Neurodegenerative Diseases

Neurodegenerative diseases are characterized by -

- **Progressive death of neurons.**
- **Reactive glia multiplication.**
- **Deposition of protein deposits.**

The clinical manifestation is diverse depending on the affected structures.

Pathogenesis

The basic pathogenetic mechanism is a *change in the secondary structure* of the affected protein when there is an increase in *the proportion of β-sheet* – the protein thus acquires other properties (it is resistant to chemical and physical influences). The cell cannot process it, so it accumulates, can be toxic or induce apoptosis. On the other hand, there is a lack of functional protein.

Diagnostics

Clinical diagnosis arises on the basis of clinical, paraclinical and genetic examinations. However, the neuropathological diagnosis using macroscopy, microscopy, and analysis of proteins (immunohistochemistry, western blot) and nucleic acids is definitive.

Alzheimer's disease

Alzheimer's disease is characterized by the presence of amyloid plaques and neurofibrillary balls.

Amyloid plaques are *extracellular deposits of amyloid-β-peptide*. Pathological amyloid-β-peptide (A-β-42) is formed from *the amyloid precursor protein (APP)* by cleavage *γ-sectresasis*. A normal product (A-β-40), which is shorter by two amino acids, forms *α-secretase*. Pathological amyloid-β-peptide induces apoptosis of neurons and stimulates glia.

Neurofibrillary clusters (tangles) are *intracellular* aggregates of hyperphosphorylated *τ-protein* (see Tauopathy).

Early Alzheimer's disease is familial – associated with genetic mutations (mutation of APP, components of γ-sectretase; the presence of the apoprotein E *ApoE4* allele is also at risk), the late form has a more complex etiology.

Tauopathy

Tauopathies are rare diseases associated with a τ-protein mutation.

τ-protein (tubulin-associated unit) strengthens the structure of microtubules. Its hyperphosphorylated form does not fulfill this role, but aggregates to form amyloid.

- Progressive supranuclear palsy (Steele-Richardson-Olszewski).
- Corticobasal degeneration.
- Pick's diseases - frontotemporal atrophy (Pick's bodies intracellularly).
- Dementia with argyrophilic grains.

Synucleinopathy

α-synuclein is abundantly present in the CNS, but its role is not entirely clear. The pathological form creates Lewy bodies inside the cells and induces apoptosis.

- Parkinson's disease
- Dementia with Lewy bodies
- Multiple systemic atrophy

Triplet diseases

The pathological protein is a product of a mutated gene in which the expansion of trinucleotide repeats occurs.

- Huntington's disease
- Spinocerebellar ataxia

Motoneuron disease

It is a group of diseases affecting the upper (in the cortex) and lower (in the spinal cord or in the trunk) motoneurons.

- Amyotrophic lateral sclerosis (ALS) – Most cases are sporadic, 5–10% are caused by a mutation in superoxide dismutase 1, which produces excessive amounts of free radicals.

Prion diseases

More detailed information can be found on the Prions page.

Links

Source

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