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Ophthalmic Manifestations of Crouzon Syndrome

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ABSTRACT

Metastatic lesions to the gingiva are rare. Lung, prostate and rectal carcinoma are the most common primary tumors with a gingival mass as a presentation of metastatic disease. The following report describes an unusual case of gingival masses in a patient with renal cell carcinoma with concomitant lung, bone, liver, meningeal, muscle and adrenal gland metastases. The sudden appearance of lesions in the head and neck region should always raise suspicion in a patient with a history of cancer that rarely metastasizes to this site.

Keywords: Renal cell carcinoma, Gingiva, Metastasis; Oral metastasis

Abbreviations: RCC: Renal cell carcinoma; UN: United Nations; CSF: Cerebrospinal Fluid; MRI: Magnetic Resonance Imaging; ENT: Ear, nose and throat

INTRODUCTION

Skull bones articulate through areas called sutures. These fibrous joints are constituted by mesenchyme that must remain unmineralized (unfused) until physiological skull growth is finalized. A tightly regulated mechanism prevents premature and persistent osteogenesis, preserving suture patency. Mechanisms of suture growth must modulate osteogenesis at the right site and timing, until growth is complete. Sutures function as key growth centers of the skull during the early years of life. Hence, as the embryonic brain grows, a proportional amount of skull growth is needed at the sutures in order to create the necessary space for the expanding brain. The main role of sutures is to ultimately permit brain growth by coordinating skull expansion in the presence of a developing brain. Suture patency is therefore critical at this stage of life [1].

Craniosynostosis, defined as the premature closure of one or more of the cranial vault sutures, results in a variety of associated skull and subsequent facial deformities secondary to skull growth restrictions that may severely impact on child wellbeing, potentially increasing ICP, commonly resulting in visual disturbances, frequent headaches and learning developmental delays. In addition, the inability of the skull to create the adequate space for brain growth by expanding perpendicularly to the fused sutures results in a compensatory expansion of the cranial vault in a direction parallel to these sutures, with a compensatory overgrowth at other suture sites, progressively rendering an abnormal head shape.

The head shape will be a product of the direction and number of the affected sutures, together with the order and timing in which these sutures synostosed. Craniosynostosis can be expressed as an isolated clinical feature, or in association with other clinical features, as a part of about 100 syndromes. Patients with syndromic craniosynostosis are much more complicated than isolated cases, requiring a multidisciplinary team to treat all their problems effectively. Crouzon syndrome (CS) is an example of such group and accounts for approximately 4.5% of all cases of craniosynostosis [2, 3].

Crouzon syndrome was first described in 1912 by a French neurologist Octave Crouzon (1874-1938), as a hereditary syndrome of craniofacial dysostosis, which included a triad of skull deformities, facial anomalies and proptosis [4]. It is a rare genetic disorder which has worldwide prevalence rate of 1 in 25,000 live births [5, 6].

PATHOGENESIS OF CS

CS is transmitted as an autosomal dominant inheritance, but in 25% of cases, it may occur sporadically because of a fresh

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mutation. The genetic defect is caused by mutation of fibroblast growth factor receptor 2 (FGFR2) on chromosome locus 10q25-q26, resulting in early fusion of skull bones during fetal development [7-9]. The underlying pathological process in CS is premature synostosis of the sagittal, coronal and occasionally lambdoid sutures beginning in the first year and completed by 2-3 years of life. No single skull shape is diagnostic of CS because the eventual shape of the head depends on the time and sequence in which the skull sutures fused. The skull deformity in CS may be brachycephaly, oxycephaly or trigonocephaly [10].

Clinical Manifestations of CS

The appearance of an infant or a child with CS can vary in severity from a mild presentation with subtle midface manifestations to severe form with multiple fused cranial sutures and marked brain, midface, orbital, and eye problems. The earlier the onset, the more dramatic the effect of these malformations on subsequent cranial and brain growth and development; whereas late synostosed cranial sutures may render a nearly normal-shaped skull [11]. However, in most affected infants, the facial and ocular abnormalities typically include protrusion of the eyeballs (proptosis) due to shallow orbital cavities; outward deviation of the eyes (exotropia); widely spaced eyes (hypertelorism); and a small, underdeveloped upper jaw (hypoplastic maxilla), with protrusion of the lower jaw (relative mandibular prognathism) [12,13]. Other reported anomalies of CS include overcrowding of teeth; narrow, high arched palate or cleft palate, bifid uvula; low set ears, pinna defects, narrow or absent ear canals, deformed middle ears, congenital otosclerosis, with conductive deafness. Approximately one-third of patients with CS suffer from hearing loss [14]. Optic atrophy has been reported in 30 to 80% of patients [15]. Some patients with CS may present with headache and seizures because of the raised ICP secondary to early closure of cranial sutures. Approximately 73% of patients have chronic tonsillar herniation, of these, 47% intervention has been recommended [16]. Mental retardation has been reported due to the premature closure of the cranial sutures which may impair brain development [3,15]. Cervical fusions are present in approximately 18% of patients (C2-C3 and C5-C6 are equally affected) [17]. Upper and lower respiratory tract obstructions may present in patients with CS. Nasal septal deviation, coanal atresia or stenosis, nasopharyngeal narrowing may cause respiratory obstruction [18,19]. The respiratory problems may also be related to the tracheal abnormalities. Complete cartilaginous trachea is very rare and is always associated with craniosynostosis syndromes [20].

Diagnosis and differential diagnosis of CS

The diagnosis of CS is based mainly on the typical clinical, dental, ophthalmological and radiological features. The combination of craniosynostosis, especially of the sagittal and coronal sutures; typical facial features; and lack of hand/foot anomalies (Syndactyly) would strongly suggest the diagnosis of CS; and also, helps to distinguish CS from other conditions which may have similar facial appearances such as Apert (acrocephalosyndactyly), Pfeiffer and Jackson-Weiss syndromes [21]. Prenatally, CS can be diagnosed by ultrasonography and molecular genetic testing for FGFR 2 gene mutation, particularly for couples at risk for having a child with CS.

Ultrasonographic features of exophthalmos [22], binocular/interorbitaldiameter [23] and unusual head shape [21] help in diagnosis. Molecular genetic testing is more accurate and reliable than ultrasonography for prenatal diagnosis and can be done by performing amniocentesis and using amniotic fluid for DNA isolation to detect mutation [24].

Treatment of CS

For complete evaluation, optimum treatment planning and comprehensive procedures, a multidisciplinary approach to the management of a patient of CS is indicated. Early and accurate diagnosis is essential. The extent and timing of treatment depend upon the severity of the disease and age of the patient. CS can vary in severity from a mild presentation with subtle midface deficiency to severe form with fusion of multiple cranial sutures and marked midface, brain and eye problems [11, 25].

Surgery is the mainstay of treatment for CS. Surgical management has two components: First is the release of prematurely fused sutures which should ideally be done during the first year of life (after 3−6 months) by a neurosurgeon. The goals of surgical treatment are to increase the intracranial volume, with the aim of reducing the risk of developing elevated ICP and to improve head shape. The techniques most commonly employed for the initial cranial vault expansion are front orbital advancement (FOA) with anterior cranial vault remodeling or posterior cranial vault expansion, although other foci for expansion may be employed in specialized circumstances [26,27]. Second is the stage of craniofacial reconstructive surgery including advancement of the maxilla and frontonasal complex, aiming to coincide with facial growth patterns and psychosocial development [26, 28]. Procedures for this purpose include the Le Fort III osteotomy or its segmental variants [28, 29]. Other surgeries such as rhinoplasty, oculoplasty and cleft lip and cleft palate repair may be indicated depending upon patient's other deformities. Evaluation of optic atrophy due to optic nerve compression is done by the ophthalmologist; psychiatric problems related to the cosmetic deformity is treated by a psychiatrist; in addition to orthodontic management for the dental problems; tracheostomy for airway obstruction and myringotomy for drainage of middle ear secretions secondary to distorted nasopharynx [30,31].

CONCLUSION

CS can present with different clinical manifestations involving the skull, orbits and eyes. The clinical and radiological findings vary in severity from a mild presentation with subtle manifestations, to a severe form with marked midface, brain, orbital and eye complications. Management of patients with CS requires a multidisciplinary approach, by a team of craniofacial experts. Early surgical intervention is highly recommended in many patients with CS. Early diagnosis and prompt treatment not only provide good cosmetic and functional results, but also prevent the dangerous complications of increased ICP and visual loss in the majority of those children.

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