shown to have a significant effect on cell growth and differentiation.[1] *FUT8*-CDG is rare; to our knowledge, only 2 individuals other than our patient have been reported with pathogenic variants,[2] and our patient is the first case of *FUT8*-CGD associated with glaucoma. Of note, whole exome sequencing revealed no abnormalities in known genes for primary congenital glaucoma or other glaucomas. Therefore, we propose *FUT8*-CDG as a new etiology of glaucoma and classify it as a "glaucoma associated with a nonacquired systemic syndrome," according to the World Glaucoma Association's childhood glaucoma classification system.[3]

Overexpression of the *FUT8* gene has been found in the trabecular meshwork of eyes with primary open-angle glaucoma and is thought to play an important role in the regulation of the aqueous outflow.[4] Imbalances in both up-regulation and down-regulation of a single gene may cause a broad range of diseases.[5] We cannot rule out the possibility that our patient had glaucoma unrelated to the mutations in *FUT8*; however, given the absence of any other glaucomatous genetic abnormalities on whole exome sequencing and the significant improvement in IOP with trabeculotomy, we suspect that reduced expression of the gene was either directly causative of the glaucoma or acted as a cofactor to exacerbate her infantile-onset glaucoma. To our knowledge, this is the first evidence to suggest that reduced expression of the *FUT8* gene dysregulates aqueous outflow at the level of the trabecular meshwork and results in an infantile-onset variant of open angle glaucoma.

The mortality in individuals with *FUT8*-CGD is expected to be high. Studies have shown that 70% of *FUT8* knockout mice usually die within 3 days of birth, and survivors display growth retardation and severe respiratory problems.[6] Two of the 3 known individuals with *FUT8*-CGD have died before 8 years of age from respiratory diseases.

FUT8-CGD should be considered in the differential diagnosis of patients with infantile-onset glaucoma who present with intrauterine growth retardation, feeding difficulties, hypotonia, microcephaly, seizures, short stature, developmental delay, and respiratory abnormalities. Children diagnosed with FUT8-CGD should be evaluated for potential glaucoma. Future studies of *FUT8*'s role in the trabecular meshwork could further elucidate the exact pathogenesis of aqueous outflow obstruction and guide therapeutic developments.

Literature Search

PubMed and Google Scholar were searched on June 16, 2019, without date restriction, for English-language results using the following terms: *congenital disorder of glycosylation* AND *glaucoma*, *fucosyltransferase 8* AND *trabecular meshwork*, *fucosyltransferase 8* AND *glaucoma*.

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Management of ocular manifestations of autosomal recessive congenital ichthyosis 4B, harlequin type, in the perinatal period

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Autosomal recessive congenital ichthyosis (ARCI4B [OMIM #242500]), also known as harlequin ichthyosis, presents at birth with extreme hyperkeratosis and thick-fissured plaques, leading to tightness of the skin around the eyes, mouth, ears, chest, abdomen, and extremities. Ocular manifestations include cicatricial ectropion and exposure keratitis. We present 2 infants with ARCI4B and cicatricial ectropion who were managed with aggressive nonsurgical therapy. Both infants avoided severe ocular sequelae and maintained corneal clarity, highlighting that management of exposure keratopathy with frequent ophthalmic ointment application can prevent severe ocular surface pathology in ARCI4B.

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Case 1

A boy born at 35.2 weeks gestation was noted at delivery to have diffuse thick desquamating plaques over the entire surface of his body, consistent with autosomal recessive congenital ichthyosis (ARCI4B [OMIM #242500]). The patient was immediately placed in a high-humidity incubator on isolation precautions. On initial ophthalmic examination, he was noted to have bilateral upper eyelid ectropion, with both eyelids fully everted. Lashes were lightly pigmented bilaterally. Both conjunctivae had trace injection, with no chemosis. The corneas were clear. The patient was started on a regimen of alternating petrolatum and erythromycin ointment every 2 hours. By the third day of life, he was started on systemic acitretin and topical tazarotene cream (vitamin A derivatives). Plastic surgery released circumferential plaques around the digits, hands and legs as a treatment for soft tissue ischemia. Genetic testing revealed homozygous p.R2482X pathogenic variant in the *ABCA12* gene. The mother and father were nonconsanguineous and of Salvadoran and Honduran descent, respectively.

By 2 months of age the skin plaques had significantly improved. Ophthalmologic examination throughout the patient's admission was consistent with bilateral upper eyelid ectropion. The corneas remained clear with improved lid closure over time. Continued improvement was noted at 6 months (Figure 1) and 18 months of age. The most recent outpatient ophthalmology examination was performed at age 2, at which time the corneas were clear, with mild upper eyelid ectropion. The patient was continued on petroleum ointment at bedtime.

Case 2

A girl born at 34 weeks' gestation was admitted to the neonatal intensive care unit with hyperkeratotic plaques over her entire body, with severe thickening of the skin around her face abdomen and extremities with outward turning of her lips (eclabium) and ectropion. The patient's family history was notable for consanguinity with parents related as double first cousins (both grandmothers were sisters, and both grandfathers were brothers.) Both parents were of Pakistani ancestry.

On the first day of life, ophthalmologic examination was notable for thickening and tightness of the skin around her eyes, with cicatricial ectropion of the upper eyelids. Good lid closure was noted, with excellent Bell's phenomenon and limited exposure. The conjunctivae appeared white and quiet and the corneas were clear in both eyes. The patient was started on ophthalmic ointment treatment every 2 hours, alternating between petrolatum and erythromycin. She was placed in reverse isolation, maintained in a humidified incubator, and started on systemic acitretin therapy. Dermatology recommended topical retinoid use, and Plastic Surgery monitored and treated extremity compression secondary to the circumferential plaques with incision as indicated. Ophthalmology followed the patient throughout her admission and she was discharged at the age of 1 month.

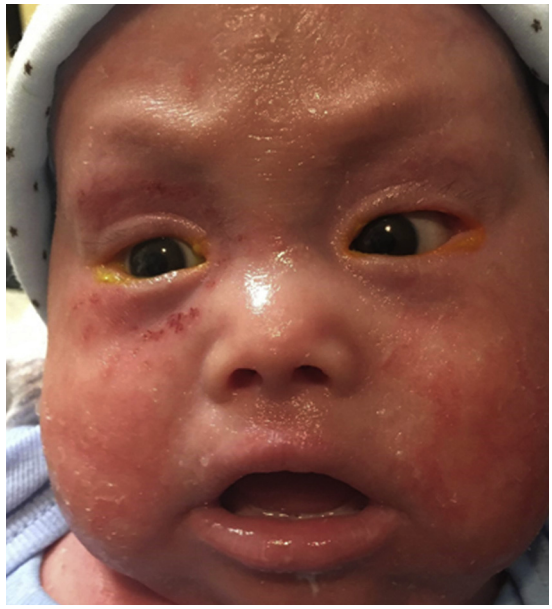

FIG 1. Case 1 at 6 months of age, showing improved hyperkeratosis and ectropion with clear corneas.

The last ophthalmic examination at 20 months of age showed no evidence of exposure keratopathy with clear corneas and resolved ectropion and she was maintained on petroleum ointment every four hours. Genetic testing was not performed on this child.

Discussion

ARCI4B is a rare autosomal recessive genetic disorder resulting in extreme hyperkeratosis with potentially lethal sequelae. It is the most severe form of autosomal recessive congenital ichthyosis. The most common disease-associated mutations for ARCI4B have been identified in the *ABCA12* gene in chromosome 2.[1] Dysfunction of the encoded adenosine triphosphate-binding cassette transporter results in abnormal lipid transport within keratinocytes. Subsequent abnormal proper skin barrier function leads to extreme hyperkeratosis as a compensatory mechanism.[2] Constriction of extremities by hyperkeratotic bands may result in necrosis and movement restriction. Subsequent high morbidity and mortality during the neonatal period are secondary to skin barrier compromise and mechanical restriction leading to secondary infection, thermal dysregulation, transepidermal water loss, delayed feeding and/or respiratory distress.[3,4]

Patients who survive infancy often have continued systemic morbidity, including recurrent skin infections, alopecia, failure to thrive, short stature, arthritis, and developmental delay.[4] Skin findings after the neonatal period after the shedding of plaques resembles severe nonbullous congenital ichthyosiform erythroderma with erythematous skin and fine white scales.[4,5] A multicenter retrospective study of clinical outcomes of 45 ARCI4B

patients at a dermatology research institution reviewed the outcomes of 25 survivors aged 10 months to 25 years (survival rate of 56%). Ophthalmological problems included persistent ectropion in 64% of survivors, epiphora in 48%, and exposure keratitis in 12%. Sequela noted included corneal scarring and corneal perforation. Cataract formation was noted secondary to corticosteroid therapy in one patient, and retinoid therapy in another patient.[4]

Cicatricial ectropion eyelid surgery and skin grafting have been described in the management of the ocular manifestations of ARCI4B to preserve corneal clarity.[6-8] Risks of surgical intervention include increased likelihood of infection and risk factors associated with sedation in the setting of systemic comorbidities.[9] Skin grafting is limited by the availability of healthy skin, and ectropion often recurs.[4] Management of ARCI4B requires a multidisciplinary approach. The use of retinoids such as acitretin as well as proper humidification and sterilization have improved outcomes of newborns with ARCI4B, reducing both morbidity and mortality.[10]

This case series of 2 newborns with ARCI4B demonstrates that medical management alone can provide good ocular outcomes without the need for skin-releasing surgery, skin grafting, or alternative surgical management. This approach was effective in reducing the ectropion and preventing ocular surface sequela in both of our patients. Aggressive lubrication with close follow-up is necessary for preservation of the ocular surface. Additionally, erythromycin may be used for antimicrobial prophylaxis. Nonsurgical management of ARCI4B in a newborn requires collaboration of care with multidisciplinary specialties to prevent sequelae of severe exposure keratopathy.

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Corneal ectasia and high ametropia in an infant with microcephaly associated with presumed Zika virus congenital infection: new ocular findings

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We report the first case of a corneal ocular ectasia in an infant with Zika virus congenital infection (CZS). We suspect that the ocular embryology and neurotropism of the Zika virus could account for the corneal involvement.

According to the World Health Organization, the number of cases of microcephaly associated with presumed Zika virus congenital infection (CZS) is increasing worldwide.[1] The first human case in Brazil was reported in the state of Bahia in 2015,[2] although cases have also been reported in the northeastern states of Pernambuco and Paraiba.[2] Children with microcephaly have also been identified in southeast Brazil.[1,2] Several ocular manifestations may occur in infants with CZS, including abnormalities of the retina, choroid, and optic nerve.[2] Anterior segment findings, such as iris coloboma, lens subluxation, and congenital glaucoma, have been described with a lower prevalence.[2,3] We report presumed corneal ocular ectasia in an infant with CZS.

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