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# *Causes of acquired oculomotor nerve palsies*

There are two groups of causes contributing to acquired oculomotor nerve palsies: traumatic and nontraumatic. Traumatic injuries are most frequently the result of road accidents, but they can also be a complication of invasive methods of medical procedures, for example operative treatment of brain aneurysms or lumbar puncture. Among the nontraumatic causes vascular brain incidences are the most common. They are also a factor in aneurysms, tumors, infections of the central nervous system and multiple sclerosis. Other significant causes of oculomotor nerve palsies are diabetes mellitus and connective tissue diseases.

Head injuries are the common cause of palsies of oculomotor nerves. The damage can occur at the moment of acting of a noxious stimulus or some hours after the injury as a result of cytotoxic processes leading to ischaemia of the nerve tissue. Additionally, the formation of intracranial haematoma, increasing oedema or ischaemia of the brain can contribute to secondary injuries of oculomotor nerves.

Injuries of cranial nerves arise mainly as a result of high kinetic energy forces, which often take place during road accidents. The most exposed to injury is the third cranial nerve (3rd cranial nerve, oculomotor nerve), because of its anatomical conditions, that is its short intracranial section with a straight course and limited reserve for tension. Data concerning the occurrence of the 3rd cranial nerve injuries vary from 2.4% to 3.0% and most frequently they are secondary injuries. Primary injuries of the 3rd cranial nerve are diagnosed in about 1% of cases of head injuries.

About 60% of primary and secondary injuries of oculomotor nerve occur in the form of internal ophthalmoplegia, in which only the parasympathetic fibres supplying the pupillary sphincter are damaged. These nerve fibres are thinner and weaker and therefore more susceptible to injury. The motor fibres of the 3rd cranial nerve are affected far less frequently. Injuries of both types of nerve fibres are also possible resulting in total ophthalmoplegia.

Clinical observations point to good regenerative abilities of the 3rd cranial nerve, which can be found in about 60% of traumatic cases. Parasympathetic fibres regenerate the worst. Clinical observations show that the faster the regeneration process of nerve fibres the better the nerve function. Lengthening of time of nerve regeneration may lead to the pathologic process known as the misdirection phenomenon. It can be responsible for the lack of 3rd nerve function return.

The injuries of the fourth cranial nerve (4th cranial nerve, trochlear nerve) happen sporadically, but if they occur, they are usually accompanied by a total and bilateral break of the nerve continuity. The regeneration of the 4th cranial nerve is extremely rare and is usually related to the misdirection phenomenon which is responsible for its abnormal functioning (11, 12).

Injuries of the sixth cranial nerve (6th cranial nerve, abducens nerve) result mainly from secondary mechanisms such as for example increasing intracranial haematoma. Primary injuries are

rarely observed because of the long, intracranial 6th nerve course which tends to decrease the risk of its break in the pull mechanism. The sixth cranial nerve can be hurt as a result of fracture of the petrosal part of the temporal bone, base of the skull or the process of the cervical vertebra (14). Niedermüller et al. described a case of a patient with 6th cranial nerve paresis as a complication of lumbar puncture. The authors suggest that the reason was prolonged cerebrospinal fluid leakage caused by a delayed closure of the duramatral defect (13). Similar cases described in the literature occurred after subarachnoid anesthetic and myelography. The probable cause of the above palsies was intracranial hypotension (3).

Oculomotor nerves can be hurt during operative treatment of aneurysms of the vertebrobasilar system. It may be either the result of direct mechanical nerve injury or vascular complications. The 3rd nerve is injured the most frequently, but literature also provides reports concerning 6th nerve palsies. In most cases spontaneous improvement occurs within a few months. In others, the effects of nerve palsies persist. The occurrence of 3rd cranial nerve palsies after operation of basilar artery aneurysms oscillates from 30% to 75%. In Horikoshi et al. study performed in a group of 105 patients with aneurysms of vertebrobasilar system [77 with basilar tip aneurysm and 28 with SCA (superior cerebellar artery) basilar aneurysm] 3rd nerve palsy was observed in 32% of the operated patients with basilar tip aneurysm and 39% of those with basilar SCA aneurysm (6). 6th nerve palsies have been described in isolated cases of aneurysm operations (10).

Nonruptured intracranial aneurysm can cause ophthalmoplegia in the pressure mechanism or it may be the result of thrombotic and embolic complications. It may occur in the case of aneurysm of the intracavernous part of the internal carotid artery which can injure all oculomotor nerves (3rd, 4th, 6th cranial nerves) (8). However, the aneurysm of the posterior communicating artery is often the cause of isolated, painful 3rd cranial nerve palsy (4). Aneurysms are rarely the cause of 6th nerve palsy (about 4%) (14). It occurs mainly in people above 50 years of age. Isolated 3rd nerve palsy with pupil involvement is rarely a result of stenosis of the internal carotid artery (4).

Another important cause of oculomotor nerve palsies is vascular (haemorrhagic and ischaemic) brain incidents including infarcts of the medial part of the pons resulting in 6th nerve palsy, haemorrhagic and ischaemic lesions in the mesencephalon causing 3rd nerve palsy and large cerebellar infarcts and intracranial haemorrhages accompanied by compression of the brain stem and secondary 6th nerve paresis (8). Also a massive intracranial haemorhage causes a fast increase in intracranial pressure which may threaten with caudal transtentorial herniation of the uncus of the hippocampal gyrus and 3rd nerve pressure. It manifests in unilateral pupil dilatation and lack of pupillary light reaction. A similar mechanism of 3rd nerve palsy is observed in fast increasing epidural or subdural haematomas (9). Intracranial hypertension (regardless of the cause) results in the pressure of the nervous tissue on the base of the skull leading to bilateral 6th nerve palsy in 25% of patients (8).

Another severe vasogenic cause of oculomotor nerve palsies (mainly 3rd and 6th cranial nerves) is cavernous sinus thrombosis which can be a complication of infection in the orbital region or paranasal sinusitis or odontogenic infection (8).

Cranial nerve palsies can be a symptom of primary brain tumor or brain metastases. The occurrence of oculomotor disorders is related to tumors localization in the nervous system. The symptoms of oculomotor nerve palsies result most frequently from tumors of the sinus cavernous and brain stem. They are also typical of tumors of the pineal gland region and cerebellum. They are rarely observed in pituitary tumors. When these tumors expand, they can cause oculomotor nerve palsies in the pressure mechanism (9). Metastases to the subtentorial region of the brain are rare (there are 3% metastases to the brain stem and 15% metastases to the cerebellum). The more frequently occurring supratentorial metastases can indirectly (because of an increase in intracranial pressure) injure the

3rd and 6th nerves and give false localization symptoms. Besides, the metastases to the cranial basis can result in characteristic clinical syndromes that may run with oculomotor nerve palsies: orbital Jacod-Rollet's syndrome (5th, 3rd, 4th, 6th nerves), Foix's syndrome (3rd, 4th, 6th), Gradenin's syndrome (5th, 6th) (9).

Meningitis, regardless of etiology, can proceed with involvement of cranial nerves. Although it most frequently concerns the 7th and 8th cranial nerves, oculomotor nerve palsies can also be observed. The involvement is the result of inflammatory reaction and fibrosis of the meninges along cranial nerve radices (8).

Inflammatory conditions of the nervous tissue, including abscesses localized in the brain stem, cavernous sinus and petrosal pyramid region, can also proceed with involvement of oculomotor nerves. There have been reports in the literature of cases of 6th nerve palsies as an otitis media complication (5, 8).

Paresis or palsies of oculomotor nerves (3rd, 4th, 6th) are observed in about 30% of people with advanced stages of multiple sclerosis. They result from the presence of demyelinizating foci in the brain stem (2, 8). Pareses of these nerves are more frequently found than palsies, which are quite rare. Only in single cases are the autonomic fibres supplying the pupil affected (8). A population based study (inhabitants of Olhmsted Couch) performed in the United States shows that multiple sclerosis was the cause of 6th nerve palsies in 7% (15).

Cases of oculomotor nerve (3rd, 4th, 6th) palsies are often described in the Guillain-Barre syndrome, however in chronic, inflammatory demyelinizating polyradiculoneuropathy they occur only in about 3–4% of patients. The 6th cranial nerve is affected most frequently (1).

Another proven factor for oculomotor nerve palsy is diabetes mellitus. The prevalence of palsy is probably related to ischaemic failure of these nerves which is caused by changes in the vasa nervosum. DM Jacobson et al. in their study stated diabetes mellitus in 41.5% of patients with isolated, ischaemic 3rd nerve palsy. Similar results have been obtained in other studies (Rush and Young – 36.1%, Berlit – 42.0%) (7). It is estimated that oculomotor nerves palsy occurs in about 0.6–1.4% of diabetics. Most frequently nerve palsy concerns the 3rd and 6th nerves, relatively rarely the 4th nerve and usually it takes the form of mononeuropathy. The clinical picture includes a sudden onset of the disease with accompanying heavy ipsilateral eyeball and frontotemporal region pain, lack of other neurological symptoms and spontaneous function return in several weeks. Neither the diabetic disease duration nor the treatment method influences the nerve palsies frequency. The dysfunction of oculomotor nerves can be the first symptom of *diabetes mellitus* (18).

Apart from diabetes mellitus other independent risk factors such as left ventricular hypertrophy and increased haematocrit have been considered to play a role in ischaemic 3rd nerve palsy. So far a direct relationship between isolated 3rd nerve palsy and factors such as: hypertension, hypercholesterolaemia, coronary heart disease, congenital heart disease, nicotine, positive family history of cardiovascular disease has not been proved conclusively (7).

The vascular mechanism in oculomotor nerve palsies has been observed in systemic connective tissue diseases such as rheumatoid arthritis, Sjogren syndrome, systemic lupus erythematosus, Wegener's granulomatosis, giant cell arteritis. The cause of the neuropathy is ischaemia of the brain stem or of the nerve only which is related with panvasculitis (mainly arteriolitis) (8, 16).

Oculomotor nerves can be harmed by toxic effects of exogenous substances. A case of a young patient with bilateral 6th nerve palsy associated with MDMA (3,4-methylenedioxymetamphetamine, "Ecstasy") abuse has been reported by Schröder and Brieden. The mechanism of 6th nerve palsy suggested by the authors is the interaction of MDMA in serotonin metabolism or mild brain oedema (17).

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## SUMMARY

Pareses and palsies of oculomotor nerves can be a symptom of many, various pathologies associated with the central nervous system (vascular brain incidents, aneurysms, primary and secondary tumors, multiple sclerosis, infections or polyradiculopathies). Besides, oculomotor nerve palsies are observed in systemic diseases such as diabetes mellitus, collagenosis or some infections. One major cause of palsies of these nerves is head injuries. The 3rd cranial nerve is injured frequently,

the 6th nerve less often and 4th nerve very rarely. Oculomotor nerves can be also partially or totally affected by toxic substances.

Przyczyny nabytych porażeń nerwów gałkoruchowych

Niedowłady i porażenia nerwów gałkoruchowych mogą być objawem licznych patologii centralnego układu nerwowego, takich jak: naczyniowe uszkodzenia mózgu, tętniaki naczyń mózgowych, guzy pierwotne i przerzutowe, stwardnienie rozsiane, neuroinfekcje, polineuropatie. Poza tym porażenia nerwów gałkoruchowych spotyka się w chorobach ogólnoustrojowych – w cukrzycy, kolagenozach czy infekcjach. Ważną przyczyną porażeń tych nerwów są urazy czaszkowo-mózgowe. Najczęściej uszkodzeniu ulega nerw okoruchowy, następnie nerw odwodzący i bardzo rzadko nerw bloczkowy. Nerwy zaopatrujące aparat ruchowy gałki ocznej mogą ulec częściowemu lub całkowitemu porażeniu także na skutek działania substancji toksycznych i odurzających.