A Case of Brown's Syndrome in Association With Goldenhar Syndrome

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ABSTRACT

A case study of a young girl diagnosed at birth with Goldenhar syndrome is presented. Ocular features are described, including the unusual finding of Brown's syndrome, suggesting a possible teratogenic link between the two conditions.

Keywords: Goldenhar syndrome, oculo-auriculo-vertebral dysplasia, Brown's syndrome

INTRODUCTION

Goldenhar syndrome was first described in 1952 by Swiss ophthalmologist Maurice Goldenhar.[1] It is a manifestation of the oculo-auriculo-vertebral spectrum (OAVS). Structural malformations found in Goldenhar syndrome are commonly unilateral and may involve the following; external and middle ears, eyes, face, skin, vertebrae and jaw.[2] Further associations may include congenital heart anomalies, cleft palate, dental anomalies, mental retardation and agenesis of corpus callosum.[3-5]

Gorlin has estimated the incidence of the syndrome at one in 5,600.[6] It has a reported male to female ratio of between 2:1 and 3:2.[1,7] The severity of the disease varies between individuals.

Ocular involvement differs from case to case. Findings can include microphthalmia, anophthalmia, upper eyelid coloboma, eyebrow coloboma, retinal coloboma, iris coloboma, ptosis, epibulbar dermoid, lipodermoid, nasolacrimal duct and canalicular obstruction, corneal anaesthesia, microcornea, peripapillary choroidal hyperpigmentation, macular hypoplasia, tortuous retinal vessels, optic nerve hypoplasia, tilted optic disc, cataract, dacryocystitis, cryptophthalmos, strabismus and Duane's syndrome.[3, 5, 8]

CASE REPORT

Miss K was born prematurely at 35 weeks gestation, weighing 1,538gms, and was diagnosed with Goldenhar syndrome. While the findings with Goldenhar syndrome can be numerous and varied, Miss K was born with the following manifestations; preauricular skin tags, mild left hemifacial microsomia and a right epibulbar dermoid. X-rays of spine and limbs, ultrasound of brain, chromosome testing and heart investigations were all shown to be normal, indicating a mild form of the syndrome. At two years of age, mild hearing loss in her right ear was also discovered.

Aged six and a half years old, Miss K had been regularly attending ophthalmology clinics since four months of age. Strabismus was recorded at four months of age, with a right essential infantile esotropia, which after some part-time occlusion was alternating. Surgery was undertaken at 19 months with bi-medial rectus recessions. The initial result post-operatively appeared straight, however, a year later a small consecutive left exotropia was apparent. At a later stage, a positive result to four diopter prism testing indicated a left microtropia with identity as no movement was seen on cover testing. It is uncommon for esotropia surgery to obtain perfect visual axis alignment and bifoveal fixation,[9] and therefore it is likely that the microtropia was residual following previous esotropia surgery.

Miss K's ocular findings included the presentation of a right epibulbar dermoid. The epibulbar dermoid in Miss K's case was a dermolipoma located in the lateral canthus region of her right eye and was relatively inconspicuous. It was not impinging on the cornea or causing astigmatism and therefore no surgical intervention had been taken.

At three years of age a right Brown's syndrome was noted. No deviation was seen in primary position and surgical intervention was not required. Since then the Brown's syndrome has not altered or resolved.

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At three and a half years of age, Miss K had an cycloplegic refraction of +2.50DS in each eye. At this point a difference in visual acuity was noticed with Right 3/6 and Left 3/9 (Kay pictures, single optotypes) and part-time patching was prescribed.

At six years of age her visual acuity was Right 3/3.8 and Left 3/4.8 (LogMAR). At this point patching was ceased due to poor compliance and given the presence of a microtropia, where it is generally accepted that levels of visual acuity greater than 6/12 or 6/9 are rarely achieved.[10]

Miss K showed classic ocular findings of Goldenhar syndrome of an epibulbar dermoid and esotropia. While Duane's syndrome has been reported in association with Goldenhar syndrome, Miss K presented with the unusual finding of a Brown's syndrome.

DISCUSSION

The aetiology of Goldenhar syndrome is poorly understood and mostly presents sporadically.[7,11] Familial cases have also been reported, although the genetic basis for the disorder is not fully understood.[11] The aetiology in Miss K's case is unlikely to be of genetic origin as there was no family history of the condition. The cause in her case was attributed to an intra-uterine event during pregnancy. Goldenhar syndrome is thought to develop due to defects on the first and second branchial arch during foetal development.[4]

Epibulbar dermoids (dermolipomas and limbal dermoids) are commonly found with Goldenhar syndrome. Dermoids are histologically normal tissue (epidermal and connective tissue) in an abnormal location, usually present at birth and show little to no growth.[5] The reported incidence of epibulbar dermoids with Goldenhar syndrome, or OAVS, varies between 32% and 78%.8,[12-14] Limbal dermoids often contain hair and can involve deep corneal structures.[5] Vision can be impaired if they encroach on the visual axis, cause astigmatism and/or amblyopia.[11]

In Miss K's case, an epibulbar dermoid was found in the form of a dermolipoma. Dermolipomas are usually located in the conjunctiva near the lateral canthus and consist of epithelial, dermal and adipose tissues.[5] Dermolipomas are yellowish or the colour of normal conjunctiva.[8] They are usually well circumscribed and are rarely a functional or cosmetic problem.[5] If removal is necessary a limited dissection should be performed to avoid symblepharon and scarring of the lateral rectus which can result in restrictive strabismus.[5, 6]

Strabismus is a common finding with Goldenhar syndrome,[3, 5, 11, 15] indicating a likely association in Miss K's case between the presentation of an essential infantile esotropia and Goldenhar syndrome.

Duane's retraction syndrome is also commonly reported in the literature in relation to Goldenhar syndrome.[8,15,16] Duane's retraction syndrome is thought to be due to branches of the oculomotor nerve innervating the lateral rectus muscle taking the place of absent or deficient abducent nerve fibres.[17]

The extraocular muscles innervated by the oculomotor nerve develop from the premandibular condensations, whereas the lateral rectus muscle and superior oblique muscles differentiate from the maxillomandibular mesoderm.[18] The extraocular muscles become separate masses of mesoderm at four weeks.[19] At around one month the extraocular muscles are innervated by the cranial motor nerves.[5] Goldenhar syndrome manifests at a similar time in embryological development of approximately 30 to 45 days,[6,14] which provides further basis for a link between Duane's syndrome and Goldenhar syndrome. Santamaria[16] described an atypical vertical retraction syndrome in a child with Goldenhar syndrome, presenting a further ocular muscle innervation variant of Goldenhar syndrome.

To the best of the authors' knowledge, Brown's syndrome has not been reported previously in a case of Goldenhar syndrome. Brown's syndrome presents as an absence of elevation in adduction, with mechanical restriction on attempts to elevate the eye in adduction with forced duction testing.[20] While there are many possible aetiologies of Brown's syndrome, the exact aetiology in Miss K's case is unknown. Her Brown's syndrome was first noted at three years of age and is likely to have been congenital or may have developed in infancy. It is believed that the majority of cases of Brown's syndrome actually develop in infancy and that very few are congenital.[17] There was no evidence of acquired trauma, juvenile rheumatoid arthritis, chronic sinusitis, systemic lupus erythematosus,[5] or other aetiology supporting the diagnosis of an acquired Brown's syndrome.

One possible theory for the aetiology of a congenital Brown's syndrome in Miss K's case is the persistence of the embryonic trabecular connections between the superior oblique tendon and trochlea, thereby causing a restriction of movement.[21-23] The trochlea and superior oblique tendon are derived from mesenchymal tissue and are indistinguishable up to six weeks gestation (22mm embryo). At 26mm (seven to eight weeks) differential degeneration occurs between the trochlea and the tendon, being discernible as separate structures connected by thick trabeculae at 78mm (approximately 12 weeks). By 26 weeks, these septae generally degenerate, with only fine remnants remaining.[21,22] This initial development of the tendon and trochlea occurs at the same time as the structures involved in Goldenhar syndrome.

A second possible aetiology is paradoxical innervation of the superior oblique similar to Duane's syndrome. Paradoxical innervation has been described with the co-contraction of the superior and inferior obliques on attempted elevation in adduction.[23-26] Instead of the superior oblique muscle relaxing in elevation in adduction, there is

maximum innervation, restricting the globe from moving upwards.[25, 26] On depression in adduction the innervation to the superior oblique is weaker, but still sufficient to move the eye in this direction.[25,26] There have been three cases reported electromyographically showing this simultaneous paradoxical innervation,[24-26] but this has not been confirmed by others.[23] However, in cases of paradoxical innervation one would expect a negative result on forced duction testing under anaesthesia, with von Noorden stating that this is never the case.[20] As forced duction and electromyography testing were not conducted in Miss K's case, this aetiological hypothesis can not be confirmed. The oculomotor nerve innervates the inferior oblique muscle at 31 days, and the superior oblique is innervated by the trochlear nerve at 33 days.[19] The manifestation of Goldenhar syndrome is at a similar time period to the innervation of the extraocular muscles, providing a further possible basis for a relationship between the two syndromes.

CONCLUSION

While Miss K presented with a variety of ocular findings, only the epibulbar dermoid and infantile esotropia were common findings in Goldenhar syndrome. The presentation of Brown's syndrome has not been reported previously with Goldenhar syndrome. While we can not be certain Miss K's Brown's syndrome was congenital and therefore a true finding in Goldenhar syndrome, there are several possible causes of Brown's syndrome that could relate to the manifestation of Goldenhar syndrome, suggesting a common teratogenic effect.

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