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Review Article

A Comprehensive Review on Oculomotor Nerve Palsy: Diagnosis and Management Strategies

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ABSTRACT

The third cranial nerve (oculomotor nerve) plays an essential role in the function of ocular movement and mainly innervates the inferior oblique, medial rectus, inferior rectus, superior rectus, levator palpebrae, pupillary sphincter, and ciliary muscle. The most frequent clinical manifestations of oculomotor nerve palsy are ophthalmoplegia, ptosis, pupillary dysfunction, and diplopia. The etiology of oculomotor nerve palsy is complex, including congenital tumors, craniocerebral trauma, intracranial inflammation, diabetes, intracranial aneurysm, cerebrovascular infarction or hemorrhagic disease, myasthenia gravis, multiple myeloma demyelinating diseases, and other uncommon causes. Each etiology of oculomotor nerve palsy has its corresponding clinical features. The present study comprehensively reviews the common etiologies of oculomotor nerve palsy and the corresponding clinical manifestations and treatment methods to help practitioners with the prompt and accurate clinical diagnosis of the causes and effective management plan.

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Introduction

Overview of anatomy

Ocular movements in different gazes are undertaken via 6 extraocular muscles (EOMs) located around the eyeball. The superior rectus, inferior rectus, inferior oblique, and medial rectus are innervated by the third nerve (oculomotor nerve), and the superior oblique and the lateral rectus muscles are innervated by the fourth (trochlear) nerve and the sixth (abducens), respectively. Congenital and acquired damage to these cranial nerves can result in malfunction in the affected EOM. Whenever the cranial nerve is deactivated, it is called cranial nerve palsy. A total deactivation of the cranial nerve is called paralysis, and a partial dysfunction of the cranial nerve is called paresis. The oculomotor nerve originates from the midbrain oculomotor nucleus, passes between the posterior cerebral artery and the superior cerebellar artery, runs parallel to and beneath the posterior communicating artery in the subarachnoid space, and passes through the dura to enter the cavernous sinus, where it passes through the cavernous, the lateral wall of the sinus, the supraorbital fissure of the middle cranial fossa. Then, the oculomotor nerve is divided into two branches, the upper branch innervates the superior rectus muscle and the levator palpebrae muscle; the lower branch innervates the medial rectus muscle, inferior rectus muscle, inferior oblique muscle, pupil sphincter and ciliary muscle [1].

Clinical features

Oculomotor nerve palsy (the third nerve palsy) is a common neurological disease and can be divided into complete or incomplete paralysis according to the clinical manifestations. Complete paralysis manifests as ptosis, disturbances in adduction, elevation, and depression, as well as mydriasis. However, incomplete paralysis has all but milder signs, the same as complete paralysis except for pupil involvement [2]. Oculomotor nerve palsy can occur alone or in combination with other ophthalmic nerve palsies. Oculomotor nerve palsy can be divided into congenital and acquired according to the time of onset. Congenital oculomotor nerve palsy occurs at birth or early after birth. Common causes include congenital developmental abnormalities, early postnatal diseases, and neonatal birth trauma and trauma. Patients often have a noticeable angle of exotropia, but most patients have no diplopia and compensatory head position, so they often visit a doctor because of their appearance. Acquired oculomotor nerve palsy is an acute onset, and the onset time is exact. Common causes include cerebrovascular disease, aneurysm, head trauma, inflammation, tumors, and endocrine and metabolic diseases. Oculomotor nerve palsy can be divided into complete and incomplete according to the degree at the onset. After complete oculomotor nerve palsy, there are only two functional muscles left in the affected eye, namely the lateral rectus muscle and the superior oblique muscle.

Etiologies and their corresponding management strategies

Oculomotor palsy is a disorder of abnormal eye movements, ptosis, and pupil damage that can be caused by various causes. Lesions in any part of the path of the oculomotor nerve can lead to different degrees of oculomotor nerve palsy [1]. There are many causes of oculomotor nerve palsy, including ischemia, infection, non-specific inflammation, and external compressive lesions. Although there are many causes of oculomotor nerve palsy, microcirculation disturbance is considered the leading cause [3] and some researchers confirm that intracranial aneurysm is a more common cause [4], resulting in differences between studies. This discrepancy can be related to the different causes of the included cases [3-6]. To understand the clinical characteristics and common causes of oculomotor nerve palsy, the first examiner can make a preliminary decision on the severity of the etiology, and prompt detection of aneurysms with a higher risk of bleeding is critical.

As mentioned earlier, the oculomotor nerve and surrounding tissue lesions can lead to oculomotor nerve palsy. The etiology of oculomotor nerve palsy is complex and diverse, and it is often closely related to intracranial lesions or systemic diseases, which can easily lead to misdiagnosis or inadequate attention. Intracranial aneurysm is one of the common causes of oculomotor nerve palsy, with high mortality and disability rates; therefore, it is imperative to timely identify the causes of the disease. In various studies of oculomotor nerve palsy, the classification of common causes and their proportions vary. Singh et al. reported that oculomotor nerve palsy is divided into congenital and acquired types [7]. Among the causes of oculomotor nerve palsy in children, congenital 43%, trauma 20%, inflammation 13%, and intracranial artery are the most apparent; however, vascular disease, intracranial aneurysm, and trauma are the most common in adults [8, 9]. Rush and Younge studied 290 patients with oculomotor nerve palsy and found that among all etiologies, the etiology was unknown in 23.1%, vascular lesions accounted for 20.7%, head trauma accounted for 16.2%, and intracranial aneurysms accounted for 13.8%,

and other reasons accounted for 14.5% [10]. Meanwhile, Berlit studied 412 patients with oculomotor nerve palsy, of which 165 were caused by vascular factors, of which 135 were related to cerebrovascular diseases caused by diabetes and hypertension [11]. Bruce et al. realized that the common causes of oculomotor nerve palsy include intracranial aneurysm, cerebral vascular ischemia or hemorrhage, nerve ischemia, neuritis, and meningitis [12].

Materials and Methods

A systematic search was conducted across multiple databases, including PubMed, MEDLINE, Scopus, Web of Science, and Google Scholar, to identify relevant articles on oculomotor nerve palsy, its diagnosis, and management strategies. The search terms included the following items: "Oculomotor nerve palsy", "Third nerve palsy", "Oculomotor neuropathy", "Oculomotor nerve dysfunction", and "Cranial nerve III palsy". Boolean operators (AND, OR) were used to combine these terms, and truncation symbols were applied where appropriate to capture variations in terminology.

Filters were applied to include only peer-reviewed articles published in English. Titles and abstracts were screened for relevance, and full-text articles were reviewed based on predefined inclusion and exclusion criteria. Reference lists of selected articles were manually searched to identify additional relevant studies. This structured search strategy was designed to encompass a broad range of evidence to comprehensively address the objectives of the review.

Results and Discussion

Intracranial aneurysm

The oculomotor nerve emerges from the nerve nuclei in the midbrain, runs between the posterior cerebral artery and the superior cerebellar artery, passes through the basilar artery, runs parallel to the posterior communicating artery, and then enters the cavernous sinus. Oculomotor nerve palsy may be caused by an aneurysm in an artery adjacent to the oculomotor nerve. Kasner et al. reported that about 30% of cases with oculomotor nerve palsy are caused by aneurysm; the most common ones are posterior communicating artery aneurysm, internal carotid-cavernous sinus aneurysm, internal carotid aneurysm, and posterior cerebral aneurysm [13]. Posterior communicating aneurysms are common, and approximately 90% of posterior communicating aneurysms present with oculomotor nerve palsy before rupture, causing subarachnoid hemorrhage. In recent years, there have also been rare reports of asymptomatic acute dilation of posterior communicating artery aneurysm leading to oculomotor nerve palsy [14].

Patients with posterior communicating artery aneurysm often present with unilateral oculomotor nerve palsy, sudden onset of persistent or progressive headache, and may be accompanied by periorbital pain, vomiting, pallor, and cold sweats. The nerve fibers that innervate the pupil are located in the dorsomedial superficial layer of the oculomotor nerve trunk and are easily compressed; therefore, aneurysmal oculomotor nerve palsy often presents with mydriasis and loss of light reflex and accommodation reflex. Oculomotor nerve palsy caused by cavernous sinus aneurysm is often combined with trochlear, abduction, and damage to the ophthalmic branch of the trigeminal nerve, which is related to the passage of the above-mentioned nerves through the cavernous sinus. Meanwhile, not all patients with aneurysm have pupillary changes. If the aneurysm compresses the oculomotor nerve from below, the pupil may not be involved, which should be differentiated from diabetic oculomotor nerve palsy and ophthalmoplegic migraine [15].

Patients with aneurysmal oculomotor nerve palsy should undergo cerebral angiography as early as possible. After diagnosis, surgical treatment is usually performed. Currently, the primary surgical methods include endovascular coil embolization and microscopic clipping. Many authors have reported that clipping is better than embolization in the treatment of oculomotor nerve palsy [16-18]. The advantage of clipping is that it can directly remove the compressive effect of the tumor on the oculomotor nerve [19, 20]; however, Mino et al. found that these two types of surgery promoted the recovery of oculomotor nerve function, and there was no significant difference in their efficacies [21]. A recent study found that embolization assisted by blood flow diverting devices can promote the recovery of oculomotor nerve function by reducing the pulsation of the aneurysm [22]. Some studies suggest that mecobalamin combined with surgery has a better curative effect [23]. The sequence of postoperative recovery of eye muscle function was levator palpebra muscle, medial rectus muscle, inferior rectus muscle, superior rectus muscle, pupillary sphincter, and ciliary muscle. In terms of the surgical prognosis of patients with aneurysmal oculomotor nerve palsy, some studies have shown that the degree of preoperative oculomotor nerve palsy is an essential factor affecting postoperative neurological recovery [16]. In another study, Leivo et al. found that the interval from the onset to the surgical treatment had a clear impact on the prognosis of oculomotor nerve palsy, and the shorter the interval, the better the effect [24].

In short, it is clinically found that patients with oculomotor nerve palsy may have fixed and dilated pupils. When the cause is unknown, intracranial aneurysm should be highly suspected, and digital subtraction angiography and other related examinations should be timely performed to make the diagnosis and early treatment possible. Once an aneurysm rupture occurs, the consequences are often more severe and even life-threatening. For patients who are suspected of an aneurysm but not shown by angiography, regular check-ups should be performed.

Vascular diseases

Cerebrovascular infarction or hemorrhagic disease

Hypertension, increasing age, and long-term smoking can easily induce vascular sclerosis and blockage of the oculomotor nerve, resulting in ischemia and hypoxia of the oculomotor nerve and causing impairment in its function [25]. Some studies have also found that atherosclerosis causes arterial expansion, deformation, and compression of nerves and, at the same time, causes a local inflammatory response. The combined effect of compression and inflammation can cause sudden oculomotor nerve palsy [26]. The medial rectus muscle is more susceptible than other ocular muscles during ischemia of the oculomotor nerve fibers [27]. Brainstem infarction and hemorrhage often show nuclear damage, manifested as bilateral involvement, with adjacent structures mostly damaged. The damage only affects part of the eye muscles, such as the lack of pupil light reflex and the presence of accommodation reflex. Therefore, patients with cerebrovascular infarction should routinely control blood pressure, lower blood lipids, and improve microcirculation. Various drugs, such as vitamin B-12 and methylcobalamin can also be used to nourish nerves and promote the regeneration of peripheral nerves. Symptoms can be controlled with steroids, such as dexamethasone and prednisolone. The treatment of patients with ophthalmoplegia caused by intracranial hemorrhage mainly includes surgery and medical treatment. Some studies suggest that minimally invasive intracranial hematoma removal combined with mild hypothermia has a good effect on hypertensive cerebral hemorrhagic diseases and has an excellent promoting effect on the recovery of neurological function. Medical treatment includes the effective reduction of intracranial pressure as well as blood pressure. Early intensive antihypertensive treatment in hypertensive patients can limit further expansion of hematoma and prevent neurological deterioration. The prognosis is the best, and neither too high nor too low blood pressure is detrimental to the patient [28]. Calcium ion antagonists, such as nimodipine can promote the absorption of brain edema, hematoma, and the recovery of neurological function. Auxiliary hyperbaric oxygen therapy can also contribute to the recovery of patients. Muthyala et al. found that pregnant women with severe preeclampsia were prone to oculomotor nerve palsy, and with the control of postpartum hypertension, the symptoms of oculomotor nerve palsy would spontaneously remediate [29].

Diabetes mellitus

Peripheral neuropathy caused by diabetes mellitus is common, and oculomotor nerve palsy is the main type of cranial nerve damage in these patients. Clinically, it is not uncommon for diabetic patients to have oculomotor nerve palsy as the first symptom, and it is likely to occur in subjects over 45 years old [30]. The onset is sudden and repeated, and it occurs simultaneously or alternately in one or both eyes, accompanied by orbital and brain diffusion. In addition, these patients may experience pain and discomfort to various degrees. Bortolami et al. maintained that pain was related to trigeminal nerve ischemia that co-runs with the oculomotor nerve and was mostly manifested as partial paralysis, exophthalmos, and ptosis [31]. However, the intraocular muscles were often not involved, which may be because nerve fibers that innervate the pupil are superficial to the oculomotor nerve trunk, and their blood supply comes from the large anastomotic branches of the pia mater, so they are not easily affected [31]. The blood supply source of the central part of the oculomotor nerve is single, and the vascular occlusion caused by diabetes mellitus only demyelinates or necroses the thick fibers in the central part; therefore, the pupil size and light reflex of patients with diabetic oculomotor nerve palsy are often normal. The involvement of the pupil is an important diagnostic factor for whether oculomotor palsy is caused by intracranial lesions, such as intracranial aneurysm, brain tumors, or diabetes mellitus. In addition, studies have found that in diabetic-induced oculomotor nerve palsy, miotic fibers are involved, and the pupil size changes between 0.5 and 1.0 mm [32]. Meanwhile, sudden oculomotor nerve palsy with pain in diabetic patients is not necessarily diabetic oculomotor nerve palsy but may also be caused by carotid-cavernous sinus leakage. Venkatesan et al. reported a 45-year-old diabetic female patient with sudden left-sided complete oculomotor nerve palsy with headache and no pupil involvement [33]. After examination and treatment, it was confirmed that the cause was internal carotid artery cavernous sinus leakage. The treatment of diabetic oculomotor palsy is mainly

to improve microcirculation and metabolic disorders. First, blood sugar should be strictly controlled; second, low-dose hormones can be used to control non-specific inflammatory reactions in the body as appropriate. Insulin can reduce blood sugar fluctuations caused by the use of low-dose hormones, and at the same time, it can improve microcirculation with anticoagulation and vasodilator therapy. Diabetic oculomotor nerve palsy has a favorable prognosis. Suppose it is clinically found that an elderly patient suddenly develops oculomotor nerve palsy, regardless of whether the patient complains of a history of diabetes mellitus. In that case, blood sugar and urine sugar should be routinely checked to avoid misdiagnosis.

Intracranial inflammation

Intracranial inflammation involves a wide range of diseases, and the resulting oculomotor nerve palsy is often a local manifestation of a syndrome. Intracranial inflammation includes acute cranial neuritis, meningitis, chronic non-specific inflammation, post-infection immune response, and so forth. It is often accompanied by a history of upper respiratory or gastrointestinal infections, is sensitive to hormone therapy, and generally has a good prognosis. Oculomotor nerve palsy caused by cranial neuritis is more common in middle-aged people, generally manifested as complete paralysis, which is acute onset and with insignificant headache, sensitive to hormone therapy, and not easy to relapse. A recent report of a middle-aged and elderly male patient infected with Chikungunya virus-induced painless oculomotor palsy [34]. The disease is also occasionally seen in children. Drenckhahn et al. reported a case of isolated oculomotor nerve palsy caused by Lyme disease in a child and found that it was mainly caused by cranial neuritis due to rubillonella infection [35]. After intravenous antibiotic treatment, full recovery was achieved. Painful ophthalmoplegia is a non-specific granulomatous inflammation of intracranial arteries, often involving the oculomotor nerve. Its main manifestations include ipsilateral ptosis, eye movement disorders, and loss of light reflex, accompanied by ipsilateral severe, intractable pain, which can be biting or drilling pain in nature and radiates to the temporal and occipital regions. The symptoms can last for several days or months but can be relieved spontaneously and may recur after intermittent months or years. In addition, corticosteroids are effective in their treatment, and the prognosis is good [36].

Traumatic brain injury

Traumatic brain injury is also a common cause of oculomotor nerve palsy. There are mechanical damage factors, such as the relative displacement of the tissue causing the oculomotor to be squeezed, pulled, or impacted. Some authors maintain that nerve damage may also result from blood supply disorders and unfavorable biochemical factors [37]. When the oculomotor nerve is entirely paralyzed by the trauma, the patient immediately encounters ptosis, mydriasis, loss of light reflex, and abnormal ocular motility. In partial paralysis, the degree of ptosis and mydriasis is mild, but patients often have diplopia, which is more apparent when gazing at the unaffected side and can be alleviated or disappear when looking at the affected side. Midbrain injury is characterized by oculomotor nerve palsy on the diseased side, mostly not involving the pupil, but may have diplopia or strabismus, contralateral cerebellar ataxia, hypotonia, and so on [38]. Traumatic patients often have disturbances of consciousness; however, pupil recovery and improvement of disturbances of consciousness may not manifest at the same time. Internal carotid-cavernous fistula caused by fracture can cause oculomotor nerve damage, and patients often have symptoms of occasional proptosis. Symptoms of oculomotor nerve palsy caused by mild traumatic brain injury usually remediate spontaneously within 6 to 12 months. During this period, if the patient has severe diplopia, some temporary measures can be taken, including covering one eye or wearing a prism. Intramuscular botulinum toxin injection or strabismus surgery may be considered when there is no further sign of improvement beyond 12 months [39]. For the oculomotor nerve palsy caused by severe craniocerebral trauma, there is currently no particular treatment method. Conservative treatment, such as hemostasis, dehydration, anti-infection, nutritional nerve, and vasodilator is given. Ineffective conservative treatment requires surgical repair, but the effect is not satisfactory. Oculomotor nerve palsy caused by mild craniocerebral trauma has an acute onset, a long course of the disease, and a poor prognosis. Early detection and treatment are relatively more effective.

Congenital oculomotor nerve palsy

Congenital oculomotor palsy is the most common cause of oculomotor palsy in children [40]. Congenital oculomotor nerve palsy is mainly related to disorders of the oculomotor nerve nucleus or abnormal development of the oculomotor nerve, perinatal ischemia and hypoxia, birth trauma, and early postnatal diseases. The disease is characterized by clinical symptoms that occur within

six months after birth and are often manifested as monocular onset, large-angle exotropia and hypotropia, mydriasis, and amblyopia in the affected eye [41]. Because strabismus occurs in the stage of visual development and before the optic reflex is fully established, the reason patients seek treatment is the cosmetic concern of strabismus rather than diplopia and compensatory head posture. In addition, the clinical manifestations of congenital oculomotor nerve palsy are closely similar to those of congenital extraocular muscle fibrosis, but patients with congenital oculomotor nerve palsy have abnormal oculomotor nerve function, but normal extraocular muscle structure and contractile function, and ocular magnetic resonance imaging. There is no obvious abnormality in the examination, while the patients with congenital extraocular muscle fibrosis mainly have fibrosis of the involved eye muscles, and ocular muscle fibrosis can be observed on ocular magnetic resonance imaging. The two types of diseases need to be differentially diagnosed. [42]. The treatment methods for congenital oculomotor nerve palsy include medical and surgical treatment. Since medical treatment is not helpful, currently, surgical treatment is the primary treatment option. Surgery can improve the appearance of the affected eye and its visual function. Surgical intervention to correct strabismus due to oculomotor nerve palsy is complicated because four of the six extraocular muscles are involved. The surgical approach is different for complete oculomotor palsy and partial oculomotor palsy. For patients with complete oculomotor nerve palsy, it is necessary to rely on the strength of other muscles and flexible surgical methods to solve the problem of eye position, such as receding and excising the rectus muscle more than the maximum amount or combining the transfer of the superior oblique muscle or even the simultaneous operation of both eyes surgery [7]. An increasing number of studies have begun to explore new surgical modalities, including the installation of ophthalmic prostheses and periosteal fixation. [43]. Gokyigit et al. found that by splitting the end of the lateral rectus muscle and connecting it to the upper and lower edges of the medial rectus muscle, the degree of strabismus could be significantly corrected [44]. Lee et al. also found that medial rectus anchoring had a significant effect on this type of patient [45]. Surgery for some patients with oculomotor nerve palsy only needs to be adjusted according to the nature and degree of extraocular muscle involvement, such as strengthening the paralyzed muscle and weakening the antagonist muscle to improve the eye position. Hence, in clinical practice, patients with congenital oculomotor nerve palsy should be inquired about their medical history in detail, improve the neurological examination, and exclude intracranial lesions before considering eye surgery.

Tumors

Tumors are an important cause of oculomotor nerve palsy, as both benign and malignant neoplasms can compress or infiltrate the nerve along its course. Common tumors include pituitary adenomas، which may compress the nerve in the cavernous sinus, presenting with diplopia, ptosis, and sometimes hormonal imbalances. Meningiomas of the skull base, particularly cavernous sinus meningiomas, cause gradual onset of oculomotor nerve palsy and are treated with surgical resection and/or radiotherapy. Skull base tumors such as chordomas and chondrosarcomas often involve multiple cranial nerves and require multimodal management, including surgery and radiotherapy. Metastatic tumors (e.g. from lung or breast cancer) and nasopharyngeal carcinoma can invade the cavernous sinus, causing rapid oculomotor nerve palsy progression, treated with systemic therapy or radiotherapy. Finally, brainstem gliomas may directly affect the oculomotor nucleus, presenting with associated brainstem symptoms, and are managed with radiotherapy and chemotherapy. Imaging, particularly MRI, plays a critical role in diagnosing tumor-related oculomotor nerve palsy, while treatment focuses on addressing the underlying tumor and symptomatic relief for ocular misalignment [46]. Summary of causes, characteristics and treatment outcomes of oculomotor nerve palsy is reported in Table 1.

Summary

The etiology of oculomotor nerve palsy is complex, including intracranial aneurysm, cerebrovascular infarction or hemorrhagic disease, diabetes, intracranial inflammation, benign and malignant tumors, craniocerebral trauma, congenital tumors, demyelinating diseases, myasthenia gravis, multiple myeloma, and other uncommon causes [47]. Oculomotor nerve palsy caused by different etiologies has its corresponding clinical characteristics, and the treatment methods also have their characteristics. In the process of diagnosis and treatment of patients with oculomotor nerve palsy, ophthalmologists should not be limited to ophthalmology diagnosis and treatment. However, they comprehensively consider craniocerebral and systemic diseases, understand clinical characteristics, reasonably perform relevant examinations, and make a clear diagnosis as early as possible to carry out a timely, reasonable, and effective diagnosis and management plan.

Table 1. Summary of findings: causes, characteristics and treatment outcomes of oculomotor nerve palsy

Author(s)	Year	Type of Study	Sample Size	Additional Explanation(s)	Outcome(s)
Rush & Younge [10]	1981	Retrospective	290	An unselected series of 219 cases of paralysis of cranial nerves III was retrospectively analyzed regarding ultimate recovery and final causal diagnosis.	The greatest number of cases had no identifiable cause. The largest number of patients with known associated diseases had vascular disorders; of these 60 patients, 25 had diabetes mellitus alone, 22 had hypertension alone, and ten had atherosclerosis. Only three had a combination of factors.
Berlit [11]	1991	Retrospective	172	Palsies of the oculomotor nerve were more frequent (n = 172) than the abducens nerve (n = 165), the trochlear nerve (n = 25) or combined ocular motor nerve palsies (n=50).	Vascular lesions plus aneurysms and trauma were the most frequent causes of oculomotor nerve palsy.
Leivo et al. [24]	1996	Retrospective	28	Twenty-eight patients having oculomotor palsy caused by ICA-PCoA aneurysm had surgery as soon as the diagnosis was made.	8 of 9 patients operated on within three days (0-3) and 4 of 6 patients operated on within 4 to 6 days the onset of oculomotor palsy had complete recovery of their third nerve function, in contrast to only 4 of 13 patients operated on later. Especially those operated on more than four weeks later had a dismal outcome: only 1 of 6 had a complete recovery.
Jacobson [32]	1998	Prospective	26	Standardized enrollment criteria were employed to identify 26 consecutive patients with diabetes-associated oculomotor nerve palsy who were evaluated in a referral-based, outpatient neuro-ophthalmology practice.	Internal ophthalmoplegia occurred in 10 (38%) of 26 patients. The size of the anisocoria was 1 mm or less in most patients. None of the patients had a fully dilated unreactive pupil.
Lee et al. [15]	2002	Retrospective	28	The medical records of 28 patients admitted to the Neurology Department at the Chungbuk National University Hospital between January 1992 and August 1999 were reviewed.	19 out of 27 patients were ischemic. They were ten men and nine women. Ocular or frontal pain was present in 15 patients. Most patients, except two women, had risk factors for ischemic vascular disease. There were nine patients with diabetes mellitus. 9 patients (32.1%) had non-ischemic etiologies: two migrainous; two had midbrain infarctions; two neoplastic; three aneurysmal.
Chen et al. [16]	2006	Retrospective	13	They retrospectively compared the outcomes of ONP in 13 patients, six of whom underwent endovascular coiling, and seven of whom underwent surgical clipping.	Clipping posterior communicating artery aneurysms was associated with a higher probability of complete recovery from ONP than coiling. The degree of preoperative ONP also affected recovery.
Keane [4]	2010	Cross-sectional	1400	To compare a large contrasting population, they reviewed 1400 personally examined municipal hospital inpatients with TNPs seen over 37 years (1971-2007).	Causes were trauma (26%), tumor (12%), diabetes (11%), aneurysm (10%), surgery (10%), stroke (8%), infection (5%), Guillain-Barre and Fisher syndromes (5%), idiopathic cavernous sinusitis (3%), benign self-limited (2%), miscellaneous (4%),and unknown (3%).
Khan et al. [17]	2013	Retrospective comparative study	17	Medical records of all patients presenting between January 2000 and February 2013 with intracranial aneurysm were searched. All patients with OMNP secondary to PCOM aneurysm were included for analysis.	Surgical clipping (seven of eight patients, or 87.5%) resulted in greater complete resolution of OMNP than endovascular coiling (four of nine patients, or 44.4%), (P=0.13).

Author(s)	Year	Type of Study	Sample Size	Additional Explanation(s)	Outcome(s)
Gokyigit et al. [44]	2013	Prospective	10	All eyes with oculomotor nerve palsy treated between May 2008 and February 2010 with Y splitting and transposition of the lateral rectus muscle to the medial rectus muscle were prospectively studied. Patients had a preoperative horizontal deviation >45 Δ (range, 45Δ-90Δ).	Of the ten patients, 5 attained stable results following surgery, and 5 with post-operative under correction between 20D and 30D required further surgeries. Postoperatively, two patients improved their sensorial status in a very limited range of gaze, and two patients had symptomatic diplopia.
Brigui et al. [20]	2014	Retrospective	22	They have reviewed the retrospective data concerning twenty-two patients treated at our institution between 2004 and 2012 for PcomA aneurysms with ONP.	This study suggests that both surgical clipping and embolization are safe and effective methods in regard to functional recovery (complete ONP recovery in about 85 % of the cases). However, coiling may lead to a delayed recurrence of third cranial nerve (CN) palsy at long-term follow-up, requiring additional treatment.
Mino et al. [21]	2015	Interventional	17	Among 17 patients with internal carotid artery (ICA) aneurysms presented with oculomotor nerve palsy (ONP), 9 (52.9%) underwent microsurgical clipping and 8 (47.1%) underwent endovascular coiling.	In the microsurgical group, complete resolution (CR) of ONP was obtained in 7 of 9 patients (77.8%), and partial resolution (PR) was seen in 2 patients (22.2%). In the endovascular group, CR was obtained in 5 of 8 patients (62.5%), and PR was seen in 3 patients (37.5%).
Ogawa et al. [27]	2016	Cross-sectional	11	The neuroradiological findings of 11 patients with midbrain infarction-induced oculomotor nerve palsy were analyzed.	Unilateral and bilateral infarcts were seen in 9 and 2 patients, respectively. External ocular muscle palsy was observed in all 11 patients. Ten patients had intranuclear oculomotor nerve palsy. Of these ten patients, 9 had adduction palsy. Internal ocular muscle palsy was detected in 4 patients. Vertical gaze palsy was detected in 3 patients who continued to exhibit Bell's phenomenon.
Shimizu et al. [26]	2016	Case- report	2	Case 1 is a 47-year-old man with a 10-year history of untreated hypertension who came to the emergency department with sudden-onset diplopia. Case 2 is a 43-year-old woman without a history of diabetes mellitus who developed sudden-onset diplopia while watching the news on television and was referred to our neurological department.	They report 2 cases of sudden-onset third nerve palsy due to vascular compression. Both cases had risk factors for atherosclerosis. Brain MRI revealed enhancement of the third nerve at the site of vascular compression. Symptoms of third nerve palsy improved gradually without surgical intervention. Inflammation superimposed on vascular compression can trigger third-nerve palsy.
Fang et al. [3]	2017	Population-based cohort	145	All newly diagnosed cases of acquired third nerve palsy from January 1, 1978, through December 31, 2014, in Olmsted County, Minnesota, were identified using the Rochester Epidemiology Project, a record-linkage system of medical records for all patient-physician encounters among Olmsted County residents.	Population-based cohort demonstrates a higher incidence of presumed microvascular third nerve palsies and a lower incidence of aneurysmal compression than previously reported in non–population-based studies. While compressive lesions had a higher likelihood of pupil involvement, pupil involvement did not exclude microvascular third nerve palsy and lack of pupil involvement did not rule out compressive third nerve palsy.
Jung et al. [5]	2020	Cohort	387	Of 1,108,253 subjects, 387 patients were newly diagnosed with CN3 palsy between 2006 and 2015.	The main cause was presumed to be vascular disease (52.7%), followed by idiopathic causes (25.8%), intracranial neoplasm (7.8%), unruptured cerebral aneurysm (5.4%), and trauma (5.2%).

Conclusion

Oculomotor nerve palsy is a multifaceted neurological condition characterized by impaired eye movements, ptosis, and pupil abnormalities, resulting from diverse etiologies ranging from vascular disorders and intracranial aneurysms to trauma and systemic diseases like diabetes. This review underscores the importance of timely and accurate diagnosis to identify potentially life-threatening causes such as aneurysms, which demand prompt intervention. Effective management strategies, including surgical techniques, pharmacological therapies, and lifestyle modifications, vary based on etiology, highlighting the need for individualized care. Future research should focus on refining diagnostic protocols to improve the early detection of critical conditions, advancing minimally invasive treatment options, and investigating novel therapeutic approaches to enhance functional recovery. Clinically, raising awareness of the condition's varied presentations among healthcare providers is crucial for reducing misdiagnosis and optimizing patient outcomes. Enhanced understanding of the disease pathophysiology will further support targeted interventions, thereby improving prognosis and quality of life for affected individuals.

Ethical Considerations

Compliance with ethical guidelines

This article is a review with no human or animal sample.

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Authors' contributions

Conceptualization, design, and literature search: Yasir Adil Shakor; Data collection: All authors; Manuscript drafting, and critical revisions for intellectual content: Ali Majdi, Raheleh Moravvej, and Yasir Adel Shakor; Supervision, review of final draft: Razieh Bahreini and Yasir Adil Shakor; Conducting the publishing process: Razieh Bahreini; Discussion, review, reading and approval of the final version: All authors.

Conflict of interest

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