

Case report

Exposure, entropion, and bilateral corneal ulceration in a newborn as a manifestation of chromosome 22 q11.2 duplication syndrome



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ABSTRACT

Purpose: Chromosome 22q11.2 micro-duplication syndrome (MDS), is a rare autosomal dominant condition, with a highly variable phenotype that ranges from unremarkable and asymptomatic, to fatal due to cardiovascular defects. Hypertelorism, downslanting palpebral fissures, superior displacement of the eyebrows, and ptosis are the most commonly reported ocular manifestations. Here, we report a newborn with bilateral exposure, entropion, and corneal ulceration related to 22q11.2 MDS.

Observation: A newborn girl presented with bilateral upper eyelid entropion, bilateral lower eyelid ectropion, and lagophthalmos. She subsequently developed bilateral corneal ulcers. Topical antibacterial drops, bandage contact lenses, medroxyprogesterone 1%, and fluorometholone 0.1%, together with partial tarsorrhaphy and correction of eyelid malposition, were used to treat the ulcers and address the underlying issues of exposure and entropion. Genetic testing revealed chromosome 22q11.2.MDS; further evaluation revealed systemic manifestations of this syndrome. The ocular surface healed well with gradual improvement of corneal opacification as well as bilateral partial tarsorrhaphy.

Conclusion and importance: This report is the first that describes a newborn with 22q11.2 MDS presenting with sight-threatening corneal ulceration. Entropion, ectropion, and lagophthalmos were identified and treated, allowing for healing of the corneal surface. Genetic testing revealed a syndrome not known to be associated with eyelid abnormalities and corneal ulceration, but with other important systemic and ocular implications. Bilateral partial tarsorrhaphy should not be excluded as a treatment option for infants who fail more conservative measures for the treatment of exposure.

1. Introduction

Chromosome 22q11.2 microduplication syndrome (MDS) is thought to be a result of nonallelic homologous recombination between low-copy repeats that result in rearrangements of 22q11.2. In most cases it is inherited from phenotypically normal parents, but it can occur *de novo* as well. The prevalence of the 22q11.2 MDS is estimated to be 2/10,000 births.^{1–3} Clinical features of this syndrome vary, with some patients being asymptomatic while some have fatal cardiovascular defects. The most common systemic presentations are developmental delay, growth retardation, behavioral abnormalities (e.g. autism or

attention deficit and hyper activity disorder), hypotonia, and various facial dysmorphias.^{1–4} The most common ocular manifestations include hypertelorism, downslanting palpebral fissures, superior displacement of the eyebrows, and ptosis.^{1,2,5} Cordovez et al. recently reported new ocular findings in these patients including Marcus Gunn jaw winking phenomenon, glaucoma, esotropia, gaze palsies, retinal detachment, retinal vascular tortuosity, and early cataract.⁵ Gandhi et al. also reported falciform macular folds and familial exudative vitreoretinopathy in a girl with 22q11.2 microduplication.⁶ We report a case of a newborn girl with novel ophthalmic manifestations of chromosome 22 q11.2 MDS.

Abbreviations: MDS, Microduplication syndrome

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Fig. 1. Congenital eyelid abnormalities in a newborn with chromosome 22 q11.2 MDS. A) Patient's eyelids on day 9 of life prior to eyelid surgery, demonstrating bilateral upper eyelid entropion, and bilateral lower eyelid ectropion. B) Patient's eyelids one month after upper eyelid entropion repair and tarsorrhaphies.

2. Case report

A newborn girl, born at 37 weeks gestation, was noted to have left lagophthalmos, a right preauricular ear tag, bilateral ear pits, and micro-retrognathia at birth. "A corneal opacity of the left eye was noted on the third day of life."

Despite treatment with antibiotic ointment and drops to both eyes the corneal opacity of the left eye worsened, and the patient was transferred to our service for inpatient cornea consultation and care. Ophthalmologic examination, at age 7 days, revealed 3 mm of lagophthalmos in the right eye; the left eye had exposure of the entire cornea, with no blink present and 9 mm of lagophthalmos. There was bilateral upper eyelid entropion causing eyelash-corneal touch, and bilateral lower eyelid ectropion. (Fig. 1 A). Portable slit-lamp examination revealed bilateral pseudomembranes of the upper and lower palpebral conjunctiva, bilateral conjunctival chemosis and injection, and bilateral keratinization of the inferior bulbar and palpebral conjunctiva, all greater in the left eye. There was diffuse coarse epitheliopathy of the right cornea with no epithelial defects. The left cornea had an infero-central infiltrate involving 60% of the cornea, with an overlying epithelial defect and 10% stromal thinning. Intraocular pressure, extraocular motility, pupil size, and dilated fundus examination were within normal limits. Gram stains and cultures of the cornea and conjunctiva, which were obtained prior to her transfer, were negative for organisms.

One day after admission, at age 8 days, a 1 × 1mm inferotemporal infiltrate of the right cornea was noted. Prednisolone acetate 1% and fortified vancomycin (25 mg/mL) and tobramycin (13.6 mg/mL) eye drops were prescribed for the right eye. Bandage contact lens placement (Air Optix Night & Day, Alcon, 13.8 mm diameter, 8.2 mm base curve) was attempted in both eyes but was abandoned because of poor fit related to small diameter and steep base curve of the newborn cornea. At age 9 days, upper eyelid entropion repair (via marginal tarsotomy) and temporary tarsorrhaphy of both eyes was performed to reduce

exposure (Fig. 1B). Although no scar band or tarsal kink was visualized at the time of surgery, incision into the posterior eyelid of both eyelids revealed an atypically small and firm structure instead of normal tarsus. Its small size created a relative posterior lamellar deficiency causing the entropion.

The corneal infiltrates appeared to have worsened on this day despite the treatments thus far (Fig. 2A and B). Both eyes were taped closed to reduce exposure, and opened only for medication instillation. Specialty custom contact lenses (SiHy, CooperVision® 11.3mm diameter, 7.7mm base curve) suitable for infant eyes were applied on an intermittent basis for support of the ocular surface. With the above protection of the ocular surface, the temporary tarsorrhaphies were intermittently opened to allow for visual input and development. Over the next several weeks the eyes began to heal with improvement in the epithelial defects and infiltrates. The contact lenses would not stay on the eye beyond several days to weeks and keratinization of the temporal conjunctiva and fine neovascularization of the corneas developed bilaterally. This was treated with medroxyprogesterone 1% and fluorometholone 0.1% drops, each two times a day. At age 18 days, chromosomal micro array analysis revealed 22q11.2 duplication. Systemic evaluation revealed laryngomalacia, hypoplastic aortic isthmus, patent foramen ovale, and truncal hypotonia. Bilateral facial nerve paresis, left greater than right, was also diagnosed; we believe this resulted in poor orbicularis oculi function and led to the lower lid ectropion.

All corneal cultures including those for Herpes simplex virus, fungus, chlamydia, and gonorrhea remained negative throughout follow-up. All topical medications were tapered to limit surface toxicity, and by age 54 days, the epithelial defects of both corneas were healed with no new infiltrates. There remained in the right eye an inferotemporal 2 × 1mm peripheral corneal opacity with keratinization of 2.5 mm of the inferotemporal cornea (Fig. 2C). The left eye had a residual 5.5 × 5.0 mm central corneal opacity with neovascularization and a ridge of keratinization of the inferotemporal cornea (Fig. 2D). At ages 2, 3, and 5 months, revision and extension of tarsorrhaphies was done under general anesthesia, along with punctal cautery and electroepilation of her eyelashes. The ultimate result was a 50% permanent lateral tarsorrhaphy in each eye with occlusion of all four puncta.

The last exam at age 23 months demonstrated visual acuity of 20/94 in the right eye on preferential looking test. "She blinked to light in the left eye, but she objected to occlusion of the right eye and thus an estimate of acuity by preferential looking testing was unable to be measured. At an earlier visit, she had measured 20/1000." Keratinization of the inferotemporal cornea of the right eye was unchanged from previous exam, with no central corneal involvement (Fig. 2E). There remained a corneal opacity of approximately 3.5 mm × 4 mm diameter of the left eye, with central corneal clearing (Fig. 2F). Occlusion therapy of the right eye, initiated at age 3 months, was continued to maximize visual potential.

3. Discussion

This is the first report of congenital entropion and lagophthalmos in a patient with 22q11.2 MDS. Congenital entropion is rare and considered an ophthalmic emergency as it can result in corneal erosion, microbial keratitis, corneal vascularization, and visual loss. Although ophthalmologic findings in patients with 22q11.2 MDS are largely limited to structural abnormalities of the orbit and adnexa, there has been some speculation of association with retinal vascular tortuosity.^{5,6}

At presentation, the differential diagnosis of the corneal opacity included microbial keratitis, sterile infiltration related to exposure and abnormal eyelid anatomy, and an underlying mucous membrane disorder such as liginous conjunctivitis. Negative smears and cultures and obvious exposure and eyelid abnormalities favored a diagnosis of sterile infiltration related to exposure and entropion. Bilateral entropion and lagophthalmos may represent a previously unreported ocular manifestation of 22q11.2 MDS.

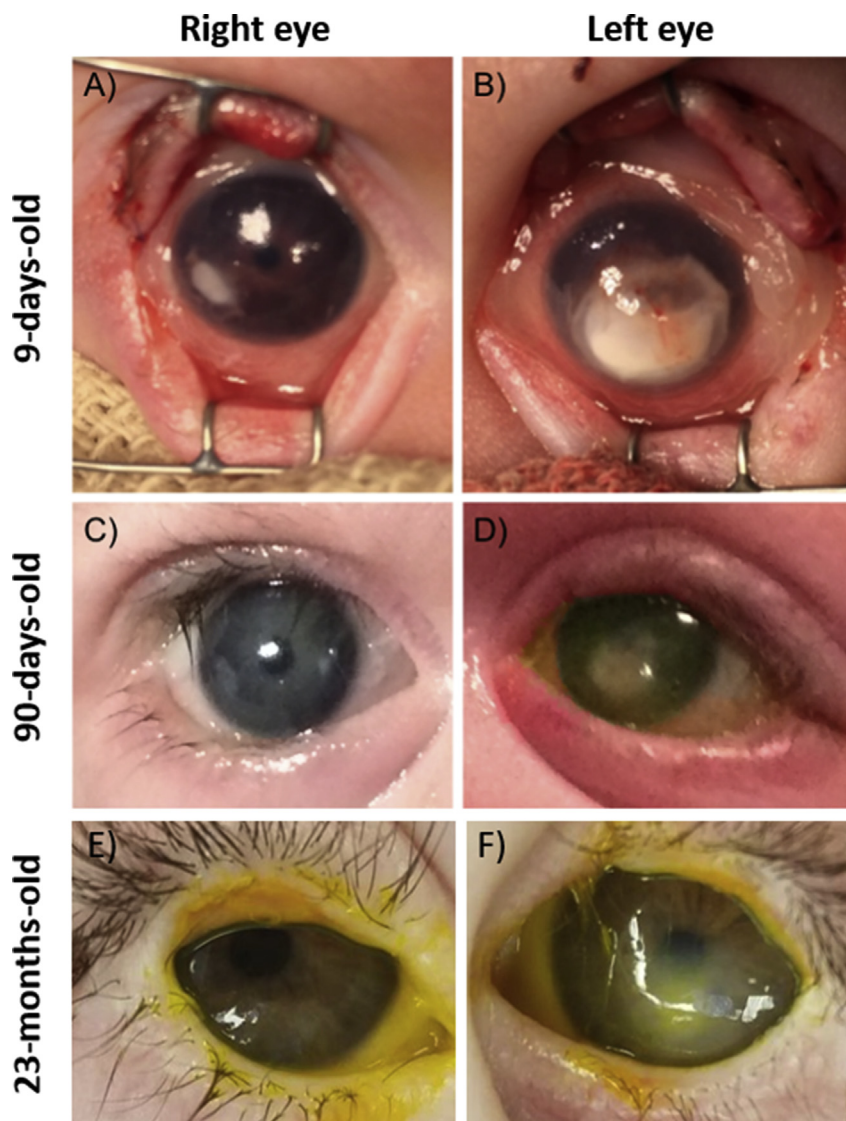


Fig. 2. Images of the patient's ocular surface on day 9 of life (A and B), day 90 of life (C and D) and most recent follow up exam at age 23 months (E and F). A) Right eye, opened with an eyelid speculum; inferotemporal 2.5 mm × 1.5 mm corneal stromal infiltrate and scarring. B) Left eye, opened with an eyelid speculum; central 6.5 mm × 7 mm stromal infiltrate with central neovascularization. C) Right eye, improved scarring with resolution of active infiltrate. D) Left eye, 5.5 mm × 5.0 mm inferocentral corneal scar. E) Unchanged compared to previous exam with clear visual axis. F) Left eye, inferocentral 3.5 mm × 4 mm corneal opacity with central corneal clearing. Fluorescein depicted in images E and F is pooling and not reflective of epithelial defect.

This case of bilateral exposure and ulceration in a newborn highlights the challenge of balancing protection of the ocular surface against the risk of deprivation amblyopia. Early intervention to correct eyelid malposition, partial tarsorrhaphies to reduce exposure, and the use of specialty contact lenses are alternatives to eyelid taping that theoretically reduce the chance of deprivation amblyopia and allow for development of the visual pathways. In this case, residual opacity and progressive opacification related to neovascularization contributed to deprivation amblyopia.

Penetrating keratoplasty or lamellar corneal transplantation commits a child and family to complex postoperative care and lifelong topical therapy, and has high risk of failure in infants.⁷ Long-term graft survival and successful visual rehabilitation can occur with early surgery, aggressive amblyopia therapy, and strong commitment from caregivers for long-term follow up.^{7,8} In this case the ocular surface stabilized with management as above and visual function was noted to improve. Corneal transplantation was not undertaken in this infant with complex medical issues because sight-limiting opacity remained unilateral.

4. Conclusion

Any child diagnosed with 22q11.2 MDS should be evaluated for entropion and lagophthalmos in addition to the other known ocular

manifestations of the syndrome to reduce the likelihood of exposure keratitis, corneal opacification, and deprivation amblyopia. Newborns with corneal ulceration warrant aggressive evaluation and treatment of possible infection and underlying predisposing factors such as entropion and exposure. Bilateral partial tarsorrhaphies in addition to contact lens use and topical therapy can stabilize the ocular surface and maximize visual potential.

Patient consent

Consent to publish this case report has been obtained from the patient's guardian in writing.

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Conflicts of interest

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ajoc.2018.11.001>.

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