Goldenhar Syndrome: Clinical Spectrum and Management at a Tertiary Care Centre

Usha Singh[1], Sonia Phulke[2,*], Amit Gupta[3]

[1]Professor & Head of Oculoplastics & Retinoblastoma Services, [2]Senior Resident, [3]Professor, Advanced Eye Centre, PGIMER, Chandigarh, Punjab

***Corresponding Author:**
Email: soniavaidya2010@yahoo.com

Abstract

Aim: To report an interventional case series of Goldenhar Syndrome with its clinical spectrum and management.

Materials and Methods: We retrospectively analyzed the clinical and surgical data of 23 patients who presented to the oculoplastics services with Goldenhar syndrome.

Results: Of the 23 patients, there were 15 females and eight males with an average age of 79 months at presentation. All had predominant ocular and aural findings associated with or without facial anomalies. Eight had bilateral involvement. The chief complaint was the presence of a white mass lesion on the eye in the majority (91%). There was a wide range of ocular signs which included refractive errors, eyelid coloboma, mechanical blepharoptosis, cystic keratinized globe, lateral canthus anomaly, conjunctival skin tags, dermolipoma, limbal dermoid, corneal opacity, microcornea, iris coloboma, congenital cataract and familial exudative vitreoretinopathy (FEVR) with retinal detachment. Non-ocular features included hemifacial atrophy in 15 (65%). None of the patients had any vertebral, cardiac anomalies, delayed developmental milestones or mental retardation. Major ocular surgical management was done in 18 (78%) patients and included excision of dermoid and dermolipoma in 10, coloboma repair in 9 and keratoplasties in three.

Conclusions: This large study was characterized by the wide ranges of clinical ocular manifestations. Management was case based and the outcome was seen in terms of improved cosmesis and maintained or improved vision.

Keywords: Goldenhar syndrome (GS), Limbal dermoid, Eyelid coloboma.

Introduction

Goldenhar syndrome (GS) is a rare constellation of congenital malformations involving the face, eyes, and ears with the prevalence of 1/3500-5600 live births. It was first described in 1952 by Dr. Maurice Goldenhar[(1)] in a patient with a triad of accessory tragi, mandibular hypoplasia, and ocular dermoid which is now named after him. Gorlin renamed it as oculo-auriculo-vertebral syndrome in 1963.[(2)] Eighty percent of malformations are unilateral and 10-30% reported bilateral cases also comprised of asymmetric presentation. Major characteristics of GS are eye anomalies, ear anomalies, vertebral anomalies, and facial asymmetry.[(3-5)] GS remains somewhat poorly understood. Many terminologies have been used to describe this syndrome such as oculo-auriculovertebral spectrum (OAVS) and hemifacial microsomia (HFM).[(4,6)] Though Tasse et al (2005)[(7)] proposed a classification system based on the presence of the main and additional clinical findings as well as the appearance of these anomalies as unilateral or bilateral. However, there is no standard system of scoring for the diagnosis or severity.

Common ocular abnormalities include epibulbar dermoid, upper eyelid coloboma, lipodermoid, and microphthalmos. Rare findings include iris or retinal coloboma, strabismus, Duane's retraction syndrome, tilted optic disc and optic nerve hypoplasia.[(3,8-10)] Aural anomalies are varied and ranged from sensorineural hearing loss, microtia, ear appendices, fistulas, atresia, and anotia. Mandibular hypoplasia leads to facial asymmetry in a majority of the patients. Less common abnormalities are congenital heart anomalies, cleft lip/palate, developmental dental disturbances, central nervous system anomalies, renal anomalies and rarely mental retardation.[(11)] Usually, children with GS have normal intelligence and normal life span.[(12)] In this report, we describe a large series of varied ocular manifestations of this syndrome without associated cardio-vertebral anomalies and its wide-ranging management. We report our series as an interventional case series in which visual, as well as cosmetic rehabilitation of the patients, was done successfully.

Subjects and Methods

We retrospectively analyzed the clinical and surgical data of 23 patients of GS, who presented to the oculoplastics services with GS, at Advanced Eye Center, from Sept 2005-2016. The study was approved by the Institutional Ethics Committee of the Post Graduate Institute of Medical Education and Research.

All included cases had predominant ocular and aural findings associated with or without facial anomalies. All underwent complete ophthalmic examination including orbital imaging (in patients, who shows hemifacial hypertrophy and mandibular hyperplasia). The pediatric evaluation was done to look for systemic involvements. The ENT evaluation was done to precisely determine hearing loss.

Results

Of the 23 patients, there were 15 females and eight males. Eight had bilateral involvement (Table 1). The average age of presentation was 79 months (range 0-312 months). There was no history of maternal exposure to any known teratogenic agents. All pregnancies were described as normal, and no perinatal complications were reported. No consanguinity was found in any parents. One pregnancy was conceived in vitro.

Chief complaint was the presence of the whitish mass in the eye in majority 21(91%).(Table 1).

Table 1: Demography and ocular anomalies in patients with Goldenhar Syndrome

Demography		Ocular Anomalies	
			No.
	No.	Dermolipoma	12
Total patients	23	Limbal dermoid	18
Male: Female	8:15	Lid coloboma	9
Unilateral: Bilateral	15:8	Conjunctival skin tags	2
Average age of presentation (months)	79	Mechanical Ptosis	2
Symptoms		Microcornea	2
		Corneal opacity	3
Whitish mass in eye	21	Cystic globe	2
Upper lid defect	9	Iris coloboma	2
Upper lid droop	2	Choroidal coloboma	1
Ocular skin tags	2	Retinal detachment	1
Forward protrusion of eye	1	Familial exudative vitreoretinopathy (FEVR)	1
Small eyes	1	Lateral canthal anomaly	2
Retinal detachment/DOV	1	Congenital cataract	1
Watering	1	Proptosis	1
		Alopecia	1

Eyelid coloboma was seen in 9 (39%) patients. The severity of the defect ranged from minimal to large. The lateral canthus was not formed in two and was associated with lax lower lids. One patient had bifid tarsus (Fig. 1, 2).

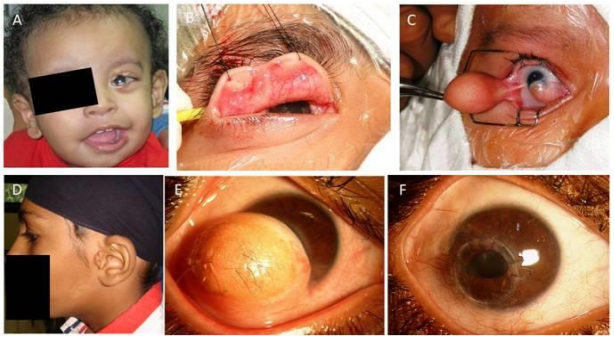

Fig. 1: Goldenhar syndrome patients with, A- lid coloboma, limbal dermoid, preauricular skin tag and macrostomia. B- Bifid tarsus. C- A large conjunctival tag, microcornea and limbal dermoid. D-E: Preauricular skin tags, limbal dermoid. F-Post keratoplasty and lens aspiration

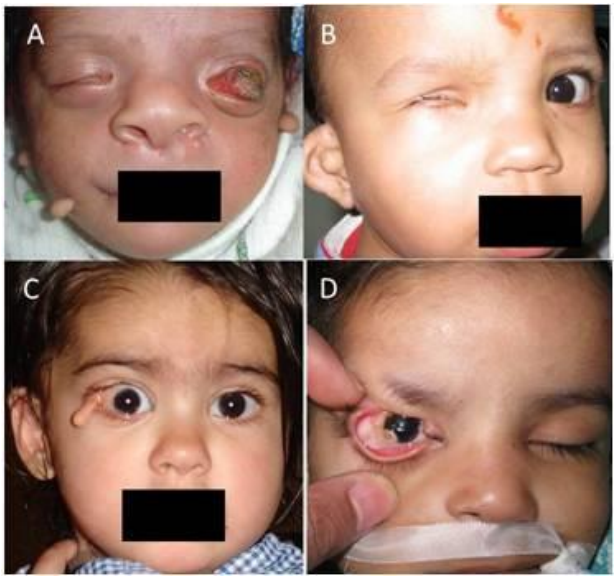

Fig. 2: Clinical presentation of Goldenhar Syndrome. A-Multiple facial skin tags, left large cystic globe with keratinized cornea. B- Right eye microcornea and cystic globe. C- A skin tag arising from conjunctiva. D- Eyebrow anomaly, large upper lid coloboma with limbal dermoid and dermolipoma

Coloboma was associated with dermolipoma in seven (77%). Dermolipoma were seen in 12 (52%). It was associated with limbal dermoid in seven (38.8%), localized to the supero-temporal quadrant in 9, was 360 degree in 2 and 180 degrees in another. In one, it involved the lateral canthus and lower fornix.

Coloboma repair was done in 9(39%) eyes. Deciding factors to operate a coloboma was based on the size, the total amount of corneal exposure and age of the child. Till the time of surgery, these infants were managed conservatively with topical antibiotic ointment, lubricants, and nightly patching. Regular follow-up and monitoring were done to look for any corneal exposure/ulceration. Parents were compliant with the above management and none required to be intervened early. The median age for surgery was 3.3 years. If coexistent dermolipoma was present, it was first excised and followed by coloboma repair, except in one patient who had 360-degree involvement. In this case, coloboma repair was clubbed with 50% excision in the first stage. The rest was removed in the second stage. This patient required extensive dermolipoma excision, fornix formation, lateral canthus fixation and amniotic membrane transplantation (Fig. 3). Her ocular movements remained full and free in all gazes. Though her cosmesis improved significantly, visual acuity gain was nil due to heavy corneal scarring.

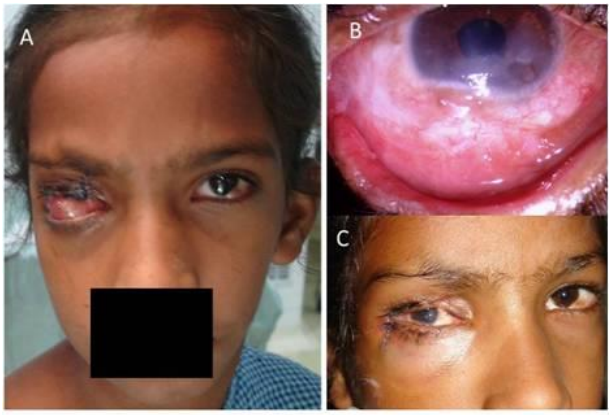

Fig. 3: A- Nine-year female has facial asymmetry, bilateral limbal dermoid, right eye 360-degree dermolipoma, repaired upper lid coloboma and left preauricular skin tag. B- After 360-degree dermolipoma with limbal dermoid excision and amniotic membrane transplantation. C- Repaired lid coloboma and lateral canthopexy

Limbal dermoid was seen in 18 (78%) cases. It was of grade-I (superficial tumor of <5mm) in seven and grade-II (tumor extending up to the descements membrane) in three. Anterior chamber structures and angle involvement was evaluated with gonioscopy and the ultrasound biomicroscopy (UBM) in cooperative patients. None had shown any angle structures involvement. Bilateral features included were limbal dermoid in two, eyelid coloboma in one and iris coloboma in two.

The limbal dermoid excisions were done in 10 (Table 2). It was excised with the aim to improve visual acuity in four with significant astigmatism and to improve cosmesis in the others. It was done with bare sclera technique in seven. Excision was augmented by keratoplasty in three. In one young child refractive error decreased from +6.0 diopter cylinder at 110 degrees to +2.50 diopter cylinder at 100 degrees following limbal dermoid excision. No recurrence was seen.

Among the total 23 patients, 18(78%) had undergone different surgical interventions. (Table 2).

Visual acuity was evaluable in eight cooperative older children and not evaluable in 10 uncooperative small children. Refractive error included significant astigmatism in four, high myopia in one and aphakic hypermetropia in one. Four with astigmatism had limbal dermoid. Astigmatism ranged from +3.0 to +7.0 D cylinder.

Post-operatively, the vision was maintained in 6, improved in one (gained vision by 4 lines) and not improved in one. The eye which did not improve had the diagnosis of FEVR and had undergone retinal reattachment surgery. Post-operative sequelae were seen as conjunctival vascularization and hypertrophy in one, shallow fornix and minimal ocular movement restriction in two and residual dermolipoma in one. Cosmetically all had improvement and were satisfied.

Non-ocular features included hemifacial atrophy in 15. None of the patients had any vertebral or cardiac anomalies. None had delayed developmental milestones or mental retardation. Facial hemiatrophy was associated with limbal dermoid, large dermolipoma and ear deformities. All five patients with anotia had hearing loss (Table 2).

Table 2: Associated clinical features and various surgical procedures done

Associated features	No.	Surgery done	No.
Hemifacial hypoplasia	15	Dermolipoma excision	10
Facial Asymmetry	8	Limbal dermoid excision	10
Pre-auricular defects	11	Coloboma repair	9
Facial skin tags	2	Keratoplasty	3
Anotia	5	Excision of conjunctival tags	2
Hyperpigmented keratinized skin on neck	1	Cleft lip/palate surgery	2
Cardiac anomaly/ vertebral anomaly	None	Amniotic membrane transplant	1
Mental retardation	2	Lacrimal syringing/probing	1
Cleft lip/ palate	1	Retinal detachment surgery	1
Microcephaly	5	Conjuctival cyst excision	1
Mandibular hypoplasia	4	Mandibular surgery	1
Eyebrow and forehead hair anomaly defect	2	Sclerosing agent into the orbital cyst	1
Small and disorganized pinna	15		

Discussion

Goldenhar syndrome (GS) is a rare congenital disorder which consists of the complete triad of epibulbar dermoid, accessory auricular appendages, and pretragal fistulae.[12] The prevalence of GS is 1/3500-5600 lives births. It occurs in a ratio of 3:2 with males more affected but in our series females were more commonly affected in a ratio of 8:15. Our 34% of bilateral cases is in sync with those of being reported in the literature.[13,14] Although some reports of autosomal dominant and autosomal recessive inheritance of GS are present in literature, it is mainly sporadic.[14] None of our patients had a positive family history which coincides with most of the available literature.[11-14] There is sparse literature on the various ocular manifestations and their management. Ocular manifestations could be the most readily evident as compared to the other features which become prominent as the child grows. None of our patients had any cardiac or vertebral anomalies.

Epibulbar choristomas are most common (32%) ocular feature of GS and are characterized by the presence of dermoid or lipodermoid which rarely enlarge and are usually inferotemporal in location.[15] Mostly these are superficial as was seen in our cases, and very few invade sclera or cornea.[16] Tumor extent and associated features such as astigmatism, irritation, and exposure keratitis decide surgical intervention.[17] Lipodermoid usually extends posteriorly in the orbit and may benefit from radiographic delineation if surgical

excision is planned. Its management tends to be conservative. Surgery should be limited to debulking as restrictive strabismus, and the relative dry eye can be induced secondary to chemically induced fibrosis from intralesional lipid.[18] Surgical correction was done for eyes with the large limbal dermoid obscuring visual axis or causing irregular astigmatism, eyelid coloboma, and dermolipoma, in order to visually rehabilitate the patient and provide better cosmesis. Limbal dermoid have been treated with bare sclera technique with and without amniotic membrane transplant and lamellar/penetrating keratoplasties. The post-operative increase in astigmatism due to pseudo-pterygium and corneal opacification can lead to decrease in visual acuity[18] as was also seen in one of our patients.

We also found some different uncommon findings, such as conjunctival skin tags, facial skin tags, bifid tarsus, blepharoptosis, lateral canthal anomaly, congenital cataract, iris and choroidal coloboma many of which have rarely been/not reported earlier. This syndrome includes a wide range of anomalies of ear, face, vertebra and viscera (heart, kidney, etc). Microtia and disorganized pinna were the most common finding, similar to report by Beleza-Meireles A et al.[19] Due to the heterogeneity of GS, not all children exhibit conductive hearing loss. Our study was characterized by the lack of cardiac and vertebral anomalies. While treatment, the emphasis was on preventing complications, buying time to allow growth of structures before the cosmetic correction, and finally intervening surgically in a stepwise fashion. The visual gain was possible to due to successful keratoplasties in selected cases, being done after the coloboma repair and or dermoid excision.

This study is one of the largest reports on the ocular manifestations of GS with a focus on the surgical management approaches of the various ocular manifestations. It is characterized by female predominance, lack of cardiac and or vertebral anomalies and rare, uncommon features of conjunctival skin tags, lateral canthus anomaly, uncommon simultaneous presentation with FEVR, cystic keratinized globe, choroidal and iris coloboma. Management was case based and the outcome was seen in terms of improved cosmesis and maintained or improved vision.

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