



Acute Binocular Diplopia: Underlying Causes, Factors Affecting Predictivity of Spontaneous Resolution

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Abstract

Objectives: In this study, we aimed to investigate the factors affecting spontaneous recovery in cases of acute binocular diplopia.

Methods: A total of 224 patients presenting with acute binocular diplopia within 7 days were included in this study. The age, gender, etiology, and radiological findings of the cases were retrospectively examined and noted. The status of diplopia in the 6th month was noted.

Results: The most commonly identified causes were presumed microvascular (28%), cerebrovascular (14%), and autoimmune-inflammatory (14%) in origin. Spontaneous recovery in diplopia was observed in 153 cases (68.3%) at 6 months. While the recovery rate was high in the presumed microvascular and idiopathic groups, it was low in the neoplastic group. Cranial nerve palsy was detected in 132 patients (58.9%). The most common were 6th, 3rd, and 4th nerve palsies, respectively. No difference was found in terms of spontaneous recovery at 6 months among cranial nerve palsies (p=0.952). The spontaneous recovery rate was found to be significantly higher in patients without radiological imaging findings (p<0.001). **Conclusion:** It is important for the physician to predict whether diplopia will resolve spontaneously. While the underlying etiology and neuronal damage are crucial factors, radiological imaging findings of the patients can also provide valuable insights.

Keywords: Acute binocular diplopia, cranial nerve palsy, radiological imaging, spontaneous recovery

Introduction

Diplopia, also known as double vision, is the perception of a single image appearing as two images to the brain. This phenomenon primarily occurs in a binocular manner but can also manifest monocularly. The causes of acute binocular diplopia are varied, and they can serve as important indicators of potentially life-threatening conditions (1). Therefore, conducting a detailed examination of patients and making a differential diagnosis is important. The primary reasons for the condition are related to microvascular causes, as well as cranial nerve palsies and ischemic events (2). Although binocular diplopia is mostly of neurological origin, patients may initially seek help from an ophthalmologist. Therefore, a multidisciplinary approach and collaboration between neurologists and ophthalmologists are important.

Radiological imaging can be helpful in diagnosing patients who experience double vision (2,3). Apart from determining

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the primary etiology of the patient, it is also important to correct diplopia by ophthalmologists to improve the quality of life. When it comes to correcting double vision, there are a few main interventions that are commonly used: prism applications, occlusion therapy, botulinum toxin injection, and surgical correction.

Research in the field of literature covers a range of studies providing causes and demographic data on acute binocular diplopia. Our investigation goes further by exploring the impact of radiological imaging and the natural recovery of cranial nerve palsies on diplopia. We argue that being able to predict the natural recovery of diplopia is important for guiding the ophthalmologist's treatment approach and for giving relevant information to the patient.

Methods

Approval for the research was obtained from our institute ethics committee (Nu:2021/514/212/10, Date: October 27, 2021) in accordance with the Helsinki Declaration. A retrospective review of the files of cases from the neuroophthalmology department with the primary complaint of double vision, who presented directly to the eye clinic or was consulted from other departments between 2017 and 2021, was conducted.

Patients with symptoms of acute binocular diplopia starting within 7 days were included in the study. However, patients with symptoms lasting more than 7 days at the time of presentation, without radiological imaging, not attending follow-up visits, and under 18 years of age were excluded from the study.

The comprehensive eye examinations of the patients, including best-corrected visual acuity, anterior and posterior segment examination, ocular movements, alternate cover test, and Worth 4-dot test, were thoroughly reviewed. All examinations conducted after the patient's presentation were duly noted to identify the causes. The patient's age, gender, and causes were documented. Patients aged over 50 with no underlying organic pathology but with microvascular risk factors were considered presumed microvascular cases. Radiological imaging findings (computed tomography [CT], CT angiography, magnetic resonance imaging [MRI], diffusion MRI, and magnetic resonance angiography) were documented as either present or absent. The resolution status of the patients' double vision complaints at 6 months was also recorded.

Statistical Analysis

Statistical data analysis was conducted using the Statistical Packages for the Social Sciences for Windows 17.0 software. The results are presented as mean±standard deviation. The homogeneity of data distribution was assessed using the Shapiro–Wilk normality test. Categorical variables were evaluated using the Chi-square test, and odds ratios (OR) were calculated. p=0.05 was considered statistically significant.

Results

In the study, a total of 224 patients were included, consisting of 131 males and 93 females. The average age of the patients was 52.6 ± 16.8 years. Among the cases, 28% showed presumed microvascular damage, whereas cerebrovascular and autoimmune-inflammatory causes were equally found in 14% of cases. Cases related to neoplastic etiology were detected in 12% of the total cases. The etiological classification and subgroups are summarized in Table 1.

Table 1. Classification and etiologies of patients with diplop	oia, n (%)
Presumed microvascular	62 (28)
Cerebrovascular	32 (14)
 Ischemic cerebrovascular stroke (n=20) 	
• Transient ischemic attack (n=7)	
 Internuclear ophthalmoplegia (n=3) 	
Aneurysmal compression (n=2)	
Autoimmune – Inflammatory	32 (14)
• Multiple sclerosis (n=8)	
• Graves ophthalmopathy (n=7)	
• Myasthenia Gravis (n=7)	
• Neurosarcoidosis (n=2)	
• Polyarteritis nodosa (n=2)	
• Covid-related, Eaton Lambert syndrome, Toxoplasma encepha encephalitis, orbital cellulitis, non-specific inflammatory (n=1 for	ılitis,Viral ^r all)
Neoplastic diseases	27 (12)
Primary intracranial tumor-related (n=12)	
• Due to intracranial metastasis (n=12)	
• Due to increased intracranial pressure caused by the tumo	or (n=3)
Idiopathic	21 (9)
Intracranial hypertension	18 (8)
 Idiopathic intracranial hypertension (n=11) 	
• Sinus vein thrombosis (n=5)	
• Subarachnoid hemorrhage, Caroticocavernous fistula (n:1 f	for all)
Traumatic	12 (5)
• Head trauma (n=7)	
• Orbital floor fracture (n=5)	
Migraine with aura	8 (4)
Decompensating heterophorias	7 (3)
Others	5 (3)
• Progressive external ophthalmoplegia, orbital apex syndror	ne, after

lacrimal gland botox, after periocular botox, after spinal anesthesia (n:1 for all) In the first 6 months, 153 out of 224 cases (68,3%) showed spontaneous resolution of diplopia. The highest rates of spontaneous resolution were observed in cases of migraine with aura, idiopathic cases, and the presumed mi-

Table 2. Resolution of diplopia according to the clinicalclassification at 6 months

Classification and etiologies of patients with diplopia, n (%)	Resolved	No change
Presumed microvascular	54 (87)	8 (13)
Cerebrovascular	22 (69)	10 (31)
Autoimmune - inflammatory	21 (66)	11 (34)
Neoplastic diseases	3 (11)	24 (89)
Idiopathic	19 (90)	2 (10)
Intracranial hypertension	13 (72)	5 (28)
Traumatic	7 (58)	5 (42)
Migraine with aura	8 (100)	0 (0)
Decompensating heterophorias	2 (29)	5 (71)
Others	4 (80)	I (20)
Total	153 (68)	71 (32)

crovascular group. The lowest rate was observed in the neoplastic group. The details of spontaneous resolution values of diplopia according to different causes at 6 months are provided in Table 2.

When cases were assessed based on the presence or absence of cranial nerve palsy, 132 patients (58,9%) had isolated cranial nerve palsy. The most commonly observed isolated cranial nerve palsies were of the 6th, 3rd, and 4th cranial nerves. Among the cases with isolated cranial nerve palsy, a spontaneous resolution was observed in 87 (65.9%) of the cases. There was no significant difference in the rates of spontaneous resolution of double vision among cranial nerve palsies (p=0.952). The causes and values of spontaneous resolution for cases with cranial nerve palsy are summarized in Table 3.

The cases were analyzed by including all groups and excluding those related to cancer, trauma, migraine, decompensated strabismus, and other causes (Tables 4 and 5). In both analyses, there was no difference in diplopia resolution between groups with and without cranial nerve palsy (OR: 1.39, p=0.261; OR: 0.901, p=0.787, respectively). It was found that the group without imaging findings had a higher resolution rate compared to the group with imaging findings (OR: 4.55, p<0.001; OR: 3.10, p=0.003, respectively).

Table 3. Comparisons of patients with cranial nerve palsy according to the clinical classification at 6 months*

Clinical classification (resolved, no change) (87, 45) (n=132)	3 rd Nerve palsy (resolved, no change) (33,18) (n=51)	4 th nerve palsy (resolved, no change) (9,4) (n=13)	6 th nerve palsy (resolved, no change) (45,23) (n=68)
Presumed microvascular (54.8)	30 (26.4)	2 (1.1)	30 (27.3)
Cerebrovascular (7.6)	7 (3.4)	I(I.0)	5 (3.2)
Autoimmune - inflammatory (4.2)**	3 (2.1)	2 (1.1)	I (1.0)
Neoplastic diseases (1.21)	9 (1.8)	I (0.I)	12 (0.12)
Idiopathic (10.2)	0 (0.0)	3 (3.0)	9 (7.2)
Intracranial hypertension (7.3)	l (l.0)	0 (0.0)	9 (6.3)
Traumatic (2.2)	I (0.1)	2 (2.0)	I (0.1)
Decompensating heterophorias (0.1)	0 (0.0)	I (0.I)	0 (0.0)
Others (2.0)	0 (0.0)	I(1.0)	l(1.0)

*Comparisons of patients with cranial nerve palsy, p=0.952 (Chi-square test was performed). **A patient with Viral encephalitis in Autoimmune – Inflammatory group not shown in this table had multiple cranial nerve palsies. There was no improvement at 6 months.

Table 4. Comparison of the resolution rate based on cranial nerve palsy and imaging findings

Al cases n=224	Spontaneous recovery at 6 months	No complete recovery at 6 months	Odds ratio	95% confidence interval	р
Cranial nerve palsy (+)	87	46	1.39	(0.77–2.49)	0.261
Cranial nerve palsy (-)	66	25			
Radiologic imaging positive	e 46	47	4.55	(2.49–8.30)	<0.001
Radiologic imaging negative	e 107	24			

n=165	Spontaneous recovery at 6 months	No complete recovery at 6 months	Odds ratio	95% confidence interval	Р
Cranial nerve palsy (+)	82	22	0.901	(0.42–1.92)	0.787
Cranial nerve palsy (-)	47	14			
Radiologic imaging positive	37	20	3.10	(1.45–6.64)	0.003
Radiologic imaging negative	e 92	16			

Table 5. Comparison of the resolution rate based on cranial nerve palsy and imaging findings, excluding neoplastic, traumatic, migraine, decompensated strabismus, and other etiologies

Discussion

Diplopia, characterized by seeing a single object as two due to disruption in the visual system, accounts for approximately 0.1% of emergency department visits (4). In addition to impairing vital functions, diplopia also bothers patients, and rehabilitation of diplopia is important for improving quality of life. Depending on the duration of exposure to damage, the regenerative capacity of nerve tissue, neuronal plasticity, and the effectiveness of treatment approaches, functional recovery can be achieved in nerve tissue (5). Predicting complete resolution is important for patients and physicians, aiding in informed consent and treatment planning. Our study compared spontaneous resolution based on cause, cranial nerve palsies, and radiological findings.

Common systemic conditions such as hypertension, diabetes, and hyperlipidemia lead to extensive microvascular damage within the body and are widespread within the population. Our findings align with prior research, demonstrating that diplopia resulting from presumed microvascular causes is the predominant etiology, as observed in our study (2,6-9). As in prior studies, diplopia stemming from autoimmune-inflammatory and cerebrovascular origins was frequently found in our research, constituting the second most common cause after presumed microvascular causes (10,11).

In cases of diplopia, intracranial tumors may cause this condition either by exerting pressure on the ocular motor nerves or by increasing intracranial pressure. Our study reveals that tumor-related causes are more prevalent than findings in other studies (1,8,10). Our findings indicate that the higher number of tumor-related cases in our investigation is likely due to our facility being a tertiary care center with a large oncology clinic, resulting in a high volume of tumor-related conditions.

Vascular malformations, edematous brain tissue, and tumors can cause double vision by putting pressure on the cranial nerves. Trauma can also directly impact cranial nerves through fractures or pressure. Furthermore, ischemia, inflammation, infection, and degenerative diseases are some of the main causes of cranial nerve palsy (12). Some studies found isolated cranial nerve palsy in cases of acute binocular diplopia at rates of 64%, 53%, 52%, and 51.4% (1,2,13,14). In our study, it was similarly observed at a rate of 58.9%. Similar to the literature, the most common finding in our study was ocular motor nerve palsy due to presumed microvascular damage (2,7,12,15). The most commonly affected cranial nerve, as previously reported, is sixth nerve palsy (6-9,12,13). A study hypothesized that the abducens nerve's lower vascular density makes it more vulnerable to microvascular damage (7).

Studies have reported spontaneous resolution rates of 89% and 98% in cases of diplopia (6,7). In contrast, various studies have reported significantly lower rates of 31.6% and 27.1% (9,13). In our study, however, the improvement rate was determined to be 68.3%. We believe that this difference is due to the higher prevalence of neoplastic cases in our study. In studies reporting high improvement rates, most cases were attributed to microvascular causes. In addition, the smaller sample size in the study reporting lower improvement rates may have contributed to the difference.

In the idiopathic group, there were high rates of spontaneous resolution (90%). Similarly, a study reported an 86% improvement rate in the group where the underlying etiology could not be determined (16). In the idiopathic group, if no pathology is found during investigations over 6 months, it may suggest that this group is not linked to significant underlying neuronal impairment. This could lead to a high rate of spontaneous resolution.

Microvascular-related diplopia results from damage to the small vessels that supply the nerves controlling eye movements. Managing risk factors such as hypertension, diabetes, and hyperlipidemia can slow down progression and aid recovery. Consistent with previous research, our study found a high rate of improvement in the presumed microvascular group (6,7). Recognition of microvascular-origin patients, control of risk factors through treatment, and the smaller affected area compared to other major cerebral vascular events may contribute to the more frequent resolution of diplopia in these patients.

One important observation from our results is that cases with neoplastic origins have a lower rate of spontaneous resolution compared to other groups. Tumors typically cause more severe damage than other lesions and are more resistant to treatment, and the lower rate of improvement in this group may be due to the prioritization of vital functions over treating diplopia.

According to a study by Phuljhele et al., (15) cranial nerve palsies caused by vascular issues showed a better rate of improvement compared to those caused by trauma. Similarly, according to Comer et al., (17) the rate of improvement in cranial nerve palsies of microvascular origin was higher compared to non-microvascular cases. A study found that diplopia associated with third nerve palsy is less likely to improve compared to other cranial nerve palsies (8). This study found that third-nerve palsy was frequently linked to traumatic origins, while fourth and sixth-nerve palsies were more inclined to be influenced by vascular-related causes (8). Like the studies conducted by Park et al., (16) our study similarly found no significant difference in the recovery rates of cranial nerve palsies. We hypothesize that the absence of a significant difference in the recovery rates of cranial nerve palsies in our cases could be due to the small number of patients with traumatic origins and the high prevalence of those with vascular-related causes.

In certain cases of diplopia, such as those associated with neoplastic, traumatic, migraine, decompensated strabismus, and other causes, the underlying cause can be identified at the time of presentation or soon thereafter, enabling an assessment of the prognosis for diplopia. Hence, during the analysis of cases involving cranial nerve palsies and imaging findings, these specific etiological categories were omitted, and the analysis proceeded accordingly. In both analyses, no significant difference was detected in the probability of spontaneous resolution between cases with and without cranial nerve palsy. While no statistical data are available in the literature on this matter, we fundamentally believe that the extent of neuronal damage and the underlying etiology are more influential in the resolution of diplopia than cranial nerve palsy itself.

Radiological imaging findings may not be present in every case of diplopia (1-3,6). However, radiological examinations can assist in identifying the underlying cause by pinpointing neurological localization anatomical abnormalities, assessing head trauma, detecting vascular issues, and evaluating inflammatory and immunological conditions. While studies in the literature have reported abnormal imaging findings in cases of acute binocular diplopia at rates of 30%, 49.8%, and 54.9%, our study observed this rate to be 41.5% (2,8,14). In our study, we also examined whether radiological imaging could predict diplopia resolution. In both analyses, we found a significantly higher likelihood of spontaneous resolution in cases without radiological imaging findings (p<0.001 and p=0.003). We hypothesize that cases with radiological findings likely exhibit more macroscopic damage and, therefore, probably have lower rates of improvement.

Conclusion

The spontaneous resolution of diplopia poses uncertainty for both patients and physicians, and predicting it is crucial. However, there is a scarcity of comprehensive data in the literature concerning extensive etiological or radiological correlations. While underlying etiology and neuronal damage are significant factors, initial radiological imaging evaluations can offer insights into diplopia resolution. Larger-scale studies are required to investigate the influence of radiological findings based on the underlying etiology.

Disclosures

Ethics Committee Approval: Approval for the research was obtained from Kartal Dr. Lütfi Kırdar City Hospital Clinical Research Ethics Committee (Nu:2021/514/212/10, Date: October 27, 2021) in accordance with the Helsinki Declaration.

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