Case Report

A Case Report of Klebsiella sepsis in an Infant with Goldenhar Syndrome: Association or Coincidence

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ABSTRACT

Goldenhar syndrome (GS) is a rare congenital disorder of the development of first and second branchial arches. The born neonate may exhibit orofacial, auricular, skeletal, and solid organ involvement with variable phenotypic expression. The pathogenesis and long-term implication of GS is still under study. Multidisciplinary management is the key in lifelong management of GS. There is a challenge identifying this syndrome in low-resource setting. We describe in this case report about a neonate with typical phenotypic features and late-onset *Klebsiella* sepsis.

Key words: Coloboma, Goldenhar syndrome, *Klebsiella*, Preauricular skin tags, Sepsis

Maurice Goldenhar in 1952 described Goldenhar syndrome (GS). It is also called oculoauriculovertebral syndrome, facioauriculovertebral syndrome [1]. GS is due to the first and second brachial arch developmental abnormalities [2-4]. GS belongs to a group of conditions together known as craniofacial microsomia. Incidence of GS is about 1:5600–1:45,000 live births with male-to-female proportion of 3:2 [4-6]. However, there is no reported incidence available in India.

Clinical presentation ranges from mild facial asymmetry to significant facial defects with internal organs and skeletal system involvement of varying degree of severity. Although unilateral facial abnormalities are commonly seen, 10–33% of the individuals can have a bilateral facial presentation [7]. The most predominant manifestations include mandibular hypoplasia, microtia, preauricular tags, and conductive hearing loss. Other abnormalities such as masticatory muscle hypoplasia and vertebral anomalies may be seen in more than 50% of cases. Coloboma involving iris, eyelids, preauricular pits, dental hypoplasia, and frontal plagiocephaly can also occur.

Cardiac anomalies and other associated craniofacial anomalies such as cleft lip or cleft palate will account for prevalence <30%, whereas sensory-neural hearing loss, pulmonary, genitourinary, central nervous system, gastrointestinal, and limb abnormalities account for a prevalence <15% [7]. Findings of short stature, delayed psychomotor development, speech disorders, psychosocial problems, and autistic behaviors are also recorded in GS [4]. Craniofacial microsomia often overlap with other syndromes, developmental anomalies, and sequences such as vertebral anomalies, anal atresia, cardiac anomalies, trachea-esophageal atresia, renal anomalies, and limb anomalies, coloboma, heart, atresia choanae, retardation of growth and development, and genitourinary and ear anomalies, Mullerian ducts anomalies, unilateral renal, cervicothoracic, and somite structures, and omphalocele, exstrophy of the cloaca, imperforate anus, and spinal anomalies. The goals of treatment involve adequate respiratory support and sufficient feeding, to maximize the hearing and communication, improve facial symmetry, and optimize dental occlusion by appropriate surgical repair.

CASE REPORT

The baby boy presented with complaints of respiratory distress, refusal to feed, decreased urine output, and faulty feeding. The baby presented to a low resource, tertiary care hospital in Northern India. He was born of non-consanguineous marriage belonging to lower socioeconomic class and was apparently well before day 33. No significant antenatal and family history was noted but history of premature normal vaginal delivery with low

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birth weight with crying immediately after birth was recorded. Baby had symptomatic hypoglycemia, shock, respiratory distress, and severe dehydration at admission.

General physical examination findings showed midline dermoid cyst (Fig. 1), ear abnormalities: Accessory tragus, microtia, preauricular skin tags, prominent anti-helix, preauricular pits, and malformed right ear (Fig. 2a). Ophthalmological examination revealed bilateral hazy cornea, coloboma involving iris, and fundus on the left side (Fig. 1), right eye: Morning glory anomaly (fundus picture not available). Added to these abnormalities, baby also had microcephaly, occipital plagiocephaly, high-arched palate, retrognathia, and pooling of secretions from mouth (Fig. 2b).

Abdominal examination showed features of septic ileus and cardiovascular examination grossly ruled out organic lesion. Investigations revealed metabolic acidosis, positive sepsis screen with *Klebsiella* species positive in blood culture, pre-renal acute kidney injury, and hypoproteinemia. TORCH profile and cerebrospinal fluid analysis were normal. Radiological examinations including echocardiography were not done as bed-side investigation facility was not available and neonate was unstable to be shifted. Due to characteristic clinical features, the infant was diagnosed as a case of GS with *Klebsiella* sepsis.

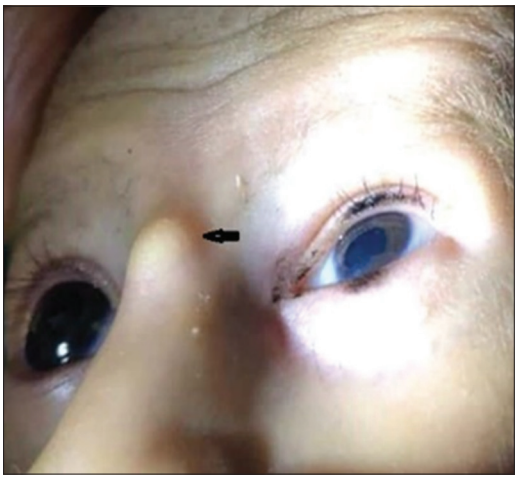

Figure 1: Midline dermoid cyst and coloboma of iris on the left side

Figure 2: Clinical image depicting (a) accessory tragus, preauricular skin tags, and malformed ear and (b) microcephaly, retrognathia, and occipital plagiocephaly

The baby received cefotaxime (100 mg/kg/day) and amikacin (10 mg/kg/day) as empirical therapy, then upgraded to meropenem (60 mg/kg/day into three divided doses), and vancomycin (45 mg/kg/day) from the 2nd day based on antibiotics sensitivity. With mechanical ventilation, inotropes, and sensitive antibiotics, the baby improved by the 3rd day. Gradually inotropes and ventilator support were weaned off by the 5th day. The baby improved on supportive care and antibiotic therapy for a period of 14 days. Screening echocardiography done in follow-up showed patent foramen ovale with good ventricular function. The baby was on follow-up with supplements (calcium, Vitamin D, and multivitamin drops) and bottle feeding with long nipple. The baby was followed up to 2 months.

DISCUSSION

GS has no established guidelines for its diagnosis. Etiopathogenesis is multifactorial involving complex interplay of genetic and environmental factors. The pattern of inheritance may be autosomal dominant or recessive with majority occurring sporadic in nature with recurrence likely 2–3% [3]. This is in accordance with our patient showing no inheritance pattern being observed.

Genetic research has shown various chromosomal abnormalities and gene defects which may lead to abnormal vascularization in the 4th week of intrauterine life hampering the development of the 1st and 2nd pharyngeal arches [3,8]. Risk factors such as gestational diabetes, hypothyroidism, celiac disease, per vaginal bleeding, premature delivery, and drugs such as cocaine, nicotine, thalidomide, and tamoxifen may affect the growth of the 1st and 2nd pharyngeal arches [3,4]. Apart from prematurity, neonate of our report had no risk factors.

The diagnosis of this congenital anomaly is based on clinical and radiological evaluation. The eye anomalies include coloboma of iris, eyelid, and retina as noted in our neonate in the left eye and morning glory abnormality in the right eye. Coloboma was also reported in an infant in an earlier case series [9]. Other ocular malformations include microphthalmia, astigmatism, cataracts, ocular dermoid, and blepharophimosis. On examination, ear abnormalities such as blind fistulas or preauricular skin tags were noted in our case study. The above-mentioned auricular abnormalities were also reported in various case series [8-11]. Artesia of the external auditory meatus, middle ear defects, and deafness may be seen [4].

The orofacial malformation includes unilateral or bilateral facial hypoplasia involving maxilla and mandible, tongue hypoplasia, cleft lip, cleft palate, arch hypoplasia, and delayed dentition, enamel, and dentine abnormalities [4] Oropharyngeal airway compromise is seen commonly in GS, our case had high arched palate and retrognathia with pooling of secretion which may suggest a compromise in the upper airway. Atrial and ventricular septal defects are commonly associated cardiac abnormalities as in index case with patent foramen ovale. Tetralogy of Fallot with aortic arch abnormalities is infrequently reported [4,5]. Urogenital anomalies include renal agenesis, fused kidneys, multicystic kidneys, ureteral abnormalities, and hydronephrosis [4].

Deformed spine, cranial abnormalities including microcephaly, and limb abnormalities such as club foot, abnormalities of radius, and thumb are frequently reported. Neonate in our study had microcephaly and occipital plagiocephaly with a negative TORCH profile, and no history of fever with rash in mother during the antenatal period which is an important risk factor for congenital infections causing primary microcephaly.

Diffuse cerebral hypoplasia, hydrocephalus, corpus callosum lipoma, absence of septum pellucidum, corpus callosum dysgenesis, facial palsy, trigeminal anesthesia, encephalocele, holoprosencephaly, Arnold–Chiari malformation, and hypothalamic hamartoma are the associated central nervous system manifestations of GS [3-5]. De Golovine *et al*. in their case series of two children with GS reported recurrent sinopulmonary infection and meningitis, and on evaluation, they eliminated primary immunodeficiency and reported secondary cause like anatomical aberration attributing to recurrent infection [11]. In our case report, the neonate presented with culture positive for *Klebsiella* sepsis.

There is lack of reported literature of the association of GS with neonatal sepsis; however, this can be contributed by low socioeconomic status, poor hygiene, faulty feeding habits, and prematurity. Studies in tertiary care hospitals in North India show *Klebsiella* species to be one of the common organisms responsible for neonatal sepsis [12,13]. Similar study was published in 2017 showed incidence of *Klebsiella* sepsis to be only 5% [14]. Hence, *Klebsiella* sepsis observed in our neonate can be a coincidence or association. Varied phenotypic presentations require a multidisciplinary approach with individualized management protocol for any child with GS.

CONCLUSION

We report this unique association of an infant with phenotypic features of GS manifesting with *Klebsiella* sepsis. Lack of genetic and radiological investigations in low-resource setting makes precise diagnosis nearly impossible. In such scenarios, diagnosing a syndromic child on clinical findings may be crucial for facilitating initial management and ensuring timely referral to higher centers.

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