Neuromuscular Diseases (Pediatrics)

Neuromuscular diseases develop as a result of a malfunction in one of the structures of the so-called motor unit, which consists of a motoneuron in the front corners of the spinal cord, a peripheral nerve, a neuromuscular plate and a muscle. A lesion can occur at all these levels, either congenital (genetically based) or acquired as a result of ischemia, inflammation, trauma, toxic effects, etc. Neuromuscular diseases affect all age groups, some typically start in childhood, others in adulthood. Most of these diseases are classified as rare diseases with a very low prevalence.

Damage to the motoneurons of the anterior horns of the spinal cord

- **Spinal muscular atrophy (SMA)** – degeneration of motor neurons of the anterior horns of the spinal cord; AR hereditary; SMA type I (Werdnig-Hoffmann disease) or acute infantile form manifests by 6 months of age with severe hypotonia and muscle weakness with respiratory insufficiency and has a very unfavorable prognosis; SMA type II, or late infantile form, manifests after 6 months of age with severe muscle weakness; children tend to be able to sit without support, but do not walk; SMA type III (Kugelberg-Welander disease) or juvenile form, manifested after 18 months by muscle weakness, first in the lower limbs; normal mental development; typical EMG finding; molecular genetic diagnosis (mutations in the SMN1 gene).
- **Poliomyelitis anterior acute** – inflammatory disease of the anterior horns of the spinal cord of viral etiology; almost eradicated by vaccination; a similar picture can be seen with enterovirus infection.

Impairment of peripheral nerves

- **Charcot-Marie-Tooth (CMT)** or hereditary motor and sensory neuropathy (HMSN) – a heterogeneous group of hereditary neuropathies; different genes and different types of inheritance apply; muscle weakness and atrophy of the distal muscles of the lower limbs, and later also of the upper limbs, typically begin slowly and progress slowly; **diagnosis**: family history including examination of relatives, neurological and EMG examination, molecular genetic examination (in the Czech Republic, not all genes related to CMT are examined yet);some types affect only motor (HMN), or only sensitive (HSN), or sensitive and autonomic nerves (HSAN); according to peripheral nerve conduction velocity during EMG: CMT 1 – clearly reduced conduction velocities due to a defect in the myelin sheath; CMT 2 – conduction velocities normal or only slightly reduced, motor potential amplitude decrease due to axon involvement; **Charcot-Marie-Tooth 1A** – AD hereditary demyelination of the myelin sheath; it begins to manifest itself in childhood with walking disorders (the so-called step-stepping, stork walking), however, the ability to walk remains preserved throughout life.
- **Polyradiculoneuritis or Gullain-Barré syndrome (GBS)** – inflammatory autoimmune disease of peripheral nerves and spinal roots; segmental demyelination or axonal degeneration; it rarely affects the cranial or autonomic nerves; 80-90% of cases: acute demyelinating form - the most common inflammation-related paresis (after eradication of poliomyelitis); other, less common forms: acute axonal, chronic demyelinating and Miller-Fisher syndrome. **Pathogenesis**: an excessive immune reaction to an infection (respiratory, gastrointestinal) or immunization (exceptionally also to a serious injury or surgery), which activates the immune system and then attacks the structures of the peripheral nerve, rapidly developing neurological symptoms (paresthesia, pain in the lower limbs or back, muscle weakness to paresis of the lower limbs first, which progresses upwards); serious complications include dysautonomic symptoms - fluctuations in blood pressure or heart rate, profuse sweating, sphincter disorders; usually 2 weeks after the insult; progresses over days to weeks, followed by a plateau phase lasting up to 2 weeks, followed by gradual regression (on the order of months); complete recovery occurs in 90-95% of cases; **Diagnosis**: anamnesis – typical course, proteinocytological dissociation in cerebrospinal fluid (elevation of protein with normal cell count) a few days after manifestation, abnormal EMG; **Treatment:** immunosuppressants (high-dose immunoglobulins, plasmapheresis), symptomatic treatment, rehabilitation.
- Peripheral nerves (their axons or myelin sheaths) are also often damaged, for example, in leukodystrophy and congenital glycosylation disorders.

Impairment of the neuromuscular junction

- **Congenital myasthenic syndromes (CMS)** – a clinically and genetically heterogeneous group of diseases caused by a mutation of one of the genes encoding proteins of the neuromuscular plate; **clinical manifestations**: e.g. impaired sucking and swallowing, weak crying, ptosis, ophthalmoplegia, hypotonia, muscle weakness, delayed motor development, arthrogryposis, sometimes even a crisis with life-threatening acute respiratory failure; in the Czech Republic, most often in the Roma ethnic group due to a mutation of the epsilon subunit of the acetylcholine receptor; symptomatic treatment with cholinesterase inhibitors.

- **Myasthenia gravis** – autoimmune disease of the neuromuscular disc, antibodies against the acetylcholine receptor are most often present; rare in children; more common in adolescence;

1. Ocular form – eyelid ptosis and oculomotor disorder with diplopia and strabismus;
2. Generalized form - in addition, weakness of the skeletal, cervical and bulbar muscles (swallowing and expectoration disorders);

Symptomatic treatment with acetylcholinesterase inhibitors, or immunosuppressants to induce remission or surgical treatment – thymectomy.

Additionally there may be cases of transient myasthenia gravis in newborns of myasthenic mothers - caused by transplacentally transferred antibodies.

- **Botulism** – reversible toxic damage to the neuromuscular disc caused by a thermolabile neurotoxin produced by the bacterium Clostridium botulinum in contaminated, poorly preserved food under anaerobic conditions. Infant botulism – with constipation, immunodeficiency or a change in the intestinal microflora, C. botulinum, colonizing the infant's digestive tract, begins to produce a toxin that causes muscle weakness and hypotonia.

Skeletal muscle diseases

- **Muscular dystrophies: Duchenne muscular dystrophy** – the most common inherited muscle disease, affects boys; caused by a mutation in the dystrophin gene (on the X chromosome); asymptomatic until 3-5 years of age, then walking disorders due to weakness of pelvic girdle muscles; calf muscle hypertrophy; sometimes present reduced intellect; around 10 years of age loss of ability to walk independently; significantly reduced life expectancy; marked elevation of CK, elevation of AST and ALT at normal GMT; molecular genetic diagnosis, possibly muscle biopsy treatment: corticosteroids, symptomatic treatment, prospective genetic therapy. **Becker muscular dystrophy** - less common, milder manifestations. **girdle muscular dystrophy, congenital muscular dystrophy.**
- **Congenital myopathy** ("structural") - a heterogeneous group that is divided according to findings in muscle biopsy; primarily myofibrils affected; genetically determined; manifestation after birth; weakness and hypotonia dominate; mostly slow progression; CK normal or slightly elevated, diagnosis based on muscle biopsy, rarely possibility of molecular genetic diagnosis.
- **Myotonic dystrophies** – degenerative, genetically determined, progressive disorders of skeletal muscles with multi-organ involvement (heart – transmission disorders, eyes – cataracts, gonads – testicular atrophy, endocrine glands – insulin resistance, brain – cognitive deficit, mental retardation, neuropathological abnormalities and neuropsychological changes) the most common adult-onset inherited neuromuscular disorder progressive muscle weakness and myotonia are typical abnormal electrical excitability of the sarcolemma causes myotonia, which is clinically manifested by impaired decontraction of skeletal muscles (e.g. when shaking hands); type I – the most common; AD hereditary; CTG trinucleotide expansion in the DMPK1 gene; the phenomenon of anticipation - an earlier start and a more difficult course in each subsequent generation
- **Congenital myotonia** – hypotonia and severe generalized weakness at birth, poor sucking and swallowing, often also respiratory insufficiency; deformity of the upper lip (so-called carp mouth) due to bilateral weakening of facial muscles; in 50-60% psychomotor retardation; myotonia is not usually clinically apparent in the first year of life; significantly reduced life expectancy (death often due to cardiopulmonary failure); the expanded allele of the DMPK1 gene is acquired almost exclusively from the mother; type II – milder manifestations; proximal myotonic myopathy; AD hereditary; CCTG tetranucleotide expansion in the ZNF-9 gene; diagnosis: EMG, molecular genetic diagnosis, CK normal or slightly elevated, elevated serum myoglobin level incurable, only myotonic manifestations can be influenced (phenytoin, carbamazepine, mexiletine), dystrophic manifestations cannot be influenced; monitoring is important (ECG, glycemia, T4, TSH, eye).
- **Periodic paralysis** – a heterogeneous group characterized by episodes of muscle hypotonia at irregular intervals; hereditary; associated with potassium disorders; based on ion channel disorders.
- **Benign acute childhood myositis** (myositis cruris) - develops during or after a respiratory infection and is manifested by significant pain in the calf muscles, for which the child walks on tiptoes, or he does not walk; CK tends to be elevated; it resolves spontaneously without treatment, rest and analgesics are suitable.

Diagnostics

- anamnesis;
- creatine kinase (CK) level – increased in (not only) muscle diseases;
- targeted molecular genetic examination;
- electromyography (EMG) of peripheral nerves or muscles;
- examination of metabolic defects;
- muscle or nerve biopsy;
- cerebrospinal fluid examination;
- immunological examination;
- magnetic resonance imaging (MRI);
- muscle ultrasound.

Links

External Links

- prof. MUDr. J. Bednařík, CSc.: Svalové dystrofie (http://www.solen.sk/index.php?page=pdf_view&pdf_id=1945)
- prof. MUDr. Z. Ambler, DrSc., prof. MUDr. J. Bednařík, CSc.: Myopatie (http://www.solen.sk/pdf/Ambler1.pdf)
- MUDr. J. Kraus, CSc. a kol.: Kongenitální myopatie (http://www.solen.sk/pdf/6f7d390f0a0f04119997d18d0330a587.pdf)
- doc. MUDr. E. Ehler, CSc, doc. MUDr. J. Zámečník, Ph.D.: Zánětlivé myopatie (http://www.neurologiepropraxi.cz/pdfs/neu/2012/04/07.pdf)

- prof. MUDr. Z. Ambler, DrSc.: Zánětlivé myopatie (http://www.solen.cz/pdfs/neu/2004/03/06.pdf)
- prof. MUDr. J. Bednařík, CSc.: Toxické a lékové myopatie (http://www.solen.sk/pdf/Bednarik1.pdf)
- MUDr. R. Mazanec, Ph.D., Mgr. Z. Mušová, Ph.D.: Myotonické dystrofie (http://www.solen.cz/pdfs/neu/2012/04/03.pdf)
- prof. MUDr. Z. Ambler, DrSc.: Myotonická dystrofie (http://www.solen.sk/index.php?page=pdf_view&pdf_id=1946)

References

- ŠIŠKOVÁ, Dana. Nervosvalová onemocnění v dětském věku. *Pediatrie pro praxi.* 2012, roč. 13, vol. 6, s. 365-368, ISSN 1213-0494.
- KRAUS, J. Kongenitální myopatie. *Neurológia pre prax* [online]. 2012, roč. 13, vol. 4, s. 192-197, dostupné také z <http://www.solen.sk/pdf/6f7d390f0a0f04119997d18d0330a587.pdf>.
- AMBLER, Z. Myotonická dystrofie. *Neurológia pre prax* [online]. 2004, roč. -, vol. 3, s. 141-144, dostupné také z <http://www.solen.sk/index.php?page=pdf_view&pdf_id=1946>.
- MAZANEC, R a Z MUŠOVÁ. Myotonické dystrofie. *Neurologie pro praxi* [online]. 2012, roč. 13, vol. 4, s. 183-187, dostupné také z <http://www.solen.cz/pdfs/neu/2012/04/03.pdf>.
- https://emedicine.medscape.com/article/1171678-overview