CRANIOSYNOSTOSIS – PATHOGENESIS, CLASSIFICATION AND CLINICAL CONSEQUENCES

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Abstract: Craniosynostosis is a congenital disorder characterized by the premature fusion of one or more cranial sutures, resulting in abnormal skull growth and potential impairment of brain development. The condition may occur as an isolated anomaly or as part of a genetic syndrome. Early diagnosis and optimal management are crucial to prevent increased intracranial pressure, neurodevelopmental delay, and aesthetic deformities. This article reviews the epidemiology, pathogenesis, classification, clinical manifestations, and potential complications of craniosynostosis.

Keywords: craniosynostosis, premature suture fusion, skull deformity, FGFR mutations, pediatric neurosurgery, intracranial pressure, syndromic craniosynostosis.

Introduction

Craniosynostosis affects approximately 1 in 2,000–2,500 live births worldwide and represents a significant challenge in pediatric neurosurgery and craniofacial surgery. Normally, cranial sutures remain open during infancy to allow for rapid brain growth. Premature fusion of these sutures restricts skull expansion perpendicular to the affected suture, leading to compensatory deformities in other regions of the skull. Understanding the biological mechanisms behind craniosynostosis is fundamental for early intervention.

Pathogenesis

The pathogenesis of craniosynostosis is multifactorial and involves genetic, molecular, and environmental factors. Mutations in fibroblast growth factor receptor genes (FGFR1, FGFR2, FGFR3), as well as TWIST1 and MSX2 genes, play a major role in syndromic and some nonsyndromic forms. These mutations lead to abnormal osteoblast differentiation and premature ossification of cranial sutures.

In addition to genetic factors, intrauterine constraints, maternal smoking, thyroid disease, and certain teratogenic exposures have been implicated as potential risk factors. Disruption of normal signaling pathways, including fibroblast growth factor (FGF), transforming growth factor-beta (TGF-β), and bone morphogenetic protein (BMP) pathways, results in accelerated suture fusion.

Classification

Craniosynostosis is classified based on the number and type of sutures involved:

- **Sagittal synostosis** (scaphocephaly) – the most common form, characterized by a long, narrow skull.

- **Coronal synostosis** (anterior plagiocephaly or brachycephaly).
- **Metopic synostosis** (trigonocephaly).
- **Lambdoid synostosis** (posterior plagiocephaly).
- **Complex (multisuture) synostosis** – involving multiple sutures.

It is also categorized as **syndromic** (associated with genetic syndromes such as Apert, Crouzon, and Pfeiffer syndromes) and **nonsyndromic** craniosynostosis.

Clinical Manifestations

Clinical features vary according to the sutures involved and include abnormal head shape, palpable ridging along sutures, facial asymmetry, and delayed closure of fontanelles in unaffected regions. Functional complications may include:

- Increased intracranial pressure
- Visual impairment due to optic nerve compression
- Developmental delay
- Feeding and respiratory difficulties

Neuropsychological deficits, including cognitive and behavioral disorders, have been reported, especially in complex and syndromic cases.

Complications

Untreated craniosynostosis may lead to chronic intracranial hypertension, hydrocephalus, Chiari malformations, and psychosocial difficulties due to craniofacial deformities. Early surgical correction significantly reduces the risk of these complications and improves long-term outcomes.

Conclusion

Craniosynostosis is a complex developmental disorder requiring early recognition and multidisciplinary management. Advances in genetics and molecular biology have significantly improved understanding of its pathogenesis, opening new avenues for targeted therapies in the future.

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