



## Etiology of Fourth and Sixth Nerve Palsies: a Single Ophthalmology Clinic's Perspective

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### Abstract

**Purpose:** To ascertain the etiology of fourth (CN4) and sixth nerve palsies (CN6) in an ophthalmology clinic.

**Methods:** This retrospective study consisted of 176 patients with fourth and sixth nerve palsies in a strabismus clinic. Demographic features and etiology were recorded.

**Results:** One hundred and three patients with fourth nerve palsy and 73 patients with sixth nerve palsy were enrolled in the study. The median follow up was 2 (1-4) years. The most common cause of the palsy was congenital palsy in CN4 group (37.9%) and trauma in CN6 group (24.7%).

**Conclusions:** Trauma and congenital palsies were the leading causes of fourth and sixth nerve palsies as described in the literature.

### Keywords

Cranial nerve palsy, Fourth nerve palsy, Paralytic strabismus, Sixth nerve palsy

### Introduction

Patients with paralytic strabismus comprise an important number of patients of ophthalmology clinics as well as of neurology and neuroophthalmology clinics. The etiology of the palsy of fourth and sixth nerves may be numerous and differ from one clinic to other in terms of patients' demographics and referral pattern.

The purpose of the study was to ascertain the etiology of fourth and sixth nerve palsies in an ophthalmology clinic and to define the clinical features.

### Materials and Methods

The series consist of patients with paralytic strabismus due to fourth or sixth nerve palsies who were seen in Strabismus Clinic between January 2001 and January 2011. The medical records of patients were reviewed upon approval of the institutional ethics

committee was obtained. Demographic data and etiology of the palsy were recorded. All patients having acquired nerve palsy were referred to neurology department in order to elucidate the underlying causes.

Cases were classified on the basis of etiology as: congenital, trauma, vascular disease (hypertension and diabetes mellitus), intracranial mass, other (lymphomas of the central nervous system, acute myeloblastic lymphoma) and undetermined.

The patients were divided into two groups according to the type of the nerve palsy they had. Patients with fourth nerve palsy were classified as CN4 group and patients with sixth nerve palsy were categorized as CN6 group.

Statistical analyses were performed using SPSS software for Windows version 15.0 (Statistical Package for the Social Sciences, SPSS, Inc., Chicago, IL). Arithmetic mean, standard deviation, median, range, frequency and percentage were used as descriptive statistics. Comparisons were made by Wilcoxon signed rank, Mann Whitney and Pearson chi-square tests. Results were accepted as statistically significant when  $p$  was  $<0.05$ .

### Results

One hundred and seventy six patients with fourth (103/176) and sixth nerve palsies (73/176) were enrolled in the study. The mean age, gender and laterality distribution within groups were described in detail in Table 1. When the mean age of each group was compared, the difference between two groups was found as significant. ( $p=0.001$ ) Patients with sixth nerve palsy were significantly older than those who had fourth nerve palsy. The median follow up time was 2 years (1-4) for each group.

The underlying etiologies for palsies were shown in Table 2. The leading determined etiological factor was congenital palsy in CN4 group (39/103, 37.9%) and trauma in CN6 group (18/73, 24.7%).

### Discussion

In the present study, a retrospective review of cases with fourth and sixth nerve palsies was performed in a strabismus clinic. Many reports are available in the literature concerning etiology of cranial

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**Table 1:** Clinical and demographic characteristics of patients with cranial nerve palsies.

Characteristics	Groups		p*	
	CN4	CN6		
N (%)	103 (51.5)	73 (36.5)		
Mean Age ( $\pm$ SD) (years)	22.5 $\pm$ 19.1	35.1 $\pm$ 21.4	0.001	
Gender No. (%)	Male	64 (62.1)	46 (63.0)	0.911
	Female	39 (37.9)	27 (37.0)	0.911
Laterality No. (%)	Unilateral	100 (97.1)	68 (93.2)	0.133
	Bilateral	3 (2.9)	5 (6.8)	0.133

\*Pearson chi-square test

**Table 2:** Etiology of fourth and sixth nerve palsies.

Etiology	Nerve Palsy No. of patients (%)	
	Fourth	Sixth
Congenital	39 (37.9)	2 (2.7)
Traumatic	13 (12.7)	18 (24.7)
Vascular	13 (12.7)	13 (17.8)
Intracranial mass	- (0)	13 (17.8)
Other*	10 (9.8)	12 (16.5)
Undetermined	27 (26.9)	15 (20.5)
Total	103 (100)	73 (100)

\*Lymphomas of the central nervous system and acute myeloblastic lymphoma.

nerve palsies in different types of clinics. We aimed to describe the clinical profile in our clinic.

Park et al. [1] analyzed clinical features of acquired third, fourth and sixth nerve palsies in their retrospective study [1]. They stated that sixth nerve was the most commonly affected nerve (52.4%) and vasculopathy was the leading cause (31.1%) [1]. The comparison of these numbers with those of the present study may cause misinterpretation because of the inclusion criteria. Congenital cases were excluded in Park's study [1] however congenital etiology was the most common cause of fourth nerve palsy in the present study. Berlit found the frequency of cranial nerve palsies as follows: 40.1% of sixth nerve palsy and 6.1% of fourth nerve palsy, and the leading cause as vascular causes (40.1%) [2]. Tiffin et al. [3] found that the most commonly seen cranial nerve palsies in their ophthalmology clinic was sixth nerve palsy (57%) followed by fourth nerve palsy (21%) in their retrospective evaluation of acquired cases [3]. The most affected cranial nerve may differ between clinics and may be interfered by many factors including the type of clinic [4-7]. In the present study, different frequencies may be explained by the referral pattern of the patients; patients who were thought as being a candidate for surgery might have been more frequently referred to our clinic by neurologists, pediatricians, general practitioners and other ophthalmologists.

As distinct from many other studies in the literature, the particular incidence and causes of pediatric fourth and sixth nerve palsy have also been reported [8-11]. Holmes et al. [11] investigated cases of cranial nerve palsy over 15- year period and calculated the incidence of third, fourth and sixth nerve palsy in this population as 7.6 per 100,000 [11]. In terms of frequency, the most common nerve palsy was fourth nerve palsy followed by sixth nerve palsy and third nerve palsy and the leading causes of these palsies were found to be as congenital, undetermined and congenital respectively [11] where as the most common cause was congenital in CN4 group and trauma in CN6 group in the present study.

Fourth nerve palsy is one of the leading causes of vertical double vision. Tamhankar et al. [12] showed in their large series including 300 patients with hypertropia based on the referral from an outpatient clinic that the congenital fourth nerve palsy comprised 23.3% of patients, whereas acquired fourth nerve palsy comprised 9% of patients [12]. In the present study, we did not investigate the frequency of etiological factors in patients with vertical diplopia but we described the distribution of fourth and sixth nerve palsies in patients with paralytic strabismus. The most common cause of acquired fourth nerve palsy was trauma in both studies 16/27

acquired fourth nerve palsy cases in the mentioned study vs 13/64 in the present study. Mollan et al. [13] reviewed the etiology and outcomes of adult superior oblique palsies [13]. They found that 38.3% of cases were congenital, 29.3% traumatic and 23.3% vasculopathic among patients who had unilateral palsy [13]. In the present study, congenital etiology, trauma, vascular disease and undetermined causes occupied 37.9%, 12.7%, 12.7% and 26.9% of cases respectively. Tarczy-Hornoch et al. [14] determined the causes of superior oblique palsy in children under 8 years old as congenital in 61%, craniofacial anomalies in 13%, trauma in 5%, intracranial tumour resection in 3% and undetermined causes in 15% [14]. The difference between numbers may stem from the difference of age of study populations and the single referral center based data of the present study.

The etiology of sixth nerve palsy may depend on the clinic where it is seen. Lee et al. [15] reviewed the causes of sixth nerve palsy in pediatric neuroophthalmology practice and disclosed that the most common cause was neurosurgical removal of neoplasms (45%), followed by elevated intracranial pressure (15%), trauma (12%) and congenital (11%) in patients with average age of 8 years [15]. They suggested a protocol containing magnetic resonance imaging, lumbar puncture and blood tests according to the patient's ophthalmological signs [15].

Aroichane and Repka [16] evaluated the characteristics of sixth nerve palsy and paresis in 64 children younger than 7 years and found that tumours were the leading causes (33%) whereas hydrocephalus and trauma were the second and third (23% and 19% respectively) [16].

Peters et al. [17] investigated the etiology of nontraumatic sixth nerve palsy in a population between 20 and 50 years old [17]. They found that sixth nerve palsy was unusual among young adults and the most common cause was central nervous system lesions or multiple sclerosis [17].

This study needs to be viewed in light of the following limitations: the results reflect the numbers of a single referral center and may have caused selection bias as mentioned many times in the text. All patients with acquired palsy were seen by a neurologist but neuroimaging was not available for all of them. Cranial imaging was arranged in cases of clinical suspicion for underlying neurological problems. Patients who were followed in neurosurgery clinics may have been omitted and only patients having manifested ocular misalignment may have been referred. Therefore, the present study should not be considered as a population based study. However, the results may give a basic idea to a clinician about possible reasons of cranial nerve palsies without regard of his profession.

With respect to the study results, the following topic is worthy of note: the etiologies of cranial nerve palsies. Finally, the management of a patient with paralytic strabismus is complex and requires multidisciplinary approach and certain follow-up period.

## Acknowledement

The study was conducted in Hacettepe University Faculty of Medicine, Department of Ophthalmology, Ankara, Turkey.

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