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Case report

Ocular surface involvements in ectrodactyly-ectodermal dysplasia-cleft syndrome☆

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ABSTRACT

Purpose: To present the ocular manifestation of 2 cases of ectrodactyly-ectodermal dysplasia-cleft syndrome, a multiple congenital anomaly syndrome caused by a single point mutation of the p63 gene that controls epidermal development and homeostasis and to present treatment options.
Case reports and discussion: Patient 1 presented with mild signs and symptoms of dry eye and limbal stem cell deficiency with retention of 20/30 vision. Patient 2 presented with severe signs and symptoms of limbal stem cell deficiency with diffuse corneal scarring and counting fingers vision. This second patient's course was complicated by allergic conjunctivitis and advanced steroid-induced glaucoma. The cause of visual loss in ectrodactyly-ectodermal dysplasia-cleft syndrome appears to be multifactorial and likely includes inflammation of the ocular surface, tear film abnormalities, eyelid abnormalities, and limbal stem cell deficiency. Treatment modalities including lubrication, contact lenses, and limbal stem cell transplantation are reviewed.
Conclusions: The ophthalmic conditions seen in ectrodactyly-ectodermal dysplasia-cleft syndrome frequently lead to vision loss. Early correct diagnosis and appropriate therapy are paramount because p63 gene mutations have a critical role in maintaining the integrity of the ocular surface in the setting of limbal stem cell deficiency, especially if there are other ocular surface insults such as lid disease, meibomian gland dysfunction and toxicity from topical medications. Patients should be monitored at regular, frequent intervals; and particular attention should be taken to avoid adverse secondary effects of these conditions and medications.

1. Introduction

Ectrodactyly-ectodermal dysplasia-cleft (EEC) syndrome is a genetic disorder caused by mutations of the p63 gene, a transcription factor [1–3]. When a family history is present, EEC syndrome is an autosomal dominant disorder displaying variable phenotypic expression and reduced penetrance. Many of the reported EEC syndrome patients appear to have the condition as the result of spontaneous mutations. Ectrodactyly (lobster claw deformities) may involve hands, feet or both; ectodermal dysplasias may involve hair, teeth, nails, skin and sweat glands; and clefting may involve lip, palate or uvula to varying degrees. EEC syndrome prominently features a variety of ocular surface abnormalities that should prompt a diligent examination for other EEC syndrome features, especially in young patients [1,4,5].

Other described ectodermal dysplasias that appear to be associated with p63 gene mutations are hypohidrotic ectodermal dysplasia, ankyloblepharon-ectodermal defects-cleft lip/palate (AEC) syndrome, Rapp–Hodgkin syndrome and ectodermal dysplasia-ectrodactyly-macular dystrophy syndrome (EEM) syndrome. All of these disorders may feature to some degree ophthalmic findings of the ocular surface [1].

This report describes two unrelated cases of EEC syndrome and discusses the importance of early, appropriate identification of the syndrome and extent of the ocular involvements, treatment of the underlying pathologic process, and recognition of common adverse effects of treatment regimens.

2. Case reports

2.1. Case 1

A 21-year-old, orphaned male with cleft lip and palate and syndactyly presented with a 2-month history of bilateral conjunctival irritation and redness. There was a history of similar recurrent episodes in early childhood as well as life-long bilateral epiphora

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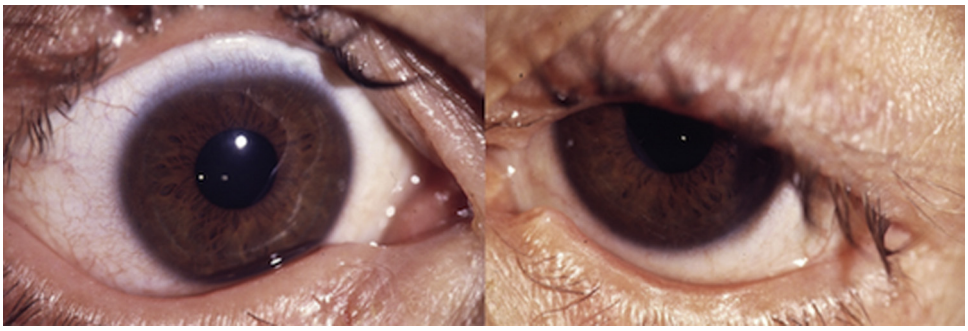

Fig. 1. Slit lamp photos of Case 1, depicting absent meibomian glands.

without a history of dacryocystitis or probing of the nasolacrimal system. The recurrent irritation and redness subsided until the onset of the current episode. His medical history included only surgical repair of cleft lip and palate as an infant. He was not aware of any family history, and he took no medications.

At initial presentation, his best-corrected visual acuity was 20/30 on the right and 20/40 on the left. The external examination detected several abnormalities including the absence of meibomian gland orifices and sparse lashes with some empty follicles bilaterally (Fig. 1). Salient features of slit-lamp biomicroscopy included punctate epithelial corneal erosions within the interpalpebral zones and 360° of superficial corneal neovascularization extending approximately 0.5 mm across the limbus of each eye. The palisades of Vogt were not identifiable on either cornea. The remainder of the examination of each eye was unremarkable including the conjunctivae, intraocular pressures and posterior poles. Tear production following topical anesthesia was 2 mm on the right and 4 mm on the left at 5 min. Irrigation and probing of the nasolacrimal system revealed bilateral obstructions. The patient achieved symptomatic relief after he was placed on chronic artificial tear replacement administered every 2 h.

2.2. Case 2

A 14 year-old male with EEC syndrome features including ectrodactyly and cleft palate was referred for evaluation and therapy of corneal scarring with a provisional referral diagnosis of Stevens-Johnson syndrome. The family history including parents and three siblings did not reveal any features of inherited EEC syndrome. The patient did not take any systemic medications. His relevant medical history included surgical repair of cleft palate and several relevant ocular items starting at birth.

Symptoms of nasolacrimal obstructions were noted soon after birth and probing was performed at 6 and 18 months of age, however, the right side continued to be partially obstructed. Throughout early life he was considered to have chronic keratoconjunctivitis that was treated with neomycin–polymyxin–bacitracin ophthalmic ointment and prednisolone, 1% drops daily in each eye until age 11 when elevated intraocular pressures were discovered. After two years of glaucoma medical therapies, a trabeculectomy was performed on the left eye. At the time of surgery the visual acuity on the right was 20/60 and on the left was light perception. The corneas were clear enough to visualize the posterior pole of each eye. On the left there was extensive glaucomatous optic nerve damage and the visual acuity remained light perception after trabeculectomy. At age 12 a right conjunctivodacryocystorhinostomy with placement of a Jones tube was performed for management of the chronic dacryocystitis. Following surgery he was maintained on topical neomycin–polymyxin ophthalmic solution.

Two years later at age 14, he was referred to the author's clinic for management of chronic bilateral corneal scarring and inflammation and was still being treated with the antibiotic combination. At this time the visual acuities were 3/200 on the right and light perception with accurate light projection in the superonasal quadrant on the left. Severe blepharospasm and photophobia were present. The external examination showed bilateral severe blepharitis with maceration of the lid margins. An eyelid speculum was required for examination of the ocular surface in each eye. All punctae appeared patent and meibomian gland orifices were stenetic or absent with difficult to express turbid secretions. The bulbar conjunctivae were moderately injected and the tarsal palpebral conjunctivae showed marked papillary hypertrophy. The filtering bleb was present on the left. The corneas had bilateral diffuse irregular epithelial surfaces, pannus formation and underlying stromal scarring (Fig. 2). The limbal palisades of Vogt were absent. These changes obscured the visual axis of each eye, however, the iris and lens appeared to be within normal limits but no details of the posterior pole of either eye could be seen. Intraocular pressures in the right and left eyes were 33 and 30 mmHg by pneumotonometer, respectively. Tear production with topical anesthetic was 15 mm on the right and 20 mm on the left at 5 min.

Intradermal scratch skin testing performed with neomycin–polymyxin–bacitracin ointment and with neomycin–polymyxin solution revealed moderate and mild hypersensitivities, respectively. Conjunctival cultures were read as no growth and conjunctival scrapings for histology showed polymorphonuclear leukocytes and basophils.

The combination topical antibiotics were discontinued and bilateral dexamethasone acetate, 1% solution five times daily and erythromycin ointment at bedtime were initiated. The patient was followed weekly, and his eyelid and conjunctival inflammation had significantly improved after 3 weeks, allowing examination without a speculum. Intraocular pressures were 18 and 16 mmHg, respectively. This improvement was felt to be due to improvement in blepharospasm. The vision in the right eye improved to 20/300 but was unchanged in the left eye (Fig. 3). The patient was maintained on erythromycin ointment at bedtime in each eye, but the dexamethasone drops were tapered and discontinued. Surgical intervention was discussed but the patient subsequently discontinued follow-up care.

3. Discussion

Despite the multiple cosmetically obvious abnormalities of EEC syndrome, the ocular involvements are often the most life-altering manifestations. Common ocular signs and symptoms include photophobia, blepharospasm, epiphora, and corneal neovascularization and scarring [6–8]. These two patients are examples of the extremes of the ocular involvements. The first case exhibits clinical findings of limbal stem cell deficiency (LSCD) and the ability of appropriate therapy to maintain an adequate ocular surface and preserve vision. In contrast, the second patient's clinical