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Goldenhar syndrome associated with lacrimal system agenesis: A case report

Mary W. Tam, Nariman Boyle *

Department of Ophthalmology, SUNY Stony Brook University, Renaissance School of Medicine, New York, USA

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ABSTRACT

Purpose: To report a case of lacrimal system agenesis in a patient with Goldenhar syndrome.
Observations: A one-month-old female preterm twin with Goldenhar syndrome presented with left upper eyelid coloboma, left central corneal ulcer and inferotemporal epibulbar dermoid. The corneal ulcer was treated and healed to a mild stromal scar. Examination under anesthesia prior to surgery revealed agenesis of the upper and lower eyelids canaliculi. Surgery was performed to correct left upper eyelid coloboma. At a second stage, the epibulbar dermoid was excised and ocular surface was repaired with amniotic membrane graft.
Conclusion and importance: Goldenhar syndrome is a rare congenital anomaly arising from the abnormal development of the first and second branchial arches. Anomalies of lacrimal drainage system are uncommon in Goldenhar including nasolacrimal duct obstruction and common canalicular obstruction. Agenesis of the lacrimal system has not been described in cases of Goldenhar syndrome. This case represents a unique and uncommonly seen feature.

1. Introduction

Goldenhar syndrome (oculo-auriculo-vertebral-dysplasia) is a rare congenital malformation arising from the abnormal development of the first and second branchial arches. In 1881, the first observation of oculo-auriculo-vertebral (OAV) dysplasia was reported by Von Arlt. In 1952, Dr. Maurice Goldenhar classified the clinical features and named the malformation complex as Goldenhar Syndrome, which consists of a triad of preauricular skin tags, ocular dermoid cyst, and vertebral dysplasia.[1] Anomalies of lacrimal drainage system in Goldenhar patients are known features,[2] but the association of Goldenhar syndrome with lacrimal system agenesis has not been previously reported. Here, we describe a unique case of a patient with Goldenhar syndrome who was found to have lacrimal system agenesis.

2. Case report

A preterm female twin, product of dichorionic diamniotic pregnancy, was born at 36 weeks to non-sanguineous parents. She presented to our oculoplastic clinic at one month of age for evaluation of left upper eyelid coloboma. She was born via primary caesarean section due to concerns of oligohydramnios and decreased growth velocity of twin A and polyhydramnios of twin B. The patient is twin A and required two weeks of neonatal intensive care unit stay upon birth. She had history of anemia of prematurity, benign cardiac murmur, left sided hydronephrosis and vertebral anomalies. She also had moderate to severe conductive hearing loss of the left ear, left preauricular skin tag, speech delay, congenital torticollis, mild left hemifacial microsomia and plagiocephaly. Her twin brother had no ocular or systemic anomalies and no nasolacrimal duct obstruction symptoms.

On initial examination, her visual acuity was fix and follow in both eyes with normal intraocular pressures. The anterior segment examination revealed a healing central corneal ulcer of the left eye and inferotemporal epibulbar dermoid (Fig. 1A). She had a central left upper eyelid coloboma, lateral canthus dystopia and preauricular appendages of the left ear (Fig. 1B). There was no evidence of microphthalmia, and extraocular movements were normal. Anterior and posterior segment findings were completely normal in both eyes apart from the cornea ulcer and epibulbar dermoid of the left eye. She was treated by the cornea service for central corneal ulcer of the left eye due to exposure keratopathy which resolved to a mild stromal scar. A panel of genes for disorders that have features of Goldenhar syndrome was done through Children's Hospital of Philadelphia (CHOP). Results did not reveal any genetic mutations in this comprehensive panel.

* Corresponding author. Department of Ophthalmology, SUNY Stony Brook, 33 Research Way, Suite 13, Setauket, NY, USA.
E-mail address: nariman.boyle@stonybrookmedicine.edu (N. Boyle).

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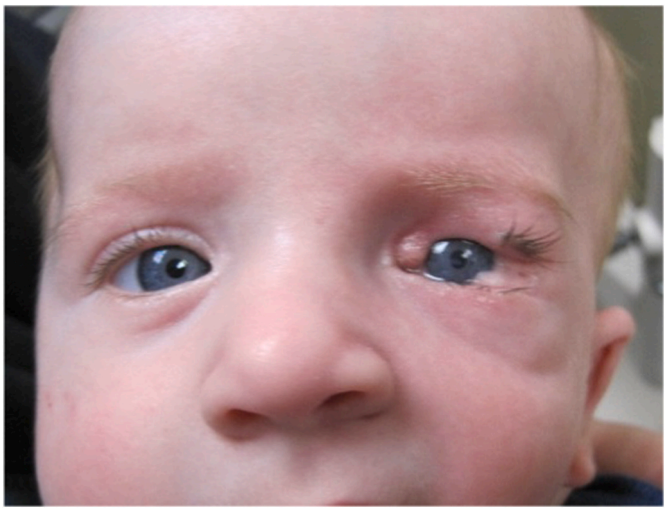

Fig. 1A. External photo showing left upper eyelid coloboma, epibulbar dermoid, lateral canthus dystopia.

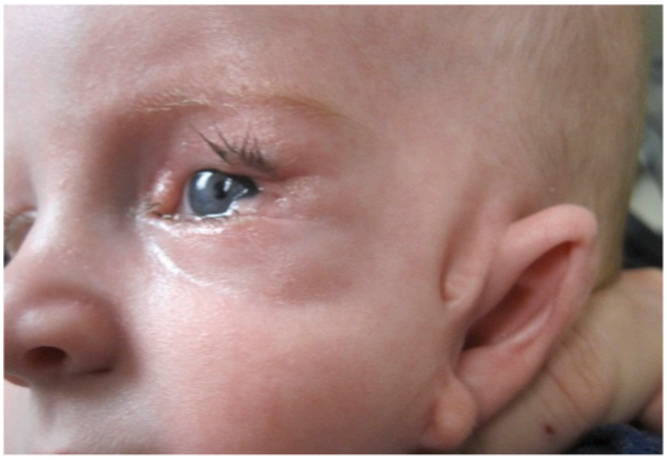

Fig. 1B. External photo showing preauricular skin tag.

She was followed closely while awaiting the uplift of restriction during the acute stage of the SARS-Cov-2 pandamic. Correction of the left upper eyelid coloboma was performed at one year of age. Examination under anesthesia at the time of surgery revealed absence of the left upper and lower canalicular system. The punctum of the upper eyelid was absent. The punctum of the lower eyelid was dystopic and laterally displaced with agenesis of the canaliculus. There were nodular lesions inferior to the canaliculus which were biopsied (Fig. 2). Attempt at irrigation and probing confirmed the atretic absence of the canalicular drainage system. The coloboma defect was repaired primarily with approximation of the tarsal plates and full thickness eyelid margin repair. The post-operative course was uneventful. A second stage excision of left limbal epibulbar dermoid was performed and ocular surface was repaired with amniotic membrane graft.

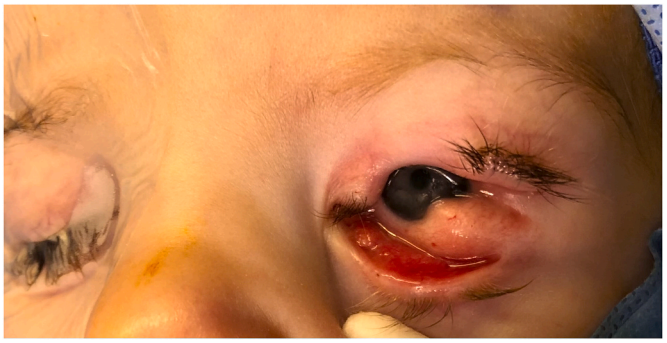

Fig. 2. External photo showing lateral punctal displacement with lengthening of the canalicular area. Also of note are palpebral conjunctival nodules inferior to the canaliculus.

Histopathology of the infra-canalicular lesions showed nodular lymphocytic infiltration associated with conjunctival epithelium.

3. Discussion

Goldenhar syndrome is a rare disorder with reported prevalence of the entire OAV spectrum of approximately 3.8/100,000 live births. It is usually sporadic, however, there has been literature reports of autosomal dominant genetic transmission and less frequent, autosomal recessive inheritance.[3] A multifactorial etiology including chromosome abnormalities, single gene mutation, vascular disruption, and teratogens have been proposed. Other factors include maternal infection with rubella and influenza, maternal diabetes, maternal smoking, and multifetal pregnancy, monzygotic and dizygotic, affecting the embryological development of the first and second branchial arches and vertebral elements during the first 3–5 weeks of embryonic life.[3] Our case supports a multifactorial etiology of Goldenhar syndrome, given the patient is a dizygotic twin. Her twin was found to be otherwise healthy.

Goldenhar syndrome has characteristic clinical appearance that is easy to diagnose. Common ocular features include upper and lower eyelid coloboma, iris coloboma, chorioretinal coloboma, epibulbar choristoma and subconjunctival dermoids. Other less frequent findings include microphthalmia, anophthalmia, strabismus, cataract, inequality of palpebral fissure, and lacrimal drainage abnormalities.[2,4] In some cases, patients may have cardiac, renal and central nervous system anomalies.[4] Goldenhar syndrome requires a multidisciplinary approach and early recognition is necessary especially in cases with eyelid coloboma to preserve the cornea and visual function.[5]

During the fourth week of embryonic gestation, the maxillary and frontal prominences appear, then enlarge and a groove forms between them.[6] The floor of the groove forms an epithelial cord arising from surface ectoderm, which fuses to become the nasolacrimal drainage system.[6] The synchronization of the embryologic development of the first and second branchial arches and the nasolacrimal drainage system can explain how anomalies of the lacrimal system may be concomitant with Goldenhar syndrome.

Lacrimal anomalies uncommonly reported in Goldenhar syndrome are mostly in the form of nasolacrimal duct obstruction and common canalicular obstruction.[7,8] Lacrimal system agenesis is a feature reported in cleft syndromes.[8] Tessier classification of facial clefting includes 15 types (type 0–14) with unique features for each type.[9] The facial clefts are represented in a clock-face manner with type 3 and 4 having an association with lacrimal anomalies. On the other hand, lacrimal anomalies are associated with an array of genetic disorders involving the gene TP63 (tumor protein 63) such as Ectrodactyly-Ectodermal Dysplasia-Clefting syndrome (EEC), Limb-Mammary syndrome (LMS) and Acro-Dermal-Ungal-Lacrimal-Tooth syndrome (ADULT).[10] TP63 gene plays a critical role in ectodermal and orofacial development.

Our patient had ocular findings of eyelid coloboma, epibulbar dermoid and lacrimal system agenesis. Goldenhar syndrome is on the spectrum of craniofacial microsomia (CFM) which is a continuum of different phenotypical presentations with various degrees of developmental abnormalities of the facial skeleton, ear and soft tissues. This can explain the severity of our patient being on the more advanced end of the spectrum. The mechanism of CFM is secondary to maldevelopment of the first and second pharyngeal arch structures composed of mesenchymal cells. Among the theories explaining the pathogenesis of CFM are failure of migration of cells from the neural crest to the pharyngeal arches and vascular disruption of the stapedial artery during the

development of the first and second pharyngeal arches.[11]

To date, this is the first case of a patient with Goldenhar syndrome associated with lacrimal system agenesis including agenesis of the upper and lower eyelid canaliculi.

4. Conclusion

Manifestations of Goldenhar syndrome may vary in scope and severity with possible features on a spectrum with craniofacial microsomia. A full ophthalmic examination under anesthesia in Goldenhar syndrome needs to include probing and irrigation of the lacrimal drainage system to have a comprehensive assessment of the malformations in the periocular area.

Patient consent

The patient's legal guardian consented to publication of the case in writing/orally.

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Authorship

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

Declaration of competing interest

None.

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