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Fraser Syndrome: case report in lacrimal system

Síndrome de Fraser: relato de caso nas vias lacrimais

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ABSTRACT

Fraser syndrome is a systemic condition characterized by cryptophthalmos, syndactyly and abnormal genitalia, which may be associated with urinary tract, ear, nose, larynx and skeletal abnormalities. Cryptophthalmos can be an isolated finding (that has been reported as an autosomal dominant trait) or associated with other congenital anomalies (reported as an autosomal recessive disorder). Child, female, nine month of life, evaluated in the lacrimal setor of Federal University of São Paulo. Child of consanguineous parents. Her physical examination showed total unilateral cryptophthalmos (left side), epiphora (right side) with mucopurulent discharge, depressed nasal bridge, low set ears, atresia of the external auditory canal, prominent labia majora and syndactyly of the fingers and toes. Ocular ultrasonography showed brachycephaly, absence of septu pellucidum prominence of the lateral ventricles, a major bone defect in the skull, the presence of thinning of the mantle tissue of the brain,a reduced anterior-posterior ocular diameter, anterior segment disorganization, absence of the lens and total retinal detachment in the left eye.

Keywords: *Lacrimal duct obstruction/congenital; Dacryocystitis; Syndrome; Case reports*

RESUMO

A síndrome de Fraser é uma condição sistêmica caracterizada por criptoftalmo, sindactilia e anomalia da genitália, podendo se associar com alterações dos rins, do ouvido, do nariz, da laringe e do esqueleto. O criptoftalmo pode representar um achado isolado, representado por herança autossômica dominante, associado a outras anomalias congênitas, relatado como herança autossômica recessiva. Criança do sexo feminino, 9 meses, avaliada no ambulatório de vias lacrimais da Universidade Federal de São Paulo. Filha de pais consanguíneos. Ao exame, foram observados criptoftalmo total à esquerda, epífora em olho direito associada à secreção mucopurulenta, nariz em sela, implantação baixa das orelhas, malformação de conduto auditivo, aumento de grandes lábios e sindactilia de mãos e pés. A tomografia de crânio evidenciou braquicefalia ausência de septo pelúcido, proeminência dos ventrículos laterais, importante falha óssea na calota craniana, presença de afilamento do manto tecidual cerebral, fossa posterior pequena, desorganização do segmento anterior, afacia e descolamento total da retina.

Descritores: Obstrução dos ductos lacrimais/congênito; Dacriocistite; Síndrome; Relatos de casos

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Introduction

Fraser syndrome[1] was first described by the Canadian geneticist Fraser in 1962 and occurs with a minimal estimated frequency of 0.43 per 100,000 live births. It is a systemic condition characterised by the following defects:[2-4]

a) Face: cryptophthalmos (93%), usually bilateral and associated with eye defects; hair growth laterally to the forehead until the side of the eyebrows (34%); depression of the underlying frontal bone; hypoplastic notched nostrils; broad nose with a depressed nasal bridge; ear anomalies (44%), such as atresia of the external auditory canal and cupped ears.

b) Performance: mental deficiency in 50% of survivors.

c) Limbs: partial skin syndactyly (57%).

d) Genitalia: incomplete development (49%); male: hypospadias, cryptorchidism; female: bicornuate uterus, vaginal atresia, clitoromegaly.

e) Other: laryngeal atresia or stenosis (21%); renal agenesis or hypoplasia (37%); microcephaly; hydrocephalus; encephalocele; myelomeningocele; cleft lip; cleft palate (4%); short tongue frenulum (96%); absence of eyelashes and eyebrows; microphthalmia; anophthalmia; corneal opacity; anal atresia; small intestine malformations; heart defects; missing phalanges; hypoplastic or missing thumb.

Diagnosis should be based on the presence of two major and one minor criteria or one major and four minor criteria. The diagnostic criteria for Fraser syndrome are:

a) Major: cryptophthalmos; symblepharon; syndactyly; genital abnormalities.

b) Minor: nose, ear, and larynx malformations; umbilical hernia; kidney abnormalities; bone abnormalities; cleft tongue or other oral clefts; mental retardation.

About 20% of affected individuals die before one year of age, usually due to kidney or laryngeal defects.

Abnormal eyelid development is generally associated with ocular abnormalities.[5]

The disease has an autosomal recessive inheritance. The aetiology of cryptophthalmos is variable.[6]

Cryptophthalmos is the most frequent finding[5,6]: it is present in 95% of cases, being bilateral in 57% and unilateral in 25%. Cryptophthalmos is the congenital fusion of eyelids due to critical defects in eye development, leading to a poor visual prognosis.

The aim of surgery[7,8] is to protect and optimise the eye's visual potential. When there is no visual potential, the secondary goal is eyelid reconstruction. Rehabilitation is challenging, and the visual prognosis should be carefully discussed with parents.

The condition may be associated with hypertelorism, microphthalmia, supernumerary eyebrows,[5,6] and an abnormal or absent conjunctival fornix. The cornea may be covered by a tissue similar to the sclera and present staphyloma. Other findings have been described such as an absent lens and iris; an anterior chamber filled with vitreous humour; microphakia with iris, ciliary body and choroidal atrophy; and retinal disorganisation.

In most cases the anterior segment is more severely affected.

The incidence of congenital obstruction of the nasolacrimal duct is 6%,[9] but it is higher in children with craniofacial anomalies.[10]

Congenital nasolacrimal obstruction may be due to incomplete development of the bony nasolacrimal canal, craniofacial anomalies, and most often due to the persistence of a mucous membrane at the level of Hasner's valve. About 82%[11] of cases resolve with conservative treatment in the first year of life. After this age, lacrimal probing is indicated.

Case Report

White female child born and raised in São Paulo and seen at UNIFESP's Lacrimal Pathways Unit since she was 9 months old. The patient had Fraser syndrome with tearing in the right eye since birth (Figure 1). Ophthalmic examination showed: mucopurulent discharge in the right eye, no hyperaemia in the bulbar conjunctiva, Milder test +++, negative oropharynx fluorescein appearance test, and cryptophthalmos in the left eye.

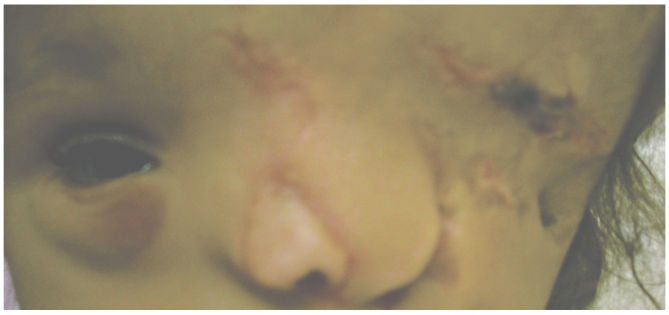

Figure 1: Part of the face of child with Fraser syndrome.

Multislice computed tomography of the head showed: brachycephaly, absent septum pellucidum, prominent lateral ventricles, major skull bone defect, thinning of the brain mantle, small posterior fossa (Figure 2).

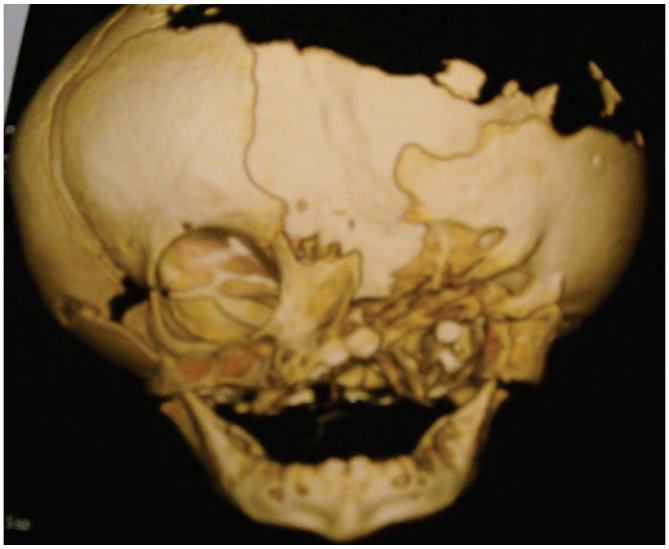

Figure 2: CT slice obtained with a thickness of 3 and 10 mm.

Conservative management was adopted, and the epiphora in the right eye resolved after 4 months.

Discussion

Craniofacial anomalies are a diverse and complex set of conditions. Craniofacial anomalies include isolated and multiple anomalies of genetic or non-genetic origin and are characterised by changes in the structure of the skull and/or face.[12,13]

A considerable proportion of patients with craniofacial anomalies have a normal life expectancy, as only a minority of presentations are lethal.[12] In Fraser syndrome, 25% of affected

individuals are stillborn and 20% die before 1 year of age due to kidney or laryngeal defects. No affected individuals have reproduced to date.[5]

Such anomalies significantly affect the speech, hearing, vision, ocular adnexa, appearance, and cognition of affected individuals, influencing their health and social integration.[13,14] In Brazil, congenital defects have consistently remained as the second leading cause of perinatal death[15] with 13% in 2003.

The diameter, height and volume of the bony nasolacrimal duct increase mainly during the first 6 months of life in term infants, coinciding with a high rate of spontaneous resolution of congenital nasolacrimal duct obstruction, as reported in the literature.[16] The increase in length of the bony nasolacrimal duct is strongly correlated with the postnatal growth of the maxilla.[16] Moreover, even in the fully-developed bony nasolacrimal duct there may be a mucous membrane at the level of Hasner's valve which can block tear drainage. In such cases, conservative management with Crigler massage[17] has been shown to be sufficient to resolve many cases of epiphora.

In our service, cases of nasolacrimal duct obstruction are managed conservatively until 1 year of age, as Crigler massage has a high rate of success until that age. After 1 year of age, however, persistent obstruction is treated surgically by probing the lacrimal pathways, as suggested in the literature.[11]

Also according to the literature[18], conservative management has a success rate of around 52.5% in children younger than 2 years.

However, good results have been reported with late probing[19,20], with success rates of 75% in children younger than 35 months and 75% in children aged 3-10 years, which is a reason to postpone dacryocystorhinostomy.

There have been reports of subjects with isolated cryptophthalmos who did not have Fraser syndrome[21].

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