A CASE OF BILATERAL CONGENITAL EUBLEPHARON OR ECTROPION

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ABSTRACT

Bilateral Congenital Eublepharon, also referred to as ectropion, is a rare condition in which at birth the eyelids do not cover the eye. It is more commonly found in Afro-Caribbean infants and in those with trisomy 21. Management is usually conservative. We review data from animal embryology to propose the condition may be related to defects in the expression of fibroblast growth factor 2 (FGFR2) in a child with this trisomy.

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Keywords: Eublepharon; fibroblast growth factors; FGFR2; trisomy 21

THE CASE

We report the case of a boy with bilateral congenital eublepharon in a male Afro-Caribbean child with trisomy 21. He was born via an elective caesarean section as the mother had undergone two previous caesarean sections. The antenatal period was significant for foetal, severe bilateral hydronephrosis and an atrioventricular septal defect which were apparent on ultrasound. On postnatal examination he was found to have complete eversion of both upper eyelids along with bilateral opacification of the lenses; he was later diagnosed with trisomy 21. The child was admitted and his eyes regularly moisturised. Topical chloramphenicol was prescribed four times a day, along with intravenous cefotaxime. In the first two days of life there was some improvement in the lid swelling, however the eyelids continued to remain everted and a left corneal ulcer developed along with extensive chemosis of both eyes. With little improvement in the child’s condition following conservative treatment and an increasing risk of a perforating
cornea surgery was proposed in the form of a full thickness skin graft. The family was counselled and following their consent surgery was carried out at 10 weeks of age employing an autograft taken from the periauricular region. The child recovered well post operatively but in terms of the eyelid eversion, at 2 week follow-up there had been little improvement. The child is having ongoing follow up and continues on topical chlormaphenicol every hour and artificial tears. The current plan is for further surgery at 6 months using an amniotic membrane graft.

DISCUSSION

Bilateral congenital eublepharon was first described by Adams in 1896 who referred to the condition as ‘double congenital ectropion.’ (1) In 1992 Seller went on to report and describe 51 other cases. Since then cases of late onset eversions have also been reported (2). The condition is most commonly bilateral but unilateral cases have been described. The underlying pathology and cause for the eversion remains unidentified, although several potential theories have been proposed. The condition tends to present more commonly in Afro-Caribbean infants and those with trisomy 21, as well as those with collodion skin disease. (2,3,4) Conditions such as orbicularis hypotonia or birth trauma commonly precede eyelid eversion. (5) Additionally vertical shortening of the anterior lamellar or vertical elongation of the posterior lamellar of the eyelid as well as failure of the orbital septum to fuse with the levator aponeurosis, have associations with this condition. (6) It is also proposed that venous stasis during delivery may cause marked chemosis and prolapse of the conjunctiva resulting in congenital eversion of the eyelids. It is thought that the chemotic conjunctiva usually protects the cornea from exposure and so there have not been many reported cases of corneal complications in these infants.

Congenital eyelid eversion can either resolve spontaneously or be treated conservatively with topical lubrication, antibiotics and eye patching in the hope of preventing desiccation of the exposed conjunctiva. Surgical intervention includes subconjunctival injection of hyaluronic acid, tarsorrhaphy (in which the eyelids are stitched together towards the palpebral fissure with excision of redundant conjunctiva) or a full thickness skin graft to the upper lid.

EMBRYOLOGICAL DEVELOPMENT OF EYELIDS

There has been little research into the embryological development of human eyelids but murine models suggest the second fibroblast growth factor receptor (FGFR2) plays a crucial role. The receptors are involved in cellular proliferation, migration and differentiation of several organ systems. (7) They comprise of a family of four transmembrane proteins with intrinsic tyrosine kinase activities. (8) Heterozygous mutations of FGFR1, 2 and 3 have been
known for some time to contribute to disorders of bone patterning and growth. A spectrum of mutations in FGFR2 in man (located on chromosome 10) is known to be associated with syndromes such as Crouzon syndrome, Apert’s syndrome, Pfeiffer syndrome, craniosynostosis and the development of a caudal appendage.(9,10)

Using genetic targeting Arman et al identified and knocked out a number of FGFR2 alleles in mice.(10) Subsequent analysis of the mutant embryos showed that FGFR2 is essential for the induction and patterning of multiple organs, including the limbs, lungs, inner ear, placenta and the skin. It is believed that loss of the FGFR2 blocks signalling interactions between the epithelium and mesenchyme leading to the failure of organogenesis as shown in this table.

Table 1: Phenotypic Abnormalities in RescuedFgfr2DIII/DIII Mutant Embryos*

<table>
<thead>
<tr>
<th>Organs</th>
<th>Dysgenesis</th>
<th>Agenesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eyelids</td>
<td>yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Hair</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hair follicle</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td>Inner ear</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td>Kidney</td>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td>Limb</td>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td>Liver</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td>Pancreas</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td>Salivary gland</td>
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<td>Yes</td>
</tr>
<tr>
<td>Skin</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td>Skull</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td>Stomach</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td>Tail bud</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td>Thymus</td>
<td>yes</td>
<td></td>
</tr>
</tbody>
</table>

*Dysgenesis and agenesis refer to malformation and absence of organs determined at multiple stages, respectively. (Taken from Li et al.)

Studies published in 2001 specifically examined mutations of the FGFR2 and the absence of eyelid formation (11). Eyelid development in mice, as in humans, consists of the protrusion of a ridge of tissue across the eye followed by fusion of the upper and lower lids. In mutant mice the initial morphogenic change from flat ectodermal cells to cubic epithelial cells was not observed. Mutant ectoderm showed a slower proliferation rate of 4% when compared to the 40% in the wild type control group. FGFR2 mediated signals from both the epithelium and the underlying mesenchyme were critical for eyelid
formation, thereby supporting the contention that eyelid malformations are likely to be the result of genetic mutations during the early stages of embryogenesis. There are no well established links between trisomy 21 and FGFR2 mutations, but it is known that intracellular transcription factors critical to fibroblast growth such as DJun are down regulated in trisomy 21. We are not aware at present of any mutations in the FGFR2 in this patient. It is possible that the condition of trisomy 21 alters expression of FGFR2 in some fashion to allow the development of eublepharon.

CONCLUSION

Congenital upper eyelid eversion is an extremely rare condition that seldom presents to paediatricians and ophthalmologists. Early recognition will help preserve the cornea and allow a more conservative approach to such patients. Cases may merit careful review to exclude any underlying chromosomal abnormality.

ACKNOWLEDGMENTS

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