

Cranial Nerve Palsy as the Most Common Presentation of Neuro-Ophthalmic Conditions at Hospital Universiti Sains Malaysia – An 8-Year Review

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Abstract

Objective: To review cranial nerve palsy as the most common presentation of neuro-ophthalmic conditions presenting to Ophthalmology Clinic, Hospital Universiti Sains Malaysia, Kelantan.

Methods: Retrospective case review of patients with neuro-ophthalmic conditions presenting to Ophthalmology Clinic, Hospital Universiti Sains Malaysia, Kelantan during the period of January 2005 to December 2012.

Results: A total of 849 case records of neuro-ophthalmic conditions were reviewed. Neuro-ophthalmic conditions affected all age groups from birth to 80 years of age. The five most common conditions were cranial nerve palsies (27.8%), traumatic optic neuropathy (12.5%), optic neuritis (8.2%), pituitary tumours (7.5%), and ischaemic optic neuropathy (6.2%). The remaining comprised of other neuro-ophthalmic conditions such as papilloedema, optic nerve compression, cerebrovascular disorders, thyroid eye disease, myasthenia gravis, pupillary abnormalities and hereditary optic neuropathies. There was only one case of suspected giant cell arteritis, but the biopsy was inconclusive. Out of the cranial nerve palsies that presented to us, the most common were isolated 6th nerve (44.5%) and isolated 3rd nerve (25.4%) palsies.

Conclusion: In our series, the most common neuro-ophthalmic conditions presented to our neuro-ophthalmology clinic were cranial nerve palsies.

Keywords: Neuro-Ophthalmology; Cranial Nerve Palsy; Third Nerve Palsy; Fourth Nerve Palsy; Sixth Nerve Palsy; Recovery

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Introduction

Neuro-ophthalmology is an ophthalmic subspecialty that addresses the relationship between the eye and the brain; specifically disorders of the optic nerve, visual pathway, ocular motility, pupil, orbit and brain, associated with visual disturbances. There are a variety of eye disorders that are associated with neurologic disease, such as brain tumours, multiple sclerosis and cerebrovascular accidents. Although some problems seen in neuro-ophthalmology are not worrisome, other conditions can worsen and cause permanent visual loss. Some may even become life-threatening. Sometimes the problem is confined to the optic nerve or the nervous system and at other times it is related to a general medical condition.

The 3rd, 4th, and 6th cranial nerves engage in the movement of the eye by extraocular muscle control [1]. Acquired palsy of these nerves can be a consequence from various factors such as trauma, vascular disease, intracranial tumours or aneurysm [1]. In adults it can be frequently attributed from presumed micro vascular ischaemia to the nerve in the background of vascular risk factors, such as older age, diabetes mellitus, hypertension and dyslipidemia [2, 3, 4, 5, 6, 7]. We

therefore conducted this retrospective study to analyse the etiology, natural history and the rate of recovery of acquired 3rd, 4th and 6th cranial nerve palsies.

Materials and Methods

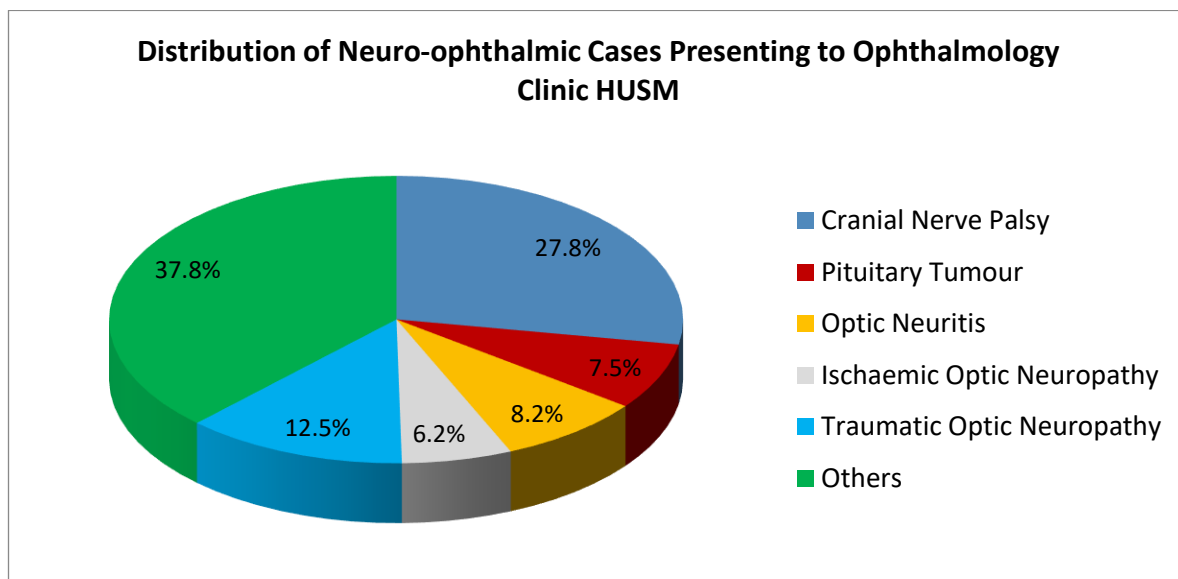
A retrospective case record review was performed on 849 cases that were evaluated by a neuro-ophthalmologist at the Neuro-ophthalmology Clinic, Hospital Universiti Sains Malaysia (HUSM), Kelantan from January 2005 to December 2012 were included in the study. Institutional review board approval was obtained for this retrospective case review study, and it was carried out in adherence to the tenets of the Declaration of Helsinki. These cases were taken from the neuro-ophthalmology registry and the case records were reviewed by the investigators which in turn entered into a standardised data entry form. These forms were then analysed and the most common presentations were studied. In this case, cranial nerve palsies were the most frequent presentation. Demographic data, underlying co-morbidities especially the presence of vascular risk factors (diabetes mellitus, hypertension and dyslipidemia), the cause of the palsy, its duration as well as the degree of recovery were recorded.

All relevant data were then entered and analysed using Statistical Package for Social Sciences (SPSS) for Windows version 22.0. Data exploration was performed to obtain the descriptive statistics for all the variables while data cleaning was performed to check the missing value and error during data entry. All the missing values data were excluded from the analysis. Mean and standard deviation were reported for normality distributed numerical variables while median and inter-quartile range were reported for non-normality distributed numerical variables. Meanwhile, the frequency and percentage were expressed for the categorical variables.

Results

Over the 8-year period, a total of 849 case records of neuro-ophthalmic conditions were reviewed. Neuro-ophthalmic conditions affected all age groups, ranging from birth to 80 years of age. The five most common conditions were cranial nerve palsies (27.8%), traumatic optic neuropathy (12.5%), optic neuritis (8.2%), pituitary tumours (7.5%), and ischaemic optic neuropathy (6.2%). The remaining 37.8% comprised of other neuro-ophthalmic conditions such as papilloedema, optic nerve compression, cerebrovascular disorders, thyroid eye disease, myasthenia gravis, pupillary abnormalities and hereditary optic neuropathies (Figure 1). There was only one case of suspected giant cell arteritis, however the biopsy was inconclusive.

Figure 1: The distribution of neuro-ophthalmic cases presenting to Ophthalmology Clinic in HUSM from January 2005 to December 2012



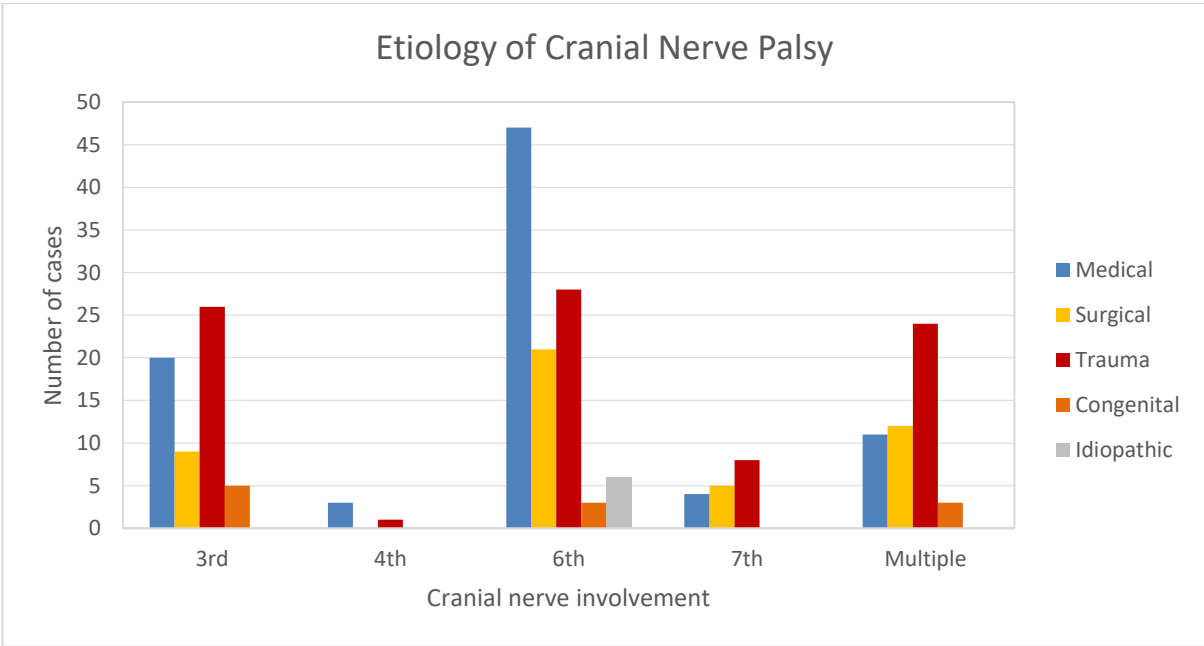
Out of the 849 case records reviewed, 236 case records were of cranial nerve palsies. Isolated 6th nerve palsy, comprising 105 (44.5%) cases was the most common condition. This was followed by isolated 3rd nerve palsy (25.4%), isolated 7th nerve palsy (7.2%) and isolated 4th nerve palsy (1.7%). Fifty (21.2%) patients presented with multiple cranial nerve involvement, mostly secondary to trauma (Table 1).

Table 1: The etiology of cranial nerve palsies

Etiology of Cranial Nerve Palsy						
	Medical	Surgical	Trauma	Congenital	Idiopathic	TOTAL
	n (%)	n (%)	n (%)	n (%)	n (%)	n
3rd	20 (33.3)	9 (15.0)	26 (43.4)	5 (8.3)	-	60
4th	3 (7.5)	-	1 (25.0)	-	-	4
6th	47 (44.8)	21 (20.0)	28 (26.7)	3 (2.8)	6 (5.7)	105
7th	4 (23.5)	5 (29.4)	8 (47.1)	-	-	17
Multiple	11 (22.0)	12 (24.0)	24 (48.0)	3 (6.0)	-	50

The most common cause of isolated 6th nerve palsy was vasculopathy, as seen in 47 (44.8%) of our patients (Table 1) (Figure 2). These patients usually had underlying co-morbidities of diabetes mellitus (23.4%) or hypertension (12.8%). A total of 18 (38.3%) patients had both diabetes mellitus and hypertension. The remaining 12 (25.5%) cases comprised of dyslipidemia, or a combination of dyslipidemia with either diabetes or hypertension. Trauma was the second most common cause, followed closely by surgical causes; both being 26.7% and 20.0% respectively.

Figure 2: A bar chart representing the etiology of cranial nerve palsies



Trauma seemed to be the most common cause for isolated 3rd nerve palsy, affecting 43.4% of the cases. Twenty (33.3%) cases were due to medical ailments such as diabetes mellitus, hypertension and dyslipidemia. Surgical causes, such as posterior communicating artery aneurysm, pituitary macroadenoma, craniopharyngioma and cavernous sinus meningioma comprised 15.0% of the cases. A minority of 5 (8.3%) cases were due to congenital disorders (Table 1).

Only 4 cases of isolated 4th nerve palsy were seen during the 8-year period. Three (75.0%) were due to medical causes such as hypertension and cerebrovascular accidents. Only one case was due to trauma. A total of 17 cases of isolated 7th nerve palsy presented to our clinic. Majority were due to trauma (47.1%). These were followed by an almost equal number of cases due to medical and surgical causes (Table 1).

Multiple cranial nerve palsy is an involvement of two or more cranial nerves. Trauma seemed to be the leading cause, affecting 48.0% of cases. The most frequently involved combination was of 3rd, 6th and 7th cranial nerves. Majority of trauma were due to motor-vehicle accidents. A handful was secondary to fall from height and industrial accidents resulting in head trauma. Other etiologies include medical and surgical causes, the former resulting in 22.0% while the latter 24.0% of cases (Table 1).

Isolated 6th nerve palsy was the most common cranial nerve palsy seen across all age groups. Trauma was the main

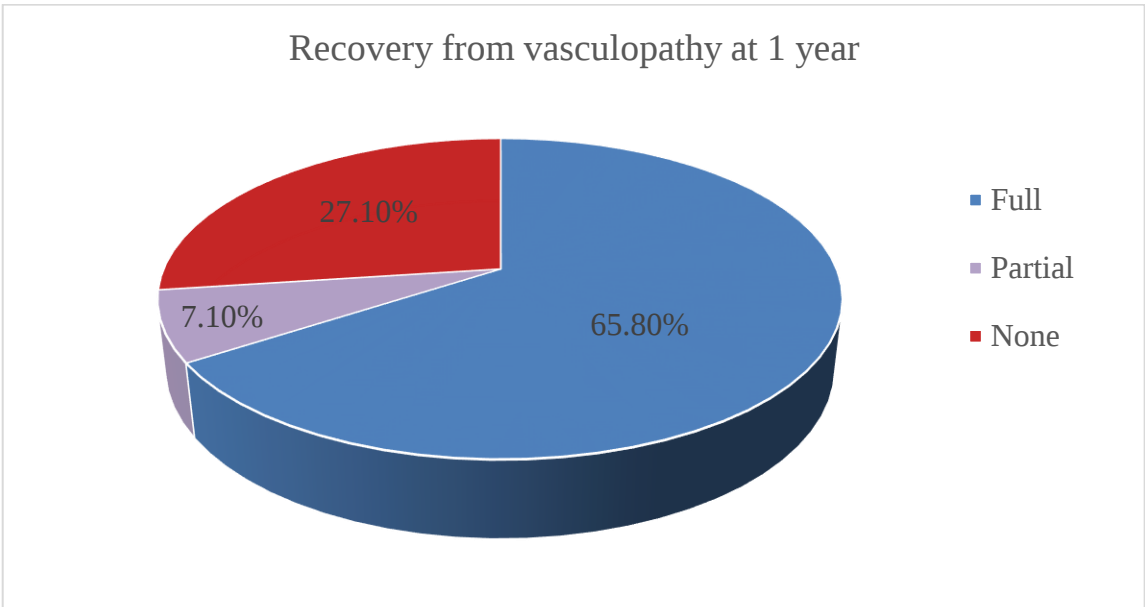
cause in 55.6% of patients aged 18 years and below. Congenital 6th nerve palsy contributed 8.3% of cases in this age group. In patients aged between 19 to 50 years, it was observed that the commonest cause was still trauma but at a lower percentage of 43.8%. This was closely followed by medical (31.2%) and surgical (25.0%) causes. In adults above the age of 50 years, the vast majority of cases were due to medical causes (71.2%). Surgical causes increased to 26.9% compared to 8.3% in the younger age group. Trauma was an unlikely cause contributing to only 1.9% of all isolated 6th nerve palsy in this age group (Table 2).

Table 2: Causes of 6th nerve palsy according to age group

Age (years)	<= 18	19 - 50	> 50
Etiology	n (%)	n (%)	n (%)
Trauma	20 (55.6)	7 (43.8)	1 (1.9)
Madical	4 (11.1)	6 (31.2)	37 (71.2)
Surgical	3 (8.3)	4 (25.0)	14 (26.9)
Congenital	3 (8.3)	-	-
Idiopathic	6 (16.7)	-	-
Total	36 (100)	17 (100)	52 (100)

The recovery period for cranial nerve palsies associated with vasculopathy ranged from 1 to 10 months. Recovery was seen in 72.9% of 236 cranial nerve palsy cases, with a majority of 62.2% recovering within 6 months. From those that recovered, 90.3% recovered fully without any residual defects, while the remaining 9.7% had some form of residual defect post recovery (Figure 3). Among those with residual defects, about 33.0% had diplopia on primary gaze and on looking down. These patients were treated with prisms for symptomatic relief. The remaining 67.0% had no diplopia on primary and down gaze. They therefore did not require any form of treatment. No surgical intervention was needed for any of the cranial nerve palsies.

Figure 3: The recovery of cranial nerve palsies at 1 year follow up



Discussion

In our study, we found that 6th nerve palsy was the most common isolated cranial nerve palsy. This finding was similar to that reported in previous studies [1, 8, 9, 10, 11, 12]. We observed that the most common cause of isolated 6th nerve palsy was vasculopathy, of which 23.4% had underlying diabetes mellitus and 12.8% had hypertension. A total of 38.3% of patients had both diabetes mellitus and hypertension. This was similar to a retrospective population-based case-control study by Patel et al. (2005) which concluded that there is a 6-fold increase in odds of having diabetes and an 8-fold increase of having both diabetes and hypertension in cases of 6th nerve palsy over controls [13]. Diabetics were also found to have a 10-fold increase in the incidence of any ischaemic cranial nerve palsies [14]. Park et al. (2008) observed that vascular disease was the most common etiology for isolated 6th cranial nerve palsy [1].

Several studies have shown that medical conditions such as hypertension, diabetes, hypercholesterolemia, ischemic heart disease and cerebrovascular accidents are significantly associated with peripheral microvasculopathy causing cranial nerve palsies [2, 9, 15, 16, 17]. It has been postulated that vasculopathic ocular motor nerve palsy is caused by thickening and hyalinization of nutrient vessels [18]. This results in ischaemic demyelination of the nerve rather than true vascular occlusion [18]. Following this insult, the area of ischaemic demyelination subsequently undergoes remyelination over time resulting in clinical recovery [18]. Microvascular ocular motor nerve ischemia is a presumptive diagnosis that is based upon the absence of other neurological signs and symptoms; no new findings during the follow-up period; and spontaneous complete recovery, usually within 4 months [5, 19, 20].

Trauma accounted for 26.7% of cases with isolated 6th nerve palsy in our study. This was in contrast to Patel et al. (2004) where trauma accounted for only 12% of the study population [3]. A study by Peters et al. (2002) found that the most common cause of 6th nerve palsy in adults aged 20- to 50-years was a central nervous system mass lesion [21]. Our study however observed that central nervous system mass lesions were more common in those aged 50-years and above.

In our study we found that isolated 3rd nerve palsy was the second most common cranial nerve palsy. This was in contrast to previous studies done on cranial nerve palsies in which the 4th nerve was the second most common cranial nerve palsy [9, 10,

11]. Berlit (1991) found that 3rd cranial nerve palsy was the commonest with 6th cranial nerve palsy being second in line [22, 23].

Fourth cranial nerve palsy was the least frequent condition encountered in our study. This finding concurred with previous studies [1, 11, 22]. Our data showed vascular risk factors seemed to be the leading cause and this was followed by head trauma. Similar observations were seen by Park et al. (2008) [1].

Most cases of medical cranial nerve palsies resolved within 6 months with conservative management. This concurs with the findings of Rush & Younge (1981), in which 71.0% of patients with isolated cranial nerve palsies secondary to vascular disease recovered, irrespective of the cranial nerve affected [8]. Other studies have also observed spontaneous recovery with vasculopathic nerve palsy [12, 20, 22]. Berlit (1991) found that 54% of cases had complete regression in 3 weeks while 16.8% only had partial recovery of symptoms [22]. Sanders et al. (2002) observed an 86% complete recovery and 14% incomplete recovery [20]. However the duration taken to recover was not stated in their study. It has been observed in a recent study that recovery takes longer if 2 or more risk factors are present [17].

Patients with acquired causes of cranial nerve palsies such as trauma and tumours have a poorer prognosis than those with medical cranial nerve palsies [8]. A longer recovery time was also seen in those patients with intracranial abnormalities [17].

In previous studies, a small proportion of patients with vasculopathic risk factors were later discovered to have secondary causes of cranial nerve palsies such as neoplasm and inflammation [9, 15]. The majority of subjects in our study, as in other studies, had medical risk factors [8]. In view of this, we would advocate a thorough systemic blood workup in all patients. Radiological investigations should be considered if the palsy is associated with other cranial nerve deficits, or if the palsy does not recover during the period of observation. As seen in our study, the period of recovery is usually within 6 months.

The results of this study are limited firstly by its retrospective nature and relatively small sample size. Some of the cranial nerve palsies might have been missed due to an inadvertent administrative error that resulted in it not being entered into the neuro-ophthalmology registry, hence underestimating the number of cranial nerve palsy. Secondly, because of the predominantly Malay population of Kelantan, our results most likely can be generalised only to the Malay

population of Malaysia. Another potential bias and error, because the patients are referred to neuro-ophthalmology clinics to seek further consultation, thereby increasing our proportion of patients with serious underlying etiologies.

Conclusion

In our series, the most common neuro-ophthalmic conditions presenting to our neuro-ophthalmology division were cranial nerve palsies, mainly 6th and 3rd nerve palsies. Cranial nerve palsies as a result of vasculopathy have very good prognosis for full recovery, usually within 6 months.

It may not be medically necessary to perform an MRI scan on every patient with an isolated 3rd, 4th or 6th cranial nerve palsy. In adults older than 50 years with an isolated mononeuropathy, physicians should carefully review the patient's history and findings to determine which patients to image at the initial evaluation.

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