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Case Report

Apert Syndrome Versus Crouzon Syndrome: aboutTwo Cases

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Introduction

Both Apert-Crouzon and Crouzon syndromes are characterized by a prematured-craniosyntosis, patients suffering from apert syndrome have also hands and feet syndactyly. They are autosomal dominant genetic disorder associated in most case with mutation in the genes of the Fibroblast Growth Factor Receptor 2 (FGFR 2) [1]. It is a rare syndrome with multiple deformities (1/100,000 births in France and 15/100.000 births in USA), occurring mostly in Caucasians, Asiatic and Afro-Americans without sex discrimination [2]. We are describing two cases of craniostenosis, one apert syndrome and one Crouzon focussing on the following aspects: clinical presentation, variants, evolution and therapeutic issues in our context.

Medical Observation

Case 1

Child X, 13 year old, presented with several months complaints of eyes pain, impaired vision and right eye lacrimation. No treatment has been taken.

From his past medical history, he has facial dysmorphia since childbirth associated with a cerebral palsy. There Is neither family history of similar case nor in breeding.

The eye examination showed: bilateral exophthalmia with hypertelorism and lagophtalmia, impaired right eye vision to light. In the left eye the acuity = 6/36 and IOP= 29mmHg.Hertel RE = 33mm and LE = 27mm with exotropia.

Slit lamp examination of anterior and posterior segments revealed:

1. Right eye:conjunctival hyperaemia associated with a central corneal yellow infiltrate of about 7-8mm up taking fluoresce in; narrow and quiet anterior chamber; iris and pupil were not seen. The posterior segment was not accessible.
2. Left eye: Conjunctival hyperaemia associated with a superficial punctuates keratitis. The funduscopic examination was blurred.

In total, she had a keratitis due to exposure and a strabismus (Figure 1).

Figure1: Exposurekeratitis and strabismus.

We had the following findings on general examination: a brachycephaly, a flattened occiput, an anterior bulging forehead, depressed nasal bridge with a tiny nose, dental retrognathism and malposition (figure 2).

Figure 2: Maxillar Hypoplasia and mandibular prognathism.

This is associated to the 2nd, 3rd, and 4th fingers bilateral and symmetric syndactyly (Figure 3), to the four toes syndactyly and stocky big toes (figure 4), To a gait with widened base and mental debility (figure5).

Figure 3: Fingerssyndactyly.

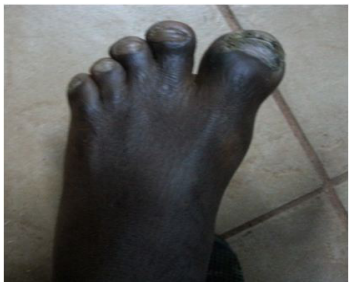

Figure 4: Fingers and feet syndactyly.

Figure 5: Typical facial features in Apert syndrome.

No limbs and brain CT scan were done.

The treatment consisted of: artificial tears, antibiotics for the ocular dryness and inflammation. Neurosurgery intervention was not done; the patient was referred to an orthopaedist for managing the syndactylies.

Case 2

KM, 13 year old, referred from the neurosurgeon for ophthalmic management of a Crouzon syndrome.

From his past medical history, he has facial dysmorphia since childbirth. There is neither family history of similar case nor inbreeding. He had a normal vaginal delivery in term.

The eye examination showed: corrected visual acuity of 10/10 in the right eye and 7/10 in the left eye, bilateral exophthalmia, Hertel LE = 25mm, irreducible, painless and axile with lagophtalmia and superficial punctuate keratitis, alternating exotropia of 45 DP (figure 6).

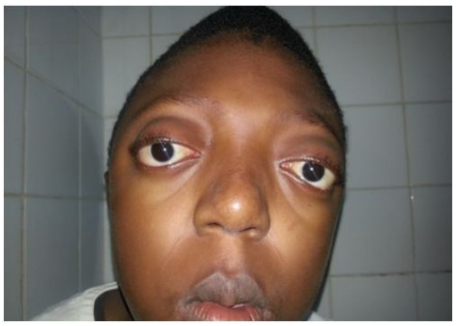

Figure 6: Bilateral exosphthalmia, telorbitism and extropia.

The posterior segment revealed:

1. Right eye: a pupil with C/D at 0.2 with temporal pallor and neat edge.
2. Left eye: a pupil with C/D at 0.2 with temporal pallor, surrounding papillary atrophy and a neat edge.

We .had the following findings on general examination: a facial dystrophy with a hypertelorbistism, an exorbitism and an inverted dental articulate.The treatment consisted on artificial tears and bilateral lateral tarsorrhaphy.

Discussion and Literature Review

Our observation illustrates both Apart and Crouzon syndromes evocative clinical features. Apart syndrome has been described by Dr Eugene Apart in 1906. It is a multiple malformations syndrome characterized by: a craniosynostosis (premature fusion of skull bones); craniofacial disorders (hypoplasia of middle floor); symmetric fingers and sometime feet syndactyly (fusion of fingers) giving mittens fingers appearance; mental retardation at variable degree; often associated with cardiac and visceral disorders [3-5].

In 1912, Crouzon described a syndrome characterized by craniosynostosis, hypertelorism, exophthalmia, parrot-beaked nose, short upper lip, hypo plastic maxilla and a relative mandibular prognathism. Cranial malformation depends on the order and rate or progression of suturalsynostosis. Brachycephaly is the most commonly observed, but scaphocephaly and trigonocephaly also are described.A shallow orbit is an essential diagnostic feature. Ocular proptosis is a consequence and results in a high frequency of conjunctivitis [1].

Epidemiology

Apert syndrome is a rare disease (occurs approximately in 1/160,000 birth) belongs to the group of craniosynostosis, where it represents only 4-5% of causes [3].

Genetic

The craniosynostoses are a heterogeneous group of syndromes characterized by a pre- mature sutural fusion that may occur alone or together with other anomalies. More than 70 syndromes are described. Apert and Crouzon syndromes are well-known craniosynostosis [1]. In the more common craniosynostosis syndrome like syndromes of Crouzon, Pfeiffer, Jackson-Weiss, and Apert, mutations were found in the gene coding for Fibroblast Growth Factor Receptor (FGFR) 2. Less frequently, mutations are observed in FGFR1 and FGFR3 in some cases of Crouzon and Pfeiffer syndrome. The mutations identified in FGFR2 are located in exons 5 and 7 of the gene that code for immunoglobulin (Ig)-like chain III and the region linking Ig II and Ig III of the receptor [2].

Age

Our two patients were seen at in advanced age of 13 year old. According to David et al in 2012, craniosynostosis are predominant in male, 56% and 66.7% in Crouzon and Apert syndromes respectively [6]. We have reported one case of Apert syndrome in a female.

Clinical Presentation

There are significant differences in the ocular manifestations of Apert and Crouzon syndromes. In Crouzon syndrome, ocular proptosis is primarily caused by retrusion of the lateral and inferior orbital margins with a very short orbital floor. In Apert syndrome, the eye globe actually protrudes in relation to the cranial base and to the orbit, probably resulting from marked protrusion of the lateral orbital wall. The implications account for some of the differences encountered. Asymmetry is associated with Apert syndrome frequently. Exotropia is found in Crouzon syndrome, whereas the V pattern is more characteristic in Apert syndrome with divergent up gaze and esotropicdowngaze [7].

Our patient suffering from Apert syndrome had exposure keratitis and central corneal ulcer due to the exopthalmia.

According to Gray et al in 2005, ophthalmic sequelae of Crouzon syndrome are numerous.The most common cause of visual impairment was amblyopia, which was present in 21% of patients, followed by optic atrophy in 7%. Ametropia occurred in 77% of patients. Strabismus occurred in 39% of patients and exposure keratopathy was observed in 15% of patients [8].

Khong et al in 2006 found 54% of patients suffering from visual impairment in a cohort of Apert syndrome. The most common cause was amblyopia, with a prevalence of 35%. Optic atrophy caused visual impairment in 5% of patients and corneal scarring in 8%. Sixty-three percent of patients had strabismus with more esotropia than exotropia. Ametropia was found in 69% of patients [9]. From those two studies, the main complications of Apert and Crouzon syndromes are first the amblyopia followed by optic atrophy, strabismus and exposure keratitis. Our two patients suffered from alternate exotropia and exposure keratitis due to the exophthalmia.

Other ophthalmic disorders are described such as lachrymal apparatus malfunction, lack of extra ocular muscles, ocular albinism, keratoconus, congenital glaucoma and cataract [9].

In sporadic cases, the prenatal diagnosis of Apert syndrome on ultrasound is difficult. It is always late during in pregnancy. The 3D ultrasound is useful. The use of molecular biology of foetal sample is essential in diagnosis. The molecular biology techniques used are those highlighting point mutations, PCR followed by ultrasound, enzymatic digestion or sequencing [3].

Treatment: The craniosynostosis are surgically treated. It is a corrective neurosurgery done soon, around three months old, aiming to stem or to decrease the orbital and ocular disorders which can threat the vision and binocular balance.

Prognosis

The severity in the management of Apert syndrome is due to the co-existence of multiple malformations with a risk of chronic intracranial hypertension responsible of blindness and mental retardation [10,11].

Conclusion

Apert and Crouzon syndromes are well known craniosynostosis. In the last 10 years, several studies have been done to provide a better comprehension of the etiology and pathogenesis of these syndromes. Both have an autosomal dominant mode of transmission and a mutation in the gene encoding for the FGFR2 as the cause in most patients.

Early detection to reduce amblyopia by correction of refractive errors, timely treatment of strabismus, and patching should be a priority for ophthalmologists and a goal of the craniofacial teams managing patients with Crouzon and Apert syndrome. Optic atrophy and exposure keratitis remains an important cause of visual impairment in these patients before decompressivecraniectomy. The management has to be multidisciplinary and done early.

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