia	3
Other brainstem lesions	1
Others	
Near reflex spasm	1
Migraine	1
Isolated inferior rectus underaction	1
Unknown	2

patients are those classified as muscular/neuromuscular junction causes or trauma. In the former group ($n=16$), patients include those with thyroid eye disease,

Table 4 Age-stratified diagnosis for binocular diplopia

Diagnosis	*0–20*	*20–40*	*40–50*	*50–60*	*60–80*	*80–100*
Microvascular	—	1	4	14	33	6
Trauma	4	9	6	2	3	—
Congenital		4	—	1	—	—
Thyroid	1	—	1	2	3	—
Inflammation	—	—	1	2	4	1
Myasthenia	—	—	2	3	1	—
Other neurological	—	3	4	—	—	—
Decompensating Phoria	2	—	—	—	2	—
Neoplastic	1	—	—	—	1	—
Migraine	—	1	1	—	1	—
Myokymia	—	2		—	—	—
Miscellaneous	1	1	1	—	—	—
Unknown	—	4	2	5	5	—

Miscellaneous = one patient each with blocked VP shunt, spasm of near reflex, and isolated inferior rectus palsy. 'Other neurological' group includes, INO, demyelination, brainstem infarct, and Miller Fisher syndrome.

myasthenia gravis, myositis, superior oblique myokymia, and previous squint surgery. The trauma group ($n=16$) was subdivided as those with either periorbital trauma or orbital floor fracture. Most patients in this group presented with vertical diplopia and orbital floor fractures were confirmed by orbital CT scan. Other orbital pathology accounted for three patients with diplopia owing to restricted eye movements, one case of cellulitis, one patient with dacryoadenitis, and one case of orbital metastases from a previously undiagnosed primary breast carcinoma. Other groups include those with decompensating heterophorias and other neurological disorders such as internuclear ophthalmoplegia and isolated brainstem lesions owing to demyelinating disease. One patient had spasm of the near reflex while a further patient had migraine, and in two cases, the cause of the diplopia was unknown. Diabetes and hypertension were not associated with cranial nerve palsies before the fourth decade of life in our study, except in the case of one 27-year-old poorly controlled insulin-dependent diabetic, whereas all other causes could occur at any age. Table 4 gives the age-stratified diagnosis for all patients in this study.

Examining the outcomes for patients with binocular diplopia, overall 118 out of 146 patients (78.5%) had resolved after 12 months. For cranial nerve palsies ($n=98$), we found that the prognosis for complete and spontaneous resolution of microvascular cranial nerve palsies ($n=58$) was very good, with 87% completely resolved at 5 months rising to 95% by 12 months with no further recovery seen thereafter (Figure 1). The rate of recovery was similar for each of the cranial nerves, with only three out of 58 patients failing to recover by 12 months. All three of these patients showed partial but

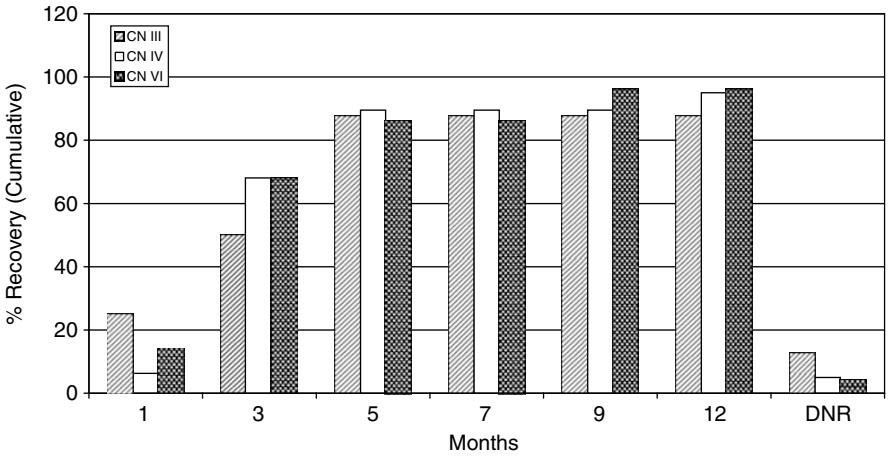

Figure 1 Recovery of microvascular cranial nerve palsies ($n = 58$).

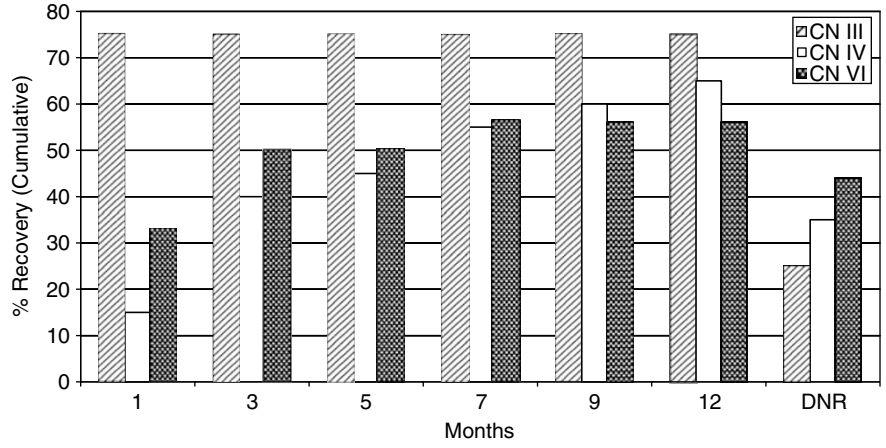

Figure 2 Recovery of nonmicrovascular cranial nerve palsies ($n = 40$).

incomplete recovery and despite neurological referral and extensive investigations including neuroimaging, no underlying cause was found. Patients with nonmicrovascular cranial nerve palsies ($n = 40$) including cases of trauma, myasthenia gravis, multiple sclerosis, and space occupying lesions (Table 2) had a worse prognosis overall with 62% showing complete recovery by 12 months (Figure 2). Of these, the nonmicrovascular sixth nerve palsies had the worst prognosis overall with 44% failing to recover by 12 months (DNR = did not recover). One patient in this group with bilateral sixth nerve palsy secondary to raised intracranial pressure recovered binocular single vision (BSV) following surgery to reposition a blocked ventriculoperitoneal shunt. Two patients with fourth nerve palsies and one patient with a sixth nerve palsy owing to demyelination made an incomplete recovery and required prisms to achieve BSV. In all, 14 out 98 patients with cranial nerve palsies (14.3%) had no specific cause for their diplopia despite extensive investigations and eight of these patients recovered spontaneously. Thirty-five out of 48 patients (73%) with binocular diplopia not caused by cranial nerve palsies recovered BSV (Table 3). Three patients in this group recovered BSV following surgery for a fractured orbital floor, one patient following bilateral strabismus surgery for thyroid eye disease, and one patient following strabismus surgery for a postviral decompensating esotropia. Three patients had incomplete recovery and required prisms in their glasses, while a further patient required an occlusive contact lens for intractable diplopia.

Discussion

Moorfields is a dedicated eye hospital located in the centre of London. The eye casualty department has a 24 h

open-access policy and currently sees approximately 50,000 patients annually. These patients are general practioner, optometrist, or self-referrals, and are thus a relatively unselected population group. Other studies including those from the Mayo Clinic have examined some of the causes and outcomes of diplopia in larger cohorts; however, their patient groups were very different from ours and included cases referred by the neurological and neurosurgical services in addition to isolated ocular motor disturbances.[6] In addition for many of their cases diplopia was not the principal complaint unlike in our study and many of the patients seen were already hospitalised with serious illness. This study of diplopia is the first to examine both the causes and outcomes for patients presenting to an ophthalmic casualty with monocular and binocular diplopia.

In 1991 at the same institution, Morris[1] carried out a study to investigate the causes of patients presenting to an ophthalmic casualty department with both monocular and binocular diplopia. However, this study did not examine the outcomes for these patients or the likelihood of spontaneous recovery of BSV. Trimble and Kelly[5] previously examined both the causes and outcomes for patients presenting with diplopia as their principal symptoms. In this study, only 67 out of 94 patients had sufficient follow-up to judge whether diplopia had resolved spontaneously and no diagnosis could be made in 44% of cases. One hundred and sixty-five patients are included in the present study with a minimum follow-up of 12 months in all cases and a diagnosis in 86% of cases. Monocular diplopia was previously thought to be a rare complaint and frequently nonorganic in origin.[7] A genuine cause was found in all 19 patients with monocular diplopia in this study despite claims that psychogenic factors are the most common cause. While ordinary spherical or astigmatic refractive errors should not in theory cause monocular diplopia, such errors either uncorrected or incompletely corrected have occasionally been reported as doing so. Coffeen and Guyton[8] demonstrated that monocular diplopia can be artificially induced using trial lenses and the effect is thought to be principally owing to spherical aberration.

Binocular diplopia accounted for 88.5% of all patients in this study. Ninety-eight patients (67%) in this group had cranial nerve palsies which are greater than that reported by Morris[1] (39%) at the same institution but similar to that reported by Nolan[3] (62.8%) and Trimble and Kelly[5] (73%). Only three cases were not isolated cranial nerve palsies: two were combined sixth and fourth nerve palsies caused by herpes zoster and migraine, respectively, while the third case involved bilateral sixth nerve palsy secondary to a blocked ventriculoperitoneal shunt. Hypertension and/or diabetes were present in 59% of those patients with isolated cranial nerve palsies. Both diabetes and hypertension have previously been cited as risk factors or causative for sixth nerve palsy.[6,9] However, more recently Patel *et al* [10], in a population-based study, concluded that while there is a six-fold increase in odds of having diabetes and an eight-fold increase of having coexistent diabetes and hypertension in cases of sixth nerve palsy over controls, systemic hypertension does not appear to be associated with increased risk. Nevertheless, hypertensive left ventricular hypertrophy, which is a marker of hypertensive end-organ damage, has previously been shown to be a risk factor for sixth nerve palsy[11] and is suggestive of a link between these two conditions. In our study, diabetes and hypertension were not associated with cranial nerve palsies before the fourth decade of life, except in the case of one 27-year-old poorly controlled insulin-dependent diabetic. Patients with nontraumatic isolated cranial nerve palsies which were associated with diabetes or hypertension had a very good prognosis with 87% recovering spontaneously by 5 months rising to 95% by 12 months (Figure 1). In those few cases that did not resolve spontaneously by 12 months despite extensive biochemical and neuroradiological investigations, no other cause were found and no further improvement seen. Trimble[5] found that 47 of 67 patients (70.1%) had spontaneous resolution of diplopia in his study with 79% recovering by 3 months. In our study, the overall recovery rate is higher which may be explained by the number of patients in Trimble's study who had insufficient follow-up to be included in the final outcome.

The incidence of hypertension or diabetes in patients with cranial nerve palsy in our study (59%) is significantly higher than the 38% previously reported in a similar study at the same institution 15 years ago.[1] This may be owing to the change in the incidence of hypertension which is rising in both obese and ageing populations, whereas its control remains inadequate worldwide.[12] However, the apparent increase in the incidence of hypertension as a cause of cranial nerve palsies in this study may also simply reflect a change in the national and international guidelines for the definition of hypertension as opposed to a rise in microvascular disease in the referring population.[13] According to changes in these guidelines, 37% of adults are now classified as hypertensive (systolic $\geq$140 mmHg or diastolic $\geq$90 mmHg) compared to only 20% in 1991 (systolic $\geq$160 mmHg or diastolic $\geq$95 mmHg) when the previous study was carried out which broadly reflects the increase seen in our study population. There were a large number of patients with diplopia owing to fourth nerve palsy, most of which were associated with either hypertension or diabetes and resolved spontaneously. Of the six patients with decompensating congenital fourth

nerve palsies, diplopia resolved completely in two cases with surgery and was controlled in the primary position and down gaze in the other four. The high incidence of traumatic diplopia seen here has previously been noted at Moorfields but has not been observed elsewhere. Injuries included blow-out fractures of the orbit in addition to soft tissue injuries. Most patients required CT scans of the orbit to exclude orbital fracture and spontaneous resolution of diplopia occurred in most cases, although three patients with orbital floor fractures resolved only following surgery. A further patient with diplopia in down gaze following an orbital floor fracture refused surgery.

A number of less common but potentially serious causes of diplopia were seen in this study, which included two patients subsequently diagnosed with multiple sclerosis, one patient with Miller Fisher syndrome, and one patient with neurosarcoidosis. Two patients were diagnosed with malignant tumours, which included a 44-year-old woman who initially presented with binocular diplopia and was subsequently diagnosed with orbital metastases secondary to a previously undiagnosed breast carcinoma. The other case involved a 10-year-old boy with isolated sixth nerve palsy who was subsequently diagnosed with a diffuse malignant astrocytoma. Tumour is more frequently the cause of a sixth nerve palsy in children than adults with the majority located in the posterior fossa.[14] Although a recent population-based study by Holmes *et al*[15] suggests that oculomotor and abducens nerve pareses occur in relation to tumours only following tumour resection, this was not the case in this study. These cases highlight the potentially serious nature of the conditions that may initially present to the ophthalmologist. In cases where the cranial nerve palsy is not neurologically isolated or where the medical history or clinical findings are suggestive of an underlying pathology, complete neurological and medical evaluation including neuroimaging and cerebrospinal fluid analysis may be appropriate. We recommend that for patients with neurologically isolated sixth, fourth, and pupil sparing third nerve palsies in the presence of microvascular disease such as hypertension and diabetes, close observation alone is initially appropriate. However, progressions of the palsy, new neurological signs or symptoms, or failure to resolve by 3 months are all indications for more extensive investigation including neuroimaging. These findings broadly agree with previous recommendations by Patel *et al*[16] in a population-based study on the incidence and associations of sixth nerve palsy.

In conclusion, we have examined the aetiologies and outcomes of patients presenting with diplopia to an eye casualty department and have found a wide range of ocular and neurological causes. Patients with clinically isolated single cranial nerve palsies associated with diabetes or hypertension are likely to recover spontaneously within 5 months and initially require observation only. However, patients with unexplained binocular diplopia and those who progress or fail to recover should be investigated to establish the underlying aetiology and managed as appropriate.

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