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 article comprehensively reviews the common etiologies of oculomotor nerve palsy and the corresponding clinical manifestations and treatment methods in order to help practitioners for the prompt and accurate clinical diagnosis of the causes and effective management plan.
Keywords: Third nerve palsy; Oculomotor nerve palsy; Strabismus; Ptosis.

Introduction:

Overview of anatomy:

Ocular movements in different gazes are undertaken via six 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 (3^{rd} 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, tumor, and endocrine and metabolic diseases. Oculomotor nerve palsy can be divided into complete and incomplete according to the degree at the onset. After affecting complete oculomotor nerve palsy, there are only 2 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.(3) 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 to be the leading cause,(4) and some authors believe that intracranial aneurysm is a more common cause,(5) resulting in differences between studies. This discrepancy can be related to the different causes of the included cases.(4-7) 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, and hence 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.(8) Among the causes of oculomotor nerve palsy in children, congenital 43%, trauma 20%, inflammation 13%, and intracranial artery are the most; however, vascular disease, intracranial aneurysm, and trauma are the most common in adults.(9, 10) 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%.(11) 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.(12) 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.(13)

Method:

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: “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.

Result and Discussion:

1. 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.(14) 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.(15)
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. It is notable that 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.(16)
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;(17-19) the advantage of clipping is that it can directly remove the compressive effect of the tumor on the oculomotor nerve.(20, 21) 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.(22) 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.(23) Some studies suggest that

mecobalamin combined with surgery has a better curative effect.(24) 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.(17) 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.(25)

In summary, 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 (DSA) 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 the aneurysm but not shown by angiography, regular check-ups should be performed.

2. Vascular diseases

2.1. 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.(26) 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.(27) The medial rectus muscle is more susceptible than other ocular muscles during ischemia of the oculomotor nerve fibers.(28) 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. 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. There are also 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.(29) 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.(30)

2.2. 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 people over 45 years old.(31) 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. believed 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.(32) However, the intraocular muscles were often not involved, which may be because of the fact that 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.(32) 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 tumor, 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.(33) It should be noted that 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.(34) 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.

3. 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.(35) 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.(36) 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.(37)

4. 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 believe that nerve damage may also result from blood supply disorders and unfavorable biochemical factors.(38) 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 disappeared 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.(39) Traumatic patients often have disturbances of consciousness; however, pupil recovery and improvement of disturbances of consciousness may do 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.(40) For the oculomotor nerve palsy caused by severe craniocerebral trauma, there is currently no particular treatment method. Generally, conservative treatment such as hemostasis, dehydration, anti-infection, nutritional nerve, and vasodilator is given. Ineffective conservative treatment requires surgical repair, but the effect is generally 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 early treatment are relatively more effective.

5. Congenital oculomotor nerve palsy

Congenital oculomotor palsy is the most common cause of oculomotor palsy in children.(41) Congenital oculomotor nerve palsy is mainly related to the 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 which represent within six months after birth and are often manifested as monocular onset, large-angle exotropia and hypotropia, mydriasis, and amblyopia in the affected eye.(42) Because strabismus occurs in the stage of visual development and before the optic reflex is fully established, the reason for patients who 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 very 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 MRI. 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 MRI. The two types of diseases need to be differentially diagnosed.(43) The treatment methods for congenital oculomotor nerve palsy include medical and surgical treatment. Since medical treatment is not very 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.(8) An increasing number of studies have begun to explore new surgical modalities, including the installation of ophthalmic prostheses and periosteal fixation.(44) 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.(45) Lee et al. also found that medial rectus anchoring had a significant effect on this type of patient.(46) 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. In conclusion, 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.

6. 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 a 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. (47)

Summary of causes, characteristics and treatment outcomes of oculomotor nerve palsy 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.(48) Oculomotor nerve palsy caused by different etiologies has its corresponding clinical characteristics, and the treatment methods also have their own 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 in order to carry out a timely, reasonable and effective diagnosis and management plan.

Conclusion:

In 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.

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Authors contributions:
Yasir Adel Shakor conceptualized and designed the review, conducted the literature search, and curated the data. Ali Majdi, Raheleh Moravvej, and Yasir Adel Shakor contributed to drafting the manuscript and performed critical revisions for intellectual content. Razieh Bahreini and Yasir Adel Shakor provided supervision, reviewed the final draft, and ensured the scientific rigor of the work. Razieh Bahreini conducted the publication process. All authors contributed to discussions, and revisions, read, and approved the final version.

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