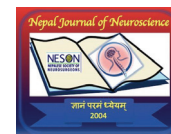


Clinical Profile of Ocular Motor Nerve Palsies in Eastern Nepal



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Abstract

Introduction: To evaluate the trends of acquired ocular motor nerve palsy in an eye care centre without a dedicated neuro-ophthalmology setup based in Eastern region of Nepal.

Methods and Materials: A retrospective, cross-sectional study was conducted after reviewing the medical records of all the patients with newly diagnosed acquired ocular motor nerve palsy. All the patients underwent comprehensive ocular examination by general ophthalmologist and detailed orthoptics evaluation by an optometrist. Necessary blood investigations were obtained and neuro-imaging were ordered as appropriate. Neurology and otorhinolaryngology consultation were advised in indispensable cases.

Results: A total of 167 patients were included in this profile. Sixth cranial nerve was found to be the most commonly affected ocular motor nerve followed by third, fourth and combined ocular motor nerves respectively. Males were predominantly affected with male: female ratio of 2.63:1. The overall mean age of the patients was 45 ± 15.33 (15 to 82) years. Diplopia was the major complaint for presentation. The etiology was undetermined in 68/167 (40.7%) cases whereas among the identifiable causes; vascular etiology accounted for 58/167 (34.7%) cases followed by trauma in 22/167 (13.2%) cases.

Conclusion: The trends in distribution and etiology of ocular motor nerve palsies can be constant even though separated by geographical location. Ocular motor nerve palsy should be examined and diagnosed properly in collaboration with other specialists where there is lack of sophisticated complementary investigations. Multi-disciplinary approach is recommended which may compensate for the missed diagnosis and indeterminate aetiologies.

Key words: Nepal, Nerve palsy, Ocular motor nerves, Retrospective

Introduction

The ocular motor nerves (OMN) are namely; oculomotor (third), trochlear (fourth) and abducens (sixth) nerve respectively. These cranial nerves synchronously control the motor functions of the extraocular muscles of the globe as well as levator muscle of the eyelid and pupil

through the parasympathetic pupillomotor fibres.¹ Ocular motor nerve palsies (OMNP) may result due to any pathology in the course of the nerve and the involvement can be categorized into nuclear, fascicular, subarachnoid, intracavernous and orbital according to their anatomical division.²

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The etiological trends of OMNP have remained fairly consistent over the decades, although there is a worldwide variation in disease pattern.³ Scientific literatures have aided in the understanding of the anatomy and vascular relationships of the OMN with respect to diagnosis and treatment of the diverse pathologic processes that can damage these nerves which includes ischemia, inflammation, and compression.⁴ Diplopia is one of the most distressing complaint that brings the patient to the eye care setup. Binocular diplopia presumably results from dysfunction of one or more of these motor nerves.⁵ Furthermore, delay in detection of pathology behind OMNP can sometimes be fatal.⁶ A collaborative interdisciplinary approach is recommended to escalate the diagnostic accuracy of OMNP.⁷

Several analogous studies were published from different parts of the globe. However, few available reports from Nepal were also mostly limited to tertiary setup in the nation capital. There is evident paucity in similar kind of reports from other parts of the country. Hence, we have conducted this review to portrait the trends of acquired OMNP in an eye care center without a dedicated neuro-ophthalmology setup.

Methods and Materials

A retrospective, cross-sectional study was performed in Mechi Eye Hospital (MEH) situated in eastern Nepal. The medical records of all the patients with ocular motor nerve palsies (OMNP) (of third, fourth, sixth cranial nerve and in combination) visiting MEH from January 2018 to December 2018 were reviewed. The study was approved by the institutional ethical committee of MEH and it adhered to the tenets of the declaration of Helsinki.

The patients with newly diagnosed acquired cases of OMNP were enrolled. Other causes of OMNP including Duane's retraction syndrome, myopathies like myasthenia gravis and chronic progressive external ophthalmoplegia, thyroid associated restrictive myopathy and traumatic orbital fracture were excluded from this study.

The collected variables from the patient included their age, gender, visual acuity (VA), presenting complaint and duration of presentation. Furthermore detailed ocular, medical and surgical history were documented. History of trauma, viral fever, meningitis, comorbid conditions like diabetes mellitus, hypertension and known event of cerebrovascular accident if present were also recorded.

All the cases underwent detailed ocular examination by an ophthalmologist followed by comprehensive orthoptic evaluation by an optometrist. Meticulous ocular examination was done by slit lamp biomicroscope (Takagi, 2ZL, Japan). VA was assessed by Snellen chart

projected on an electronic monitor at six meters distance guided by International Council of Ophthalmology standards.⁸ Tumbling 'E' chart was utilized for patients with no formal education. Detailed examination of the pupils were checked for position, size, shape, direct and consensual light reflexes and accommodation reflex. Case based notes of ptosis and proptosis evaluation, corneal and peri-orbital sensations were recorded. Meticulous review of ocular motility for both duction and version movements were noted. Diagrams and nine-point scoring system were used for representation of ocular motility.⁹ Force duction test and force generation test done whenever required, was documented. Furthermore, prism cover test was performed for both near and distant target fixation and amount of deviation was estimated. Modified Krimsky test was performed where the prism cover test was not reliable. Parks three step test and diplopia charts were applied for diagnostic interpretation.¹⁰ Torsional deviation was estimated by double Maddox rod test. A graphical method was adopted to represent cyclovertical muscle palsy.¹¹

Blood investigations comprising of haemoglobin level, total and differential counts, erythrocyte sedimentation rate and blood sugar level were ordered as appropriate. Diagnostic imaging studies computed tomography (CT) scan and magnetic resonance imaging (MRI) and angiography were performed as appropriate. Issues regarding the site of the lesion were not included in this study. Inter-departmental neurology and otorhinolaryngology consultation was advised in indispensable cases.

The collected data were analysed with Statistical Package for the Social Sciences Software (SPSS v.20, Armonk, NY, USA). Descriptive statistics was used for the presentation of data. Continuous variables were represented as mean \pm standard deviation, and categorical variables were represented as frequency and percentage. One-way ANOVA test was computed for independent variables. Chi square test or Fisher's exact tests (as appropriate) were used to assess differences between categorical variables. A p value <0.05 was considered as statistically significant.

Results

A total of 167 patients (with 178 eyes) were included in this retrospective series. Among them, 121 (72.5%) were males and 46 (27.5%) were females. Average age at presentation was 45 ± 15.33 (15 to 82) years. Most common presenting complaint was diplopia in 88 (52.7%) (Figure 1) with 44 patients (26.3%) frequently presented between two to four weeks from the onset of symptoms (Table 1).

Sixty three out of 167 (37.7%) patients had known co-morbidities, where hypertension (HTN) was the most common and present in 28 (16.8%) cases followed by diabetes mellitus (DM) in 25 (15%) cases (Table 2).

After clinical and orthoptic evaluation, sixth nerve was found to be the most commonly involved among 84/167 (50.3%) participants followed by third nerve among 64/167 (38.3%) cases (Figure 2). Frequency distribution of various categories for each nerve palsy is shown in Table 2. The average age was younger in the cases with fourth nerve palsy whereas the average age was relatively higher in the cases with sixth nerve palsy ($p=0.394$). Males were found to be commonly affected in fourth nerve palsy but it was not statistically significant ($p=0.112$). Bilateral eyes were commonly affected in the mixed OMNP ($p=0.001$). Among all other complaints, patients with fourth cranial nerve palsy frequently presented with diplopia ($p=0.001$). Similarly, among the known co-morbidities, hypertension was commonly associated with third nerve palsy and diabetes mellitus with sixth nerve palsy ($p=0.013$). The diacritic description of oculomotor nerve is presented in Table 3.

The etiology remained undetermined in 68 cases (40.7%) and among the identified cause in 99 cases (59.3%), vascular etiology was most commonly identified

among 58/167 (34.7%) cases. Aneurysm was identified in the region of posterior communicating artery in a single case (1.6%) of third nerve palsy. Neoplasm responsible for OMNP was encountered in four cases (2.4%), among them pituitary macroadenoma was identified in third nerve palsy and a single case of multiple OMNP, nasopharyngeal carcinoma in sixth nerve palsy and meningioma in another case of multiple OMNP respectively. Two cases of sixth nerve palsy had distinctive otorhinolaryngology origin which was identified as sinusitis and acoustic neuroma. Twelve (7.2%) cases were categorized under ‘others’ category which comprised idiopathic orbital inflammatory syndromes in two cases (3.1%) of third nerve palsy and two cases (2.4%) of sixth nerve palsy. Similarly, features of meningitis was present in the remaining two (3.1%) third nerve palsy and five cases (5.9%) of sixth nerve palsy. Possible demyelination findings suggestive of multiple sclerosis was determined in remaining one (1.2%) case of sixth nerve palsy. The etiology remained undetermined in most of the cases of third nerve palsy, head trauma in fourth nerve palsy and vascular etiology was frequently associated with sixth nerve palsy. The association of the etiology and OMNP was found statistically significant ($p=0.001$). The etiology of OMNP is depicted in table 4. Imaging studies were retrieved in only 101/167 (60.5%) cases. Among them, majority had done only CT scans 62/101(61.4%) accompanied by MRI in 28/101(27.7%) and both investigations in remaining 11/101 (10.9%).

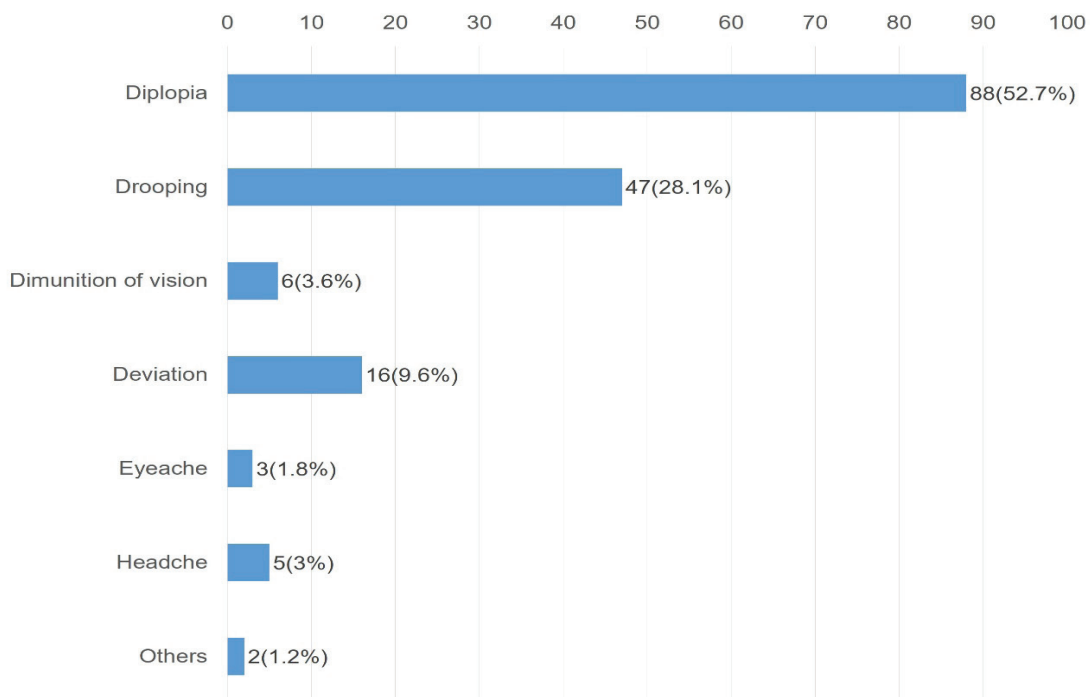


Figure 1: Complaints of patients at presentation

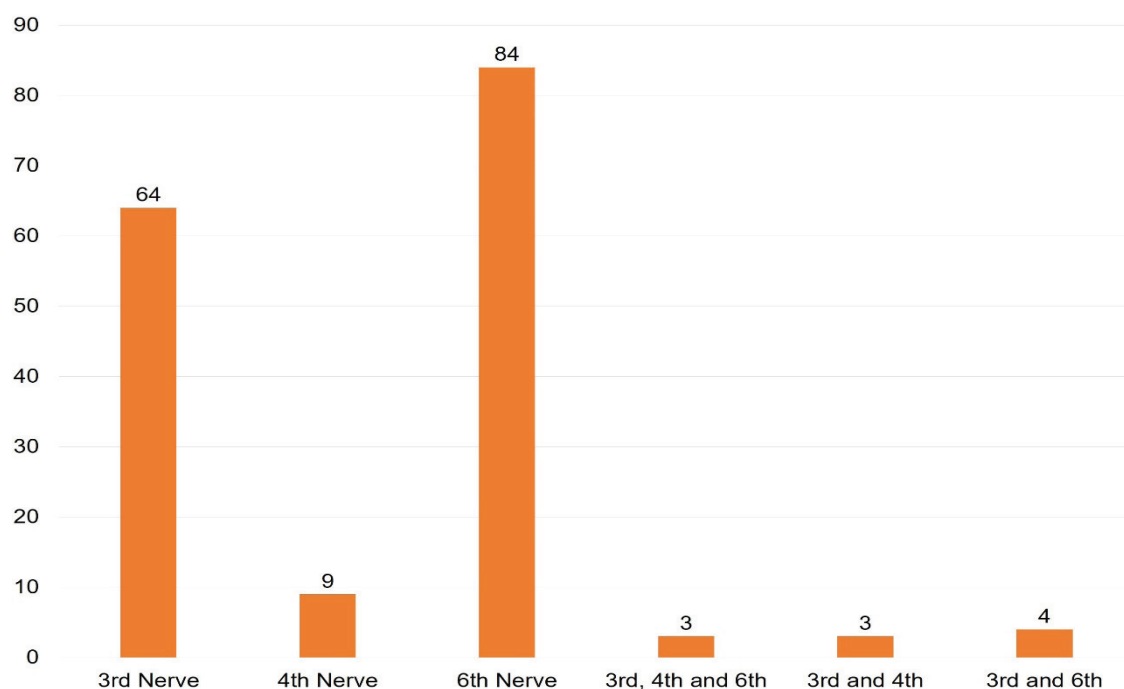


Figure 2: Involvement of ocular motor nerve among the cases

Duration	Number (%)
<1 week	25 (15)
1 to 2 weeks	28 (16.8)
2 to 4 weeks	44 (26.3)
1 to 3 months	30 (18)
3 to 6 months	13 (7.8)
6 months to 1 year	7 (4.2)
1 year to 3 years	8 (4.8)
3 years to 5 years	7 (4.2)
>5 years	5 (3)
Total	167 (100)

Table 1: Duration of Presentation from the onset of symptoms

Parameters	3 rd Cranial Nerve N (%)	4 th Cranial Nerve N (%)	6 th Cranial Nerve N (%)	Mixed Ocular Motor Nerve N (%)	p-value
Frequency	64 (38.3)	9 (5.4)	84 (50.3)	10 (6)	
Mean age (years)	44.11 ± 16.22	39.67 ± 13.54	46.71 ± 15.04	41.1 ± 12.67	0.394
Age Range (years)	15 to 76	25 to 61	19 to 82	23 to 62	
Gender					
Male	40 (62.5)	8 (88.9)	66 (78.6)	7 (70)	0.112
Female	24 (37.5)	1 (11.1)	18 (21.4)	3 (30)	
Laterality					
Unilateral	63 (98.4)	9 (100)	81 (96.4)	3 (30)	0.001
Bilateral	1 (1.6)		3 (3.6)	7 (70)	

Presenting complaints					
Diplopia	13 (20.3)	9 (100)	64 (76.2)	2 (20)	0.001
Drooping	39 (60.9)	-	2 (2.4)	6 (60)	
Diminution of vision	4 (6.3)	-	1 (1.2)	1 (10)	
Deviation of eyes	3 (4.7)	-	12 (14.3)	1 (10)	
Others	5 (7.8)	-	5 (5.9)	-	
Co-morbidities					
HTN	14 (21.9)	1 (11.1)	12 (14.3)	1 (10)	0.013
DM	2 (3.1)	1(11.1)	22 (26.2)	-	
HTN + DM	5 (7.8)	-	4 (4.7)	-	
CAD	-	-	1 (1.2)	-	
None	43 (67.2)	7 (77.8)	45 (53.6)	9 (90)	

Abbreviations HTN= Hypertension, DM= Diabetes mellitus, CAD= Coronary artery disease

Table 2: Distribution of cases by age, gender, laterality, presenting complaints and co-morbidities

Features	Number (%)
Complete nerve palsy	32 (50)
Incomplete nerve palsy	32 (50)
Total	64 (100)
Isolated muscle paresis among the cases of incomplete nerve palsy (n=10)	
Superior rectus	1 (1.6)
Medial rectus	1 (1.6)
Inferior rectus	1 (1.6)
Inferior oblique	7 (10.9)

Table 3: Profile of third cranial nerve palsy

Causes	3 rd Cranial Nerve N (%)	4 th Cranial Nerve N (%)	6 th Cranial Nerve N (%)	Mixed Ocular Motor Nerve N (%)	Total N (%)	p-value
Undetermined	35 (54.7)	3 (33.3)	27 (32.2)	3 (30)	68 (40.7)	0.001
Vascular	17 (26.5)	2 (22.2)	38 (45.2)	1 (10)	58 (34.7)	
Head trauma	6 (9.4)	4 (44.5)	8 (9.5)	4 (40)	22 (13.2)	
Aneurysm	1 (1.6)	-	-	-	1 (0.6)	
Neoplasm	1 (1.6)	-	1 (1.2)	2 (20)	4 (2.4)	
ORL causes	-	-	2 (2.4)	-	2 (1.2)	
Others	4 (6.2)	-	8 (9.5)	-	12 (7.2)	
Total	64 (38.3)	9 (5.4)	84 (50.3)	10 (6)	167 (100)	

Abbreviations ORL= Otorhinolaryngology

Table 4: Etiology of ocular motor nerve palsy

Discussion

This retrospective review of 167 patients with acquired ocular motor nerve palsies (OMNP) affirmed that the abducens (sixth cranial) nerve palsy (50.3%) was the most commonly involved followed by oculomotor (third cranial) nerve (38.3%) and trochlear (fourth cranial) nerve (5.4%). Similarly, mixed OMN accounted for 6% cases.

Our study had a male preponderance with the male to female ratio of 2.63:1 which was comparable with other studies.^{12, 13} However higher number of female patients were also reported in few instances.¹⁴ This scenario might represent our social disparity where males are the economically active earning group and males get earlier access to health care compared to female.¹⁵ Male preponderance might also depicts the fact that co-

morbidities like hypertension and diabetes mellitus are more prevalent among the males.^{16,17}

The mean age of the total patients in our study was 45 ± 15.33 (15 to 82) years which was similar to a reported average age at presentation of 48.1 years.¹³ Our series divulged younger average age groups compared to other study where the mean age reported was 54.7 years¹⁸ to 65.6 years¹⁹ for OMNP. Age at presentation has become important due to high prevalence to structural, inflammatory and infectious causes. The mean age for third, fourth, sixth and combined nerve palsies were 44.11 ± 16.22 years, 39.67 ± 13.54 years, 46.71 ± 15.04 years and 41.1 ± 12.67 years respectively. Younger patients less than 18 years with OMNP should have aggressive diagnostic approach because of high probability of tumours, susceptibility to trauma and remote possibility of vascular aetiology.

The commonest duration of presentation from the onset of symptoms was within two to four weeks among 44/167 (26.3%) of cases in our review. Likewise, a similar mean duration of presentation of 2.02 weeks was reported from a study conducted in a tertiary centre from the capital of Nepal.²⁰ The commonest presenting complaint was doubling of vision in 88/167 (52.7%) patients followed by drooping of upper eyelid, diminution of vision, deviation of eyes, ocular pain and headache which was also justified by previous studies.^{18,20} In contrast, ocular deviation was defined as the preeminent complain in another series.²¹

The aetiology in majority of the OMNP was undetermined 68/167 (40.7%) and has no particular underlying cause as well as not related with any systemic diseases. Furthermore in other articles also, the leading cause remained unknown.^{14,20,22,23} Despite of long follow up and advanced neuroimaging techniques, the cause of OMNP could be irresolute and assumed probable vascular microangiopathy of microscopic origin.²² Dropout from extended follow-up as well as lack of incorporation of appropriate imaging might be attributed to the undetermined cause. The established co-morbidities accounted for presumed vascular aetiology with HTN prevalent in 28/167 (16.8%), followed by DM in 24/167 (13.2%) and then both HTN and DM in 10/167 (6%) cases. Likewise with reference to another study, HTN accounted for (11.57%) of cases, DM (3.93%) cases and (3.1%) of patients had both HTN and DM.¹² In disagreement with our findings, DM was identified as major risk factors for OMNP with (42%) followed by HTN (28%).²⁴ The distinction between vascular and undetermined aetiology may pose a challenge and presumed vascular cause was usually based on the presence of vascular risk factors.¹² However, we did not come across any cases of orbital apex secondary to herpes zoster, HIV related OMNP,

benign intracranial hypertension which were reported as underlying cause in few other instances.^{14,20,22}

Head trauma, ranked third leading cause 22/167 (13.2%) in our review was also quoted in other series from Nepal where (15.4%)²⁰ and (26.08%)¹² were trauma related OMNP. Though we only had a handful of OMNPs caused by aneurysm and neoplasm, Rucker (26.3%),²⁵ Menon et al (12.2%),²⁶ Rush and Young (14.3%)²³ described it as a significant etiological factor. This could be due to lack of proper inter-department referral trends prevalent in our region.

We found a higher number of unilateral OMNP which was also supported by various literatures.^{24,27} We had a single case (1.6%) of bilateral third nerve palsy out of 64 and 3/84 (3.6%) cases of bilateral sixth nerve palsy in our study. No any cases of bilateral fourth nerve palsy was reported which was in accordance to similar reports by Menon et al,²⁶ and Sitaula et al.²⁰ Etiology was undetermined and there was no any history of vascular disease and head trauma in those bilateral sixth and third nerve palsies. Nonetheless bilateral third nerve palsy represents a devastating pathology and mandates a meticulous work-up.²⁰

Sixth nerve palsy is often commonest among the cases of OMNP.^{12,14,18,20,21,23,25,26,28} Literature had reported microvascular disease^{13,29} and undetermined^{13,25,29} etiology for sixth nerve palsy. Risk of vascular disease with age might be a factor for sixth nerve palsy being most common. Additionally, the longest intracranial course of abducens nerve especially make it susceptible to direct and indirect insults.¹⁰ Sixth nerve palsy was the highest among the OMNP accounting for 84/167 (50.3%) of all cases in our study. However, palsy of third nerve may also be predominant.^{24,27} We had third nerve palsy in succession reported in 64/167 (38.3%) cases. Vascular pathology was surmised as the main causative factor.²⁴ In addition, third nerve palsy should be considered in patients with OMNP which could not be related to neurological signs or pain.²⁷ The number of third nerve palsies in our present series was comparable where incidence of third nerve palsy ranged from 27.4% to 33.5%.^{23,25,26,28} Our study also revealed half 32/64 (50%) of cases with pupillary involvement and categorized as complete third nerve palsies and 10/64 (15.6%) of isolated third nerve paresis.

The least common among the OMNP was the fourth nerve. Nine out of total cases (5.4%) were of fourth nerve palsies and multiple OMNP accounted for 10/167 (5.9%) of cases. The incidence of fourth nerve palsy was similarly reported to be (6.1%) by Menon et al.²⁶ Exclusion of the congenital cases in our study might have resulted in less incidence of fourth nerve palsy, where congenital cause accounted for majority of the cases.³⁰ Other than congenital

etiology, trauma and head injury is held responsible for fourth nerve palsy.³¹⁻³³ Combined OMN palsies were lesser in comparison to previous studies.^{23, 25, 26} Also head trauma was not predominant factors for combined nerve palsies in our study. Recovery from cranial palsy depends upon the type of cause. However, some studies suggest good prognosis and recovery of OMNP with successful management of curable underlying disease.^{13, 23}

The role of neuroimaging is emphasized in the evaluation of patients above 50 years.¹⁹ The imaging was found within normal limits without any relatable pathology in isolated fourth and sixth nerve palsy in maximum cases. So, imaging in isolated fourth and sixth nerve paralysis without any neurological features might not be necessary.²⁰ However, imaging studies should be preferred in all the cases of third nerve and combined OMN paralysis as they may have diverse etiology. MRI/magnetic resonance angiography¹⁵ is superior and should be preferred whenever available compared to CT in cases other than head trauma for evaluation.³⁴

There are several limitations of our study. Retrospective nature and single center-based series. Lack of dedicated neuro-ophthalmology setup which is prevailing in most of the eye care centers due to which majority of the cases remain under diagnosed. Limited availability of neuroimaging due to financial constraints on the patient's side and lack of prospective nature hence prognosis of the OMNP could not be determined. Nonetheless our study also failed to localize the lesion.

Conclusion

Incidence of sixth nerve palsy is more common followed by third nerve palsy among the cases of OMNP. Though majority of the causes were undetermined, distinguishable cause was vascular pathology. OMNP should be examined and diagnosed properly in collaboration with other specialists where there is a lack of sophisticated complementary investigations.

Conflict of Interest: None

Source(s) of Support: None

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