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ETIOPATHOGENESIS AND EARLY DETECTION OF MICROCEPHALY IN CHILDREN

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ABSTRACT:

Microcephaly is one of the most severe neurodevelopmental disorders in childhood and is characterized by reduced brain size and head circumference, frequently accompanied by pronounced cognitive, motor, and neurophysiological impairments. In recent years, an apparent increase in microcephaly prevalence has been reported, which may be explained by improved diagnostic capabilities as well as a higher frequency of adverse perinatal factors.

The aim of this study is to systematize current concepts of the etiopathogenesis of microcephaly and to analyze clinical and instrumental approaches to its early detection. Genetic, infectious, hypoxic–ischemic, and metabolic mechanisms underlying microcephaly are reviewed, alongside the role of molecular diagnostics, neuroimaging, and neurophysiological methods.

The findings highlight the multilevel nature of microcephaly pathogenesis and underscore the need

for a comprehensive, multidisciplinary approach to early diagnosis and prognostication of neurological outcomes.

Introduction

Microcephaly belongs to the group of congenital and early acquired anomalies of central nervous system development and is defined as a head circumference more than two standard deviations below the age- and sex-adjusted mean. This condition reflects insufficient growth and development of the brain and serves as an important marker of severe neuroontogenetic disturbances. According to international epidemiological studies, the prevalence of microcephaly ranges from 1 to 5 cases per 1,000 live births; however, in low- and middle-income settings the reported rates may be substantially higher. The clinical significance of microcephaly is determined not only by its frequency but also by the high risk of disability, persistent cognitive deficits, and epileptic syndromes.

Current concepts consider microcephaly not as an isolated disease but rather as a syndrome reflecting a broad spectrum of pathological processes that disrupt normal brain development at different stages of ontogenesis.

Etiopathogenesis of Microcephaly

Genetic forms of microcephaly are associated with mutations in genes regulating the proliferation of neuronal progenitor cells, neuronal differentiation, and synaptic network formation. The most extensively studied genes include MCPH1, ASPM, WDR62, and CDK5RAP2, which participate in mitotic control and the symmetric division of neuroblasts.

At the molecular level, these mutations may lead to premature termination of neurogenesis, reduction of the neuronal cell pool, and, consequently, decreased cerebral cortical volume. Disruption of key developmental signaling pathways—such as Wnt/β-catenin, Notch, and Sonic Hedgehog—also plays a crucial role, as these pathways regulate neuronal population growth during embryogenesis.

Infectious and Neuroinflammatory Factors

Intrauterine infections can cause direct neuronal injury and activate neuroinflammatory cascades. Increased production of proinflammatory cytokines (IL-1β, TNF-α, IL-6) may impair neuronal migration and promote apoptosis within nervous tissue. In recent years, Zika virus infection has gained particular importance because of its tropism for neural stem cells and its ability to suppress their proliferation, leading to severe forms of microcephaly.

Hypoxic–Ischemic Mechanisms

Hypoxia during the antenatal and intrapartum periods disrupts neuronal energy metabolism and triggers oxidative stress cascades. Oxygen deficiency results in free-radical accumulation, mitochondrial injury, and activation of programmed cell death pathways. Under conditions of chronic hypoxia, delayed myelination, white matter reduction, and impaired formation of neuronal networks may develop.

Metabolic and Toxic Factors

Metabolic disorders may be accompanied by accumulation of toxic metabolites with neurotoxic effects. Fetal alcohol spectrum disorder is a classic example of secondary microcephaly, caused by the teratogenic impact of ethanol on the developing brain.

Overall, microcephaly arises from complex interactions between genetic and exogenous factors that disrupt fundamental processes of neuroontogenesis.

Modern Approaches to Early Detection of Microcephaly

Anthropometric Screening - Measurement of head circumference remains the principal and most accessible method of primary diagnosis. Regular longitudinal monitoring of this parameter enables detection of both congenital and progressive forms of microcephaly.

Neuroimaging

MRI allows assessment of the degree of brain volume reduction, severity of cortical atrophy, white matter status, and the extent of delayed myelination. Advanced techniques (DTI, fMRI) provide insights not only into structural abnormalities but also into functional connectivity between brain regions.

Neurophysiological Methods

EEG reflects functional immaturity and dysfunction of the cerebral cortex. In children with microcephaly, diffuse abnormalities of bioelectrical activity, reduced rhythm synchrony, and increased seizure susceptibility are commonly observed.

Biomarkers and Emerging Directions In recent years, biochemical and molecular markers of neural injury—such as neuron-specific enolase (NSE), S100B protein, and neurofilament light chain (NfL)—have been actively investigated. Elevated levels may correlate with CNS injury severity and could contribute to outcome prediction.

Prognostic Value of Early Diagnosis - Early identification of microcephaly enables prediction of the severity of cognitive and motor impairment and supports timely initiation of corrective and rehabilitative interventions. The most unfavorable prognosis is typically

associated with microcephaly combined with epilepsy, pronounced delayed myelination, and structural cortical abnormalities.

Comprehensive early rehabilitation—including neurostimulation, psychological and educational interventions, and pharmacological support—may facilitate partial functional recovery and improve quality of life.

Conclusion

Microcephaly is a complex, polyetiological syndrome caused by disruption of key molecular and cellular mechanisms of brain development. Early diagnosis based on integration of clinical findings with neuroimaging and neurophysiological data is critical for prognosis and prevention of severe neurological outcomes. Contemporary research supports the incorporation of biomarker-based and functional approaches into early screening systems for microcephaly.

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