PARKINSON'S DISEASE – PATHOGENESIS, CLINICAL FEATURES, AND DIAGNOSTIC STRATEGIES

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Abstract: Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by motor and non-motor symptoms that significantly impair quality of life. The disease results primarily from degeneration of dopaminergic neurons in the substantia nigra pars compacta and the presence of intracellular α-synuclein aggregates known as Lewy bodies. This article reviews current understanding of the molecular mechanisms, clinical manifestations, and diagnostic approaches in Parkinson's disease.

Keywords: Parkinson's disease, α-synuclein, Lewy bodies, substantia nigra, bradykinesia, tremor, neurodegeneration, biomarkers.

Introduction

Parkinson's disease is the second most common neurodegenerative disorder after Alzheimer's disease, affecting approximately 1% of the population over 60 years of age. The disease is multifactorial, involving genetic susceptibility, environmental exposures, mitochondrial dysfunction, and neuroinflammatory processes. Early and accurate diagnosis remains challenging, particularly in the prodromal stage.

Molecular and Cellular Pathogenesis

Central to PD pathology is the progressive loss of dopaminergic neurons in the substantia nigra and subsequent dopamine depletion in the striatum. Abnormal aggregation of α-synuclein leads to the formation of Lewy bodies, which disrupt intracellular transport, synaptic function, and neuronal survival.

Mitochondrial dysfunction, particularly impairment of complex I of the electron transport chain, contributes to increased oxidative stress and energy failure. Dysfunction of the ubiquitin–proteasome system and autophagy–lysosomal pathways results in impaired clearance of misfolded proteins. Neuroinflammation mediated by activated microglia and proinflammatory cytokines further accelerates neurodegeneration.

Genetic and Environmental Factors

Several genes have been implicated in familial and sporadic PD, including SNCA, LRRK2, PARK2 (parkin), PINK1, and DJ-1. Environmental risk factors include pesticide exposure, heavy metals, traumatic brain injury, and rural living. Protective factors such as smoking and caffeine consumption have been described, though the mechanisms remain unclear.

Clinical Manifestations

Motor symptoms classically include resting tremor, bradykinesia, rigidity, and postural instability. Non-motor symptoms such as depression, anxiety, sleep disorders, autonomic dysfunction, constipation, hyposmia, and cognitive impairment frequently precede the onset of motor signs.

Disease progression follows a variable course and is often described by the Hoehn and Yahr staging system.

Diagnostic Strategies

Diagnosis remains primarily clinical, supported by response to dopaminergic therapy. Neuroimaging techniques, such as dopamine transporter single-photon emission computed tomography (DaT-SPECT) and transcranial sonography, may assist in differentiating PD from atypical parkinsonian syndromes.

Emerging biomarkers include cerebrospinal fluid α-synuclein, neurofilament light chain, and genetic profiling.

Complications

Advanced PD is associated with motor fluctuations, dyskinesias, freezing of gait, falls, psychosis, and dementia. These complications significantly increase caregiver burden and healthcare costs.

Conclusion

Parkinson’s disease is a heterogeneous and complex disorder. Advances in molecular biology and imaging are improving understanding of disease mechanisms and opening new avenues for early diagnosis and disease-modifying therapies.

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