Clinical Manifestation of Ocular Motor Nerve Palsies in a Tertiary Eye Hospital of Kathmandu, Nepal

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Abstract

Introduction: Ocular motor nerve palsies are one of the leading causes of ocular morbidity in the neuro-ophthalmology clinic.

Objective: This study was aimed to determine the aetiology of ocular motor nerve palsies in a tertiary referral eye center of Nepal.

Methods: This hospital based cross-sectional descriptive study was carried out over a period of one and a half years. All cases of ocular motor nerve palsies were evaluated and relevant laboratory investigations and imaging studies were done.

Results: Ninety-one patients with ocular motor nerve palsies were examined, of which 53 (58%) were males and 38(42%) were females. The mean age was 39.4 years ±18.29 years. Majority of the cases (n=78, 86%) had unilateral involvement and the most common chief complaint was double vision (n=58, 63.7%). The sixth cranial nerve palsy was most commonly seen (n=49, 53.85%) followed by third nerve palsy (n=22, 24.18%). Fourth cranial nerve palsy and combined cranial nerve palsies accounted for 10.99% each (n=10). Aetiology of ocular motor nerve palsies could not be determined in 31.8% of the cases. Among the identifiable etiologies were vascular diseases (n=24, 26.3%), infections (n=14, 15.3%), trauma (n=14, 15.3%) and neoplasms (n=9, 9.8%). Imaging studies were done in 92% (n=84) of cases. In cases of combined cranial nerve palsies, positive diagnostic findings were noted in 50% (n=5) of the cases with imaging studies.

Conclusion: The sixth cranial nerve palsy was the most common ocular motor nerve palsy in our study. The most common identifiable aetiology was vascular diseases followed by trauma. Besides ophthalmic examination, neurological evaluation and imaging plays an important role in diagnosis.

Keywords: Aetiology, imaging, ocular motor nerve palsy.

Introduction

Dysfunction of the ocular motor nerves can result from lesions anywhere along their path between the nuclei and the extraocular muscles within the orbit. To increase the chance of identifying the causes of ocular motor nerve palsies (OMNP), close collaboration between the different specialists has been recommended.¹ The largest report from the Mayo Clinic, which included 4278 patients over 30 years, identified sixth nerve palsy and undetermined cause as having the highest prevalence.² However, other studies showed a variety in the aetiology, affected nerve distribution and recovery rates.
The previous report presented the retrospective clinical profile of oculo-motor nerve palsy that showed the most common EOM involved and possible causes in a Nepalese clinical population presenting with EOM palsy/paresis.3 The present study was carried out to determine the most common EOM involved and possible causes and systemic association in clinical patients presenting with EOM palsy/paresis in Kathmandu.

Methods

Sample size

In a hospital based prospective and cross-sectional study, 91 consecutive cases of acquired third, fourth, sixth and combined cranial nerve palsies were enrolled in to the study from neuro-ophthalmology clinic at B. P. Koirala Lions Centre for Ophthalmic Studies (BPKLCOS) from 1st January 2010 to 30th June 2011. Congenital causes of ocular motor nerve palsy including Duane’s retraction syndrome and birth injuries, myopathies like myasthenia gravis and chronic progressive external ophthalmoplegia (CPEO), restriction syndromes including thyroid related restrictive myopathy or orbital diseases like orbital fracture and inflammation were excluded from the study. They were seventeen patients excluded from the study for having diagnosis of congenital (2 cases), myasthenia gravis (6 cases), CPEO (3 cases), orbital wall fracture with muscle entrapment (2 cases) and pseudo-tumour (4 cases).

Ethical consent

Verbal consent was received from every patient before enrolment into the study. The study was approved by the institutional review board of Institute of Medicine, Maharajgunj, and Kathmandu. The study adhered to the declaration of Helsinki.

Assessment

Detailed examination of the patients was carried out by a consultant ophthalmologist and a consultant neurologist.

The detailed history included patient’s age, sex, the time from onset of symptoms to presentation, trauma, previous medical history of hypertension, diabetes, vascular disease including stroke, viral fever and meningitis.

Visual acuity was assessed using the internally illuminated Snellen multiple optotype and the best–corrected visual acuity was recorded. For illiterate patients the E-chart was used to record the visual acuity.

Ptosis evaluation was done when necessary. Proptosis evaluation was done using the Hertel’s Exophthalmometer. Corneal sensations and periorbital sensation was also measured to find out neurological signs.

Both duction and version eye movements were noted. Forced-Duction test and Force generation test were done using a fixation forceps under topical anesthesia to rule out any restrictive pathology when required.

Prism cover test was performed in both near and distant target fixation and amount of deviation was measured. The Krimsky test was performed in those patients prism cover test couldn’t be performed reliably. Torsional deviation was measured objectively with a double Maddox rod test.

The pupils were checked for size, shape, direct and consensual light reflexes and accommodation.

Investigations

Hematological investigations including ESR were done. Blood sugar levels were checked.

Cerebrospinal fluid (CSF) analysis, computerized tomography (CT), magnetic resonance imaging (MRI) and angiography were performed wherever necessary.

Oto-rhino laryngological and neurosurgical consultation were performed in necessary cases. The cause of palsy was considered to be vascular based on the presence of existing vascular diseases and risk factors.

Results

Among 91 patients, the mean age of the subjects was 39.4 years ±18.3 years with male to female ratio of 1:1.4. The distribution pattern of various ocular motor nerve palsies, the mean age of distribution for each nerve, the gender distribution and the laterality of the involved nerves are shown in Table 1.
Table 1  Distribution of patients by age, sex, laterality and symptom in cranial nerve palsy

<table>
<thead>
<tr>
<th>No (%)</th>
<th>3rd Nerve</th>
<th>4th Nerve</th>
<th>6th Nerve</th>
<th>Combined</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>91 (100)</td>
<td>22 (24.2)</td>
<td>10 (11.0)</td>
<td>49 (53.8)</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>39.4±18.3</td>
<td>45.1±18.2</td>
<td>37.8±13.0</td>
<td>35.6±18.0</td>
</tr>
<tr>
<td>Age range</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
<td>53 (58.2)</td>
<td>16 (72.7)</td>
<td>5 (50)</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>38 (41.8)</td>
<td>6 (17.3)</td>
<td>5 (50)</td>
</tr>
<tr>
<td>Laterality</td>
<td>Unilateral</td>
<td>78 (85.7)</td>
<td>21 (95.4)</td>
<td>10 (100)</td>
</tr>
<tr>
<td></td>
<td>Bilateral</td>
<td>13 (14.3)</td>
<td>1 (4.6)</td>
<td>0</td>
</tr>
<tr>
<td>Main Symptom</td>
<td>Diplopia</td>
<td>55 (60.4)</td>
<td>7 (31.8)</td>
<td>10 (100)</td>
</tr>
<tr>
<td></td>
<td>Eye lid drooping</td>
<td>20 (22.0)</td>
<td>14 (63.6)</td>
<td>--</td>
</tr>
<tr>
<td></td>
<td>Blurring of vision</td>
<td>10 (11.0)</td>
<td>1 (4.6)</td>
<td>--</td>
</tr>
<tr>
<td></td>
<td>Deviation</td>
<td>6 (6.6)</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

The most common complaint among the patients was binocular double vision, followed by drooping of lids and deviation of eyes. The mean duration of symptoms at the time of presentation was 2.02 weeks (SD).

Etiological diagnosis of various ocular motor nerve palsies

In our study, the etiology could not be determined in 31.87% of cases. The vascular causes accounted for cranial nerve palsies in 26.37%. Others like infectious causes and miscellaneous ones accounted for 15.38%; trauma was associated with 15.38% and tumours with 9.89% cases. One case (1.10%) was due to idiopathic intracranial hypertension. There were no cases of aneurysmal ocular motor nerve palsy in our study. The aetiology of individual ocular motor nerve palsy is given in Table 2.

Table 2  Aetiology of various ocular motor nerve palsies

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>3rd Nerve No. (%)</th>
<th>4th Nerve No. (%)</th>
<th>6th Nerve No. (%)</th>
<th>Combined No. (%)</th>
<th>Total No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vascular</td>
<td>8(36.30)</td>
<td>2(20.00)</td>
<td>10(20.30)</td>
<td>3(30.0)</td>
<td>24(26.37)</td>
</tr>
<tr>
<td>Trauma</td>
<td>3(13.60)</td>
<td>7(70.00)</td>
<td>4(8.16)</td>
<td>1(10.0)</td>
<td>14(15.38)</td>
</tr>
<tr>
<td>Tumour</td>
<td>3(13.60)</td>
<td>0</td>
<td>2(2.04)</td>
<td>4(40.0)</td>
<td>9(9.89)</td>
</tr>
<tr>
<td>*BIH</td>
<td>0</td>
<td>0</td>
<td>1(1.02)</td>
<td>0</td>
<td>1(1.10)</td>
</tr>
<tr>
<td>Others</td>
<td>2(9.10)</td>
<td>0</td>
<td>12(24.40)</td>
<td>0</td>
<td>14(15.38)</td>
</tr>
<tr>
<td>Undetermined</td>
<td>6(27.0)</td>
<td>1(10.00)</td>
<td>20(40.80)</td>
<td>2(20.0)</td>
<td>29(31.87)</td>
</tr>
<tr>
<td>Total</td>
<td>22(24.18)</td>
<td>10(10.99)</td>
<td>49(53.85)</td>
<td>10(10.99)</td>
<td>91(100.0)</td>
</tr>
</tbody>
</table>

*BIH- Benign Intracranial Hypertension
Clinical Manifestation of Ocular Motor Nerve Palsies

Third cranial nerve palsy
There were 22 cases with isolated third cranial nerve palsy. Majority of them were due to vascular problems (37%; n=8). Among them, 3 cases had uncontrolled hypertension, 3 had uncontrolled diabetes and 2 had both diabetes and hypertension.

In 27% (n=6) of cases, no cause could be isolated and they were grouped as undetermined cause. Infectious causes accounted for 9.09% (n=2) of cases. Out of them, one was HIV infected patient with tubercular meningitis and the other had herpes zoster Ophthalmicus.

Similarly, tumours accounted for 3 cases (13.6%). Two cases had pituitary macro adenoma and one had orbital cysticercoids. Rest 3 cases were traumatic third cranial nerve palsy.

All the cases had unilateral involvement, except one, which was in an HIV infected patient with tubercular meningitis. In this study, 41% (n=9) cases had at least some degree of pupillary involvement. Rest 59% (n=13) cases had complete pupillary sparing.

Fourth cranial nerve palsy
Majority of the cases (7 out of 10 cases; 70%) of fourth cranial nerve palsy were due to trauma. Two cases were due to vascular aetiology, and in one case, no cause could be determined. We did not include any congenital cases. In our study we did not come across any bilateral fourth cranial nerve involvement.

Sixth cranial nerve palsy
Out of the 49 cases of sixth cranial nerve palsy, cause could not be determined in 20 cases (40.8%).

We categorized 12 cases (24.4%) into ‘others’ group which included 11 infectious causes and 1 case which had possible multiple sclerosis. Among the infectious causes, 2 cases were due to Herpes Zoster Ophthalmicus. Nine cases were due to meningitis. Among them, 2 cases had viral fever during the time, but since we could not be certain that it was the cause of sixth cranial nerve palsy, we classified them as undetermined.

Ten cases (20.3%) were vascular in origin. Three cases had uncontrolled diabetes and 3 had uncontrolled hypertension. Four cases had both diabetes and hypertension.

Four cases (8.16%) were due to trauma. Two cases were due to tumours; among them 1 was due to pituitary macro adenoma with lateral extension and the other was due to nasopharyngeal carcinoma.

One case of a 45-year-old lady with bilateral sixth cranial nerve palsy had benign intracranial hypertension (BIH).

Ten patients had bilateral sixth cranial nerve palsies; out of them, 4 cases were of undetermined cause, 3 cases were due to meningitis, 2 cases were due to trauma and one had BIH.

Combined cranial nerve palsies
We encountered 10 cases of combined cranial nerve palsies. Among them, 4 cases (40%) were due to tumours; 2 pituitary macro adenomas, and 1 each of maxillary carcinoma and naso-pharyngeal carcinoma with orbital extension. Three cases (30%) had vascular aetiology; two had uncontrolled diabetes and one had uncontrolled hypertension. In two cases, no cause could be identified and one case was due to trauma.

There were two cases of bilateral combined cranial nerve palsies; one was of nasopharyngeal carcinoma and the other was of vascular origin.

The distribution pattern analysis of multiple ocular motor nerve palsies revealed that the percentage of combined involvement of third and fourth nerve palsies and third, fourth and sixth nerve palsies were equal (40% each) followed by third and sixth nerve (20%).

Imaging studies
In our study, imaging studies were done in 92% of cases. Most often MRI studies were done (58%), followed by CT scan (37%). In 5% of cases, both CT scan and MRI scan were done.

In 22.7% of cases (n=5) of third cranial nerve palsy, positive findings were present in imaging studies. Similarly, in fourth and sixth cranial nerve palsy, positive imaging findings were present in 20% (n=2) and 16.3% (n=8) respectively. However 50% of combined cranial nerve palsies had positive imaging findings.

Discussion
In our present series of 91 cases of ocular motor nerve palsies, the most common one was the sixth cranial nerve palsy (53.85%), followed by the third (24.18%), the fourth (10.99%) and combined cranial nerve palsies (10.99%). Similar distribution pattern was found in the study by Menon et al (1984) where the sixth cranial nerve was most frequently affected (n=88; 44.6%), followed by the third cranial nerve (n=63; 32%). There were 12 (6.1%) cases of fourth cranial nerve palsy while 34 (17.3%) patients had multiple nerve involvement in the same study. Published literatures also suggested similar results with the highest incidence of sixth nerve palsy, followed by third nerve palsy and fourth nerve palsy being the least common. The mean ages were 45 years, 37 years, 35 years and 47 years respectively for third, fourth, sixth and combined cranial nerves palsies in our series. In contrast, in a study...
done by Tiffin et al (1996), the mean age was 62 years, 59 years, 67 years and 60 years for the third, fourth, sixth and the combined OMNPs respectively. The decrease in mean age among all the OMNPs was due to a larger number of pediatric populations included in our study.

Among the 13 cases with bilateral involvement, 10 cases were of sixth cranial nerve palsy. There were 2 cases of bilateral combined cranial nerve palsies; one was of vascular origin and the other had intracranial tumour. The remaining one case was of bilateral third cranial nerve palsy in a 30-year-old male in a known case of HIV infection with tubercular meningitis under anti-retroviral therapy. There was no case of bilateral fourth cranial nerve palsy in our study.

This result was comparable to the study done by Menon et al (1984), where there was only one case of bilateral third nerve palsy of undetermined aetiology. There was no case of bilateral fourth nerve palsy but nine cases (10%) had bilateral sixth nerve paralysis. Bilaterality was observed in 5 cases (14.7%) of multiple nerve palsies.

Similar findings were noticed by Tiffin et al (1996) where there were 12 bilateral cases; out of them, majority (n=11) were of sixth cranial nerve involvement and 1 had fourth cranial nerve involvement.9

In the series by Rush and Younge (1981), bilateral interruption of the sixth cranial nerve was the most frequently seen symmetric nerve palsy, occurring in 33 patients (8%), whereas in our study 20% (10 out of 49) had bilateral sixth nerve involvement. The higher incidence of bilateral sixth cranial nerve palsy in our study can be attributed to a greater number of referred patients with serious infections like meningitis to our hospital, as it is a tertiary referral centre.

In our study, the occurrence of bilateral third cranial nerve involvement was 4.5% (One out of 22 cases) whereas, 8 patients (2.8%) were reported in the series by Rush and Younge (1981).6 Bilateral third cranial nerve palsy was usually indicative of a sinister pathology.

In our study, the etiology was undetermined in 31.86% of cases, whereas, vascular causes attributed to 26.37%. Infections and others accounted for 18.68% of cases; trauma was associated with 13.18% and tumours with 9.89% of cases. In the study by Menon et al (1984), 30.5% of cases were of undetermined aetiology.2 Similarly, aetiology was not clearly determined in 26.3% and 35% of cases in the study done by Tiffin et al (1996)9 and Rush and Younge (1981)6 respectively.

Cases with palsies due to vascular disease and aneurysms were similar to study by Tiffin et al (32%).9 However in the study done by Menon et al (1984),2 only 7.1% of cases were of vascular origin.

Neoplasm was noted to be less common than that reported by Menon et al (12.2%)9 or Rush and Younge (14.3%). It was much less common when compared to older reports of 26.3% by Rucker (1958).4 Thus, there was a decline in neoplasm induced ocular motor nerve palsy.

Most of the cases of third cranial nerve palsy in our study were of vascular origin (37%), diabetes and hypertension being the common causes. Twenty seven percent cases had undetermined aetiology. Trauma and tumours each accounted for 13.6% of cases. Among the rest 9% of cases, one case had herpes zoster Ophthalmicus and the other had tubercular meningitis. Our result was similar to the study reported by Rush and Younge (1981).6 Tiffin et al (1996) reported that 46% of cases were of vascular origin (slightly higher than ours);9 32% were of unknown causes; 7% were due to tumour, and 14% were of other causes. There was no aneurysmal third nerve palsy which was similar to our study. However unlike our study, those reports did not have any traumatic cases.

In previous studies, pupillary involvement had been documented in up to 95% of cases of third cranial nerve palsy due to aneurysm, and in 60-80% of vascular cases.10 In our study, 41% had some degree of pupillary involvement although none of them showed any evidence of intracranial aneurysms despite thorough neuroimaging studies.

Seventy four percent of fourth cranial nerve palsy in our study was due to trauma; 20% were vascular and 10% were idiopathic. In most of other series, trauma have accounted for 25-35% while the most common group of diagnosis was undetermined.2,6,7,9

In the present study, cause was not identified in 40% of cases of sixth cranial nerve palsy. Twenty four percent of cases were included in the ‘others’ category which included meningitis, herpes zoster Ophthalmicus and 1 case of multiple sclerosis. Twenty percent of cases were of vascular in origin and 8% were due to trauma. Tumours were present in 4% and 1 case had benign intracranial hypertension. These results do not match with the reports of Shakya et al (2004)10 where 57% were of undetermined cause; 25% were of vascular origin; 9% were due to tumours and 9% were ‘others’. The distribution pattern in the report by Rush and Younge (1981)6 was quite different from ours where 30% were of undetermined cause; trauma and tumours consisted of 16% and 14% respectively. Vascular and ‘others’ categories each contributed to 17% and aneurysm was present in 3.5% of cases.

Combined ocular nerves palsies were mostly due to serious pathology and demanded more detailed workup. In our study, 40% were due to tumours; 30% were vascular; 20% were undetermined and 10% were due to trauma. Rush and Younge (1981) had reported 32% of cases with tumours; 21% with trauma; 6.5% with vascular cause; 8.6% as undetermined and 28% with ‘other’ causes.6
In this study we did not come across any aneurysmal nerve palsy. In studies done in India by Menon et al. (1984)² and Rama et al. (1980)³, the incidence of aneurysmal nerve palsy was 1%. In one western report by Rush and Younge (1981)⁴, the incidence of aneurysmal OMNP was as high as 7.1% whereas Tiffin et al.(1996)⁵ reported an incidence of 1%. Trimble and Kelly (1979)⁶ reported only 2 cases of aneurysm in 94 patients presenting with diplopia. Hence acute ocular palsy due to underlying aneurysm is quite rare.

Ninety two percent of cases underwent imaging in our study. Out of them, 58% of patients had MRI done; 37% had CT scan done and 5 % had both CT and MRI done. Fifty percent of patients with combined nerve palsies had positive diagnostic findings in imaging. Hence it is always recommended to do an imaging study in cases of combined cranial nerve palsies.

From our experience, immediate imaging studies in patients with isolated fourth or sixth nerve palsy without any other associated neurological features is unlikely to be abnormal and is therefore unnecessary. As the number of cases of third cranial nerve palsy is relatively less and they have multitude of causes it is preferable to perform imaging studies in all of these cases. An exception to this may be in total, pupil-sparing palsy, especially if occurring in a known diabetic.

Tiffin et al (1996) suggested that partial palsies should be viewed with suspicion and initially monitored closely for signs of progression, unless associated with pain or occurring in a younger or ‘non-vascular’ patient.⁷ In that case, early angiography would be more appropriate.

Although we did not come across any aneurysm associated ocular motor nerve palsy in our study, it is necessary to exclude this condition. Conventional angiography itself is associated with definite risk in elderly vasculopathic individuals.⁸ Comparatively, Magnetic Resonance Angiography (MRA) is much safer. Jacobson and Trobe (1999)⁹ reported that MRA alone might overlook only 1.5% of aneurysms producing third cranial nerve palsy that will, if untreated, rupture during the subsequent 8 years.

**Conclusion**

Our study gives information regarding clinical and aetiological pattern of ocular motor nerve palsies in Nepalese population. The sixth cranial nerve palsy was the most common ocular motor nerve palsy in our study. The most common identifiable aetiology was vascular (26%). However, undetermined causes accounted for significant number of cases (32%). Besides, radiological investigations yielded more positive results in cases of combined cranial nerve palsies compared to cases with isolated ocular motor nerve palsies. Hence, the radio-imaging is strongly indicated in the former cases.

**Conflict of interest:** None declared.

**References**

5. Rucker CW. The causes of paralysis of the third, fourth, and sixth cranial nerves. Am J Ophthalmol 1966; 61:1293-1298,