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CROUZON SYNDROME: PATHOGENESIS, CLINICAL MANIFESTATIONS AND RESULTS OF OWN CLINICAL OBSERVATION

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Abstract: Crouzon syndrome is a rare genetic craniosynostosis syndrome characterized by the premature fusion of one or more cranial sutures, leading to distinctive craniofacial deformities. It is most commonly caused by autosomal dominant mutations in the FGFR2 (fibroblast growth factor receptor 2) gene, resulting in abnormal signaling pathways that regulate bone growth and differentiation. The pathogenic mechanism is based on accelerated osteogenesis of the cranial sutures, which restricts normal skull expansion and causes compensatory growth in other cranial regions. Clinically, Crouzon syndrome is manifested by craniosynostosis with brachycephaly or scaphocephaly, midface hypoplasia, shallow orbits with ocular proptosis, hypertelorism, and malocclusion. Neurological complications may include increased intracranial pressure, headaches, visual impairment due to optic nerve compression, and, in some cases, cognitive or developmental delays. Unlike some other craniosynostosis syndromes, limb abnormalities are typically absent, which is an important diagnostic feature. Diagnosis is based on clinical examination, radiological findings (computed tomography and magnetic resonance imaging of the skull and brain), and molecular genetic testing to confirm FGFR2 mutations. Management requires a multidisciplinary approach involving neurologists, neurosurgeons, maxillofacial surgeons, ophthalmologists, and geneticists. Early surgical intervention aimed at cranial decompression and correction of craniofacial deformities plays a crucial role in preventing neurological and ophthalmological complications and improving functional and cosmetic outcomes.

Key words: Crouzon syndrome, craniosynostosis, FGFR2, craniofacial abnormalities, optic canal stenosis.

Introduction

Crouzon syndrome is a rare hereditary craniofacial disorder belonging to the group of craniosynostosis syndromes and is characterized by the premature fusion of one or more cranial sutures. First described by the French neurologist Louis Édouard Octave Crouzon in 1912, the syndrome represents a clinically and genetically heterogeneous condition with significant variability in severity and clinical presentation. The estimated incidence of Crouzon syndrome is approximately 1 per 25,000 live births, making it one of the more frequently encountered syndromic forms of craniosynostosis, although it remains a rare disease in general clinical practice.

The etiopathogenesis of Crouzon syndrome is primarily associated with autosomal dominant mutations in the *FGFR2* gene, which encodes the fibroblast growth factor receptor 2, a key regulator of osteogenesis and cranial suture development. These mutations lead to dysregulated fibroblast growth factor signaling, resulting in premature ossification of cranial sutures and abnormal craniofacial growth. While most cases are inherited, a significant proportion arise from de novo mutations, often associated with increased paternal age. The early closure of cranial sutures restricts normal brain and skull growth, leading to compensatory deformities and, in some patients, to elevated intracranial pressure and secondary neurological complications.

Clinically, Crouzon syndrome is characterized by distinctive craniofacial abnormalities, including brachycephaly or other skull shape deformities, midface hypoplasia, shallow orbits

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with marked ocular proptosis, hypertelorism, and dental malocclusion. Neurological manifestations may vary from mild headaches to more severe consequences such as increased intracranial pressure, hydrocephalus, visual impairment due to optic nerve compression, and, less commonly, developmental delay. Importantly, unlike other craniosynostosis syndromes such as Apert or Pfeiffer syndromes, Crouzon syndrome typically lacks abnormalities of the hands and feet, which aids in differential diagnosis.

The diagnosis of Crouzon syndrome is based on a combination of clinical features, neuroimaging findings, and genetic confirmation. Advances in imaging techniques, particularly high-resolution computed tomography, have significantly improved the assessment of cranial suture involvement and intracranial structures. Molecular genetic testing allows definitive diagnosis, facilitates genetic counseling, and supports early detection in affected families. However, due to phenotypic variability and the progressive nature of craniofacial deformities, early diagnosis remains a clinical challenge, especially in mild cases.

Management of Crouzon syndrome requires a multidisciplinary and staged approach, involving specialists in neurology, neurosurgery, craniofacial and maxillofacial surgery, ophthalmology, otolaryngology, and medical genetics. Timely surgical intervention is essential to prevent irreversible neurological and ophthalmological complications and to improve functional, aesthetic, and psychosocial outcomes. Despite advances in surgical techniques and perioperative care, long-term follow-up remains necessary due to the risk of recurrent intracranial hypertension and progressive craniofacial anomalies.

In this context, detailed clinical observations and case-based analyses remain highly relevant, as they contribute to a better understanding of the disease course, diagnostic pitfalls, and optimal therapeutic strategies. The present study aims to highlight the pathogenetic mechanisms, clinical manifestations, and management aspects of Crouzon syndrome through an in-depth analysis of our own clinical observation.

Materials and Methods

The study included an analysis of current literature data on the pathogenesis, clinical manifestations, diagnosis, and treatment of Crouzon syndrome, as well as a retrospective evaluation of an own clinical observation.

The patient underwent: clinical and neurological examination; ophthalmological assessment including visual acuity testing and fundus examination; neuroimaging (CT and MRI of the skull and brain); molecular genetic testing for FGFR mutations.

Surgical interventions and postoperative outcomes were evaluated during follow-up.

Results. Clinical manifestations

The main clinical features of Crouzon syndrome include craniosynostosis with deformities of the cranial vault, midface hypoplasia, shallow orbits with exophthalmos, hypertelorism, malocclusion, and dental anomalies. Ophthalmological manifestations are common and include amblyopia, astigmatism, strabismus, optic nerve compression, and secondary optic atrophy.

Neurological complications are secondary and result from cranial deformities and impaired cerebrospinal fluid dynamics. The most frequent conditions are intracranial hypertension, hydrocephalus (20–40% of patients), headaches, sleep disturbances, and, rarely, epileptic seizures.

Own clinical observation. A 6-year-old boy with a genetically confirmed FGFR2 mutation was diagnosed with Crouzon syndrome. From birth, the patient presented with severe craniosynostosis, craniofacial deformities, increased intracranial pressure, and mixed hydrocephalus. Ventriculoperitoneal shunting was performed at the age of 9 months.

Despite multiple craniofacial reconstructive surgeries, progressive visual impairment developed due to bilateral optic canal stenosis, accompanied by partial secondary optic nerve atrophy. The patient underwent bilateral surgical decompression of the optic canals, which resulted in partial improvement and stabilization of visual function during early postoperative follow-up.

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Discussion. Crouzon syndrome demonstrates marked phenotypic variability and a wide spectrum of complications. Although cognitive functions are usually preserved, secondary neurological and ophthalmological disorders significantly influence long-term outcomes.

Optic canal stenosis is a severe but potentially reversible cause of visual loss in Crouzon syndrome. Early detection using high-resolution neuroimaging and timely surgical decompression are critical for preserving visual function. Molecular genetic diagnostics not only confirm the diagnosis but also enable genetic counseling and preimplantation genetic testing (PGT-M) in affected families.

Management of patients requires a staged, interdisciplinary approach involving neurosurgeons, maxillofacial surgeons, ophthalmologists, neurologists, orthodontists, and geneticists. Drug therapy plays an auxiliary role and does not replace surgical correction of intracranial hypertension.

Conclusion. Crouzon syndrome is a complex genetic craniofacial disorder with multisystem manifestations. Diagnosis is based on phenotypic assessment, neuroimaging, and molecular genetic testing. An interdisciplinary approach is essential for preventing severe complications such as intracranial hypertension and vision loss.

The presented clinical observation highlights the importance of early recognition and surgical treatment of optic canal stenosis. Timely decompression allowed stabilization of visual function and improvement in the patient's quality of life. With adequate and early management, the neurological prognosis in Crouzon syndrome is favorable in most cases.

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