Goldenhar syndrome: rare case reported from secondary health care facility in Himachal Pradesh

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Abstract

Dr. Maurice Goldenhar, a renowned Swiss ophthalmologist classified the clinical features and named the malformation complex as Goldenhar Syndrome and described it as a congenital defect characterized by constellation of malformations classically involving the face, eyes and ears. Principal deformities of the Goldenhar syndrome are often combined with various malformations, like Cleft lip and/or palate, tongue cleft, unilateral tongue hypoplasia, and parotid gland aplasia, Rib anomalies, Congenital heart disease (ventricular septal defects). A 12-year-old female patient diagnosed with Goldenhar syndrome at secondary care Regional Hospital Bilaspur, Himachal Pradesh. She was diagnosed with a case of Goldenhar syndrome on clinic-radiological investigations. The patient reported to ophthalmology OPD of the hospital with the chief complaint of soft tissue structure in left eye with decreased vision. On examination limbal dermoid was observed. Patient was having pre-auricular tissue tag on both sides, hemifacial micrognathia and microstomia. Correlating the history and physical findings a provisional diagnosis of Goldenhar Syndrome was made with differential diagnosis of Franschetti syndrome or Treacher – Collins syndrome, Nager syndrome or acro-facial dysostosis and Townes-Brocks syndrome. Based on the clinical and radiographic findings a diagnosis of Goldenhar syndrome was made. Severe cases of GS can affect the routine and social life of the patient. Early detection can help avoid complications at a later stage of life. Such patients will have an increased risk for psychosocial difficulties. The study of this condition is still controversial because the symptoms and the physical features may vary greatly in range and severity from case to case.

Keywords: Goldenhar syndrome, Oculo-auriculo-vertebral (OAV) dysplasia, Congenital defects

Introduction

Goldenhar syndrome (GS) is also known as oculo-auriculo-vertebral (OAV) dysplasia. It is considered a variant of hemifacial macrosomia [1]. In 1881, the first observation of oculo-auriculo-vertebral (OAV) dysplasia was reported by Von Arlt and in 1952, Dr. Maurice Goldenhar, a renowned Swiss ophthalmologist classified the clinical features and named the malformation complex as Goldenhar Syndrome and described it as a congenital defect characterized by constellation of malformations classically involving the face, eyes and ears [2,3].

Reported incidence of this syndrome is 1:3500 to 1:5600 with a male to female ratio of 3:2 [4]. Although most cases are sporadic, autosomal dominance inheritance has also been described. Though, the etiology of Goldenhar syndrome is not well established, it is thought to be due to exposure to various viruses or chemicals during pregnancy. Some researchers also suggested gestational diabetes mellitus as one of the causes. The MSX homeobox genes play a crucial role in the pathogenesis [5,6].

Other clinical features include limbal dermoid or lipo-dermoid, Preauricular skin tags, Unilateral facial hypoplasia, Neck: Branchial cartilage, branchial fistula, webbing, short neck, abnormalities of sternocleidomastoid muscle.

Unilateral macrostomia (lateral facial cleft). Back: Pilonidal dimple, kyphoscoliosis, Sprengel’s deformity, Hands / Fingers: clubbing, polydactyly, clinodactyly, single palmar crease, and Vertebral column anomalies (atlas occipitalization, synostosis, hemivertebrae, fused vertebrae, scoliosis, and bifold spine) [7].
The multifactorial etiopathogenesis includes nutritional and environmental factors that result in blastogenesis disorders. Information to identify these etiological factors do not exist [8]. The anomalies of 1st and 2nd branchial arcs have been observed in children born from mothers who were exposed to thalidomide, primidone and retinoic acid, in addition to diabetic mothers [9,10]. Embryologically, the ocular-auricle-vertebral defect has been considered an anomaly of 1st branchial arc, but this alteration does not explain the anomalies in the brain, heart, kidneys or dorsal spine [11].

**Case Report**

A 12-year-old female patient diagnosed with Goldenhar syndrome at secondary care Regional Hospital Bilaspur, Himachal Pradesh. She was diagnosed with a case of Goldenhar syndrome on clinic-radiological investigations. The patient reported to ophthalmology OPD of the hospital with the chief complaint of soft tissue structure in left eye with decreased vision. On examination limbal dermoid was observed. With a syndromic suspicion, patient was referred to Pediatrics department for further clinical examination.

![Image showing limbal dermoid](image1)

**Fig-1: Image showing limbal dermoid**

On physical examination in pediatrics department, it was found that the patient was having pre-auricular tissue tag on both sides, hemifacial micrognaethia and microstomia.

![Image showing tissue tags pre-auricular tissue tags and blind fistula on right side](image2)

**Fig-2: Image showing tissue tags pre-auricular tissue tags and blind fistula on right side**

Principal deformities of the Goldenhar syndrome are often combined with various malformations, like Cleft lip and/or palate, tongue cleft, unilateral tongue hypoplasia, and parotid gland aplasia, Rib anomalies, Congenital heart disease (ventricular septal defects), anomalies of the urogenital and gastrointestinal system, mental retardation, Venous anomalies, associated juvenile glaucoma in Turner’s syndrome, Congenital Facial nerve palsy and Growth hormone deficiency [7].

![Image showing mandibular hypoplasia](image3)

**Fig 3: Image showing mandibular hypoplasia**
There was no family history of any genetic abnormality or infections. The parents were healthy and their marriage was non-consanguineous. Correlating the history and physical findings a provisional diagnosis of Goldenhar Syndrome was made with differential diagnosis of Franchetti syndrome or Treacher–Collins syndrome, Nager syndrome or acro-facial dysostosis and Townes-Brocks syndrome. On investigations patient was showing normal ECHO, USG Abdomen & KUB, audiometry & blood investigation while there was refractive error with astigmatism.

On NCCT face with screening whole spine with 3D construction, following observations were made:
- Right sided mandible is hypoplastic predominantly in region of ramus as well as mandibular condyle.
- Mandibular condyle is located anteromedially compared to left side and shows ill formed temporomandibular joint.
- Bilateral preauricular tags and blind fistula in front of preauricular tag on one side.
- Screening spine with intervertebral discs showing grossly normal study.

![Image A)](image1.png)

![Image B)](image2.png)

![Image C)](image3.png)

Fig-4: A, B and C Showing right hypoplastic mandible in the region of ramus and condylar area with anteromedial location of mandibular condyle ill formed temporomandibular joint
Based on the clinical and radiographic findings a diagnosis of Goldenhar syndrome was made. The genetic analysis was planned but couldn't be done due to affordability issues to the family. (All other blood investigations are done at regional hospital Bilaspur free of cost under RBSK scheme and radiological investigations were done free of cost). The patient was referred to tertiary care hospital for multidisciplinary management.

**Discussion**

A number of case reports of Goldenhar syndrome have been described in literature. In 1997, Araneta et al. described the occurrence of Goldenhar syndrome among children of Persian Gulf War veterans and found that 7 infants out of an estimated 75,414 infants had Goldenhar syndrome [12]. As similar to previously reported cases, our patient had marked right facial hypoplasia

Tsai and Tsai reported a family in which seven members in three successive generations were diagnosed with Goldenhar syndrome [13]. Clinical features in all were highly suggestive of Goldenhar syndrome [7]. Anderson and David reported spinal anomaly in seven patients with wide range of abnormalities including butterfly vertebrae, hemivertebrae, kyphosis and rib anomalies [14]. Ozdemir et al. reported a case of 12-year-old male with postaxial polydactyly, congenital heart disease, vertebral anomaly and facial asymmetry [15]. Berker, Acaroglu, and Soykan reported a patient with congenital facial nerve paralysis in conjunction with Goldenhar syndrome [16]. Kumar et al. reported polydactyly and hydrocephalus as rare associations with Goldenhar syndrome [17]. Zaka-ur-Rab and Mittal reported a case where drusen of the optic nerve head was found in association with this syndrome [18].

**Table-1: Differential diagnosis of Goldenhar Syndrome**

| Differential diagnosis       | Classical presentation                                                                                                                                 |
|------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------|
| Our Index Case               | Hemifacial microsmia  
Mandibular hypoplasia  
Micrognathia  
Preauricular appendages/tags with blind fistula on one side  
Limbal dermoid  
Multifactorial inheritance with variable penetrance/Heterogeneity                                                                                                                                 |
| Goldenhar syndrome          | Unilateral cleft lip or palate is associated with other facial anomalies such as  
Facial asymmetry  
Asymmetric malformation of 1st and 2nd branchial arch  
Unilateral orbital anomalies  
Ear abnormalities: with appendix or pre-auricular tag (common sign)  
Retrognathia / micrognathia (common sign)                                                                                                                                 |
| Treacher – Collins Syndrome: | Symmetrical deformity of the face:  
Cleft palate  
Symmetrical malar and mandibular hypoplasia but without agnathia  
Severe micrognathia  
Abnormal auricles/External ear deformities/Microtia  
Coloboma of lower eyelid with deficient eyelashes  
Disruption of scalp hair in the preauricular region (Sideburn)  
Bilateral malformation of 1st and 2nd branchial arch  
AD inheritance (mostly)                                                                                                                                 |
| Nager syndrome               | Pre axial limb anomalies like:  
(Hypoplasia or absence of radius, hypoplasia or absent thumbs, triphalangeal thumbs, radioulnar synostosis)  
Facial anomalies like:  
(Malar hypoplasia with downward slanting palpebral fissures, lower eyelid coloboma, severe micrognathia)  
AD or AR inheritance                                                                                                                                 |
| Townes-Brocks syndrome:      | Lop ears/Dysplastic ears  
Imperforate anus  
Sensorineural and/or conductive hearing loss  
Thumb malformations  
(triphalangeal/duplication/hypoplastic thumb)  
AD inheritance                                                                                                                                 |
Our patient was provisionally diagnosed as Goldenhar syndrome but a number of other first and second arch syndromes were considered in the differential diagnosis [19]. A recent study detected multiple congenital anomalies in ecography findings in 20 cases. The gestational age in the diagnosis varied from 15 to 35 weeks and in more than half of the cases it was associated to the polyhydramnios or oligohydramnios.

The characteristics observed were: face malformations present in 52% of the cases, as microptalmia, auricular abnormalities, face asymmetry and face cleft; amongst the neurological alterations, occipital encephaloele, hydrocephaly and cerebellar hypoplasia were observed, which occurred in 47% of the findings; cardiac defects, radial aplasia and renal agenesia were seen less frequently [20,21].

Preauricular tags can be associated with several genetic conditions such as: Oculoauriculovertebral dysplasia, Chromosome arm 11q duplication syndrome, Chromosome arm 4p deletion syndrome and Chromosome arm 5p deletion syndrome but our case doesn’t have classical findings of these syndromes and fit only in Goldenhar syndrome phenotype. Both laboratorial and image tests are important for the diagnosis, once they are directly related to provoked alterations. The X-ray of the zigomatic bones shows a macroscopic deficiency of bone symmetry development.

Also a possibility of agenesia of these bones exists, with defect of fusing of the zigomatic arc and agenesia of the palatine bones. Palatine cleft must radiographically be observed. Ophthalmological and otorhinolaryngological examinations are also important for the final diagnosis [22].

Table-2: Comparatives studies.

| Name of the authors | Year of the study | Clinical Features |
|---------------------|-------------------|-------------------|
| Our index case      | 2020              | Limbal dermoid, Preauricular skin tags, Unilateral facial hypoplasia, Blind fistula in front of preauricular tag on one side. |
| Vasudev et al [23] | 2005              | Reported a case with juvenile glaucoma in Turner’s syndrome, along with loss of vision in one eye, preauricular appendages, absence of uterus and right kidney. |
| Sharma et al [6]   | 2006              | Reported a patient with polyductyly hand, facial asymmetry; hypoplastic maxilla, LMN facial palsy, dysmorphic ear, slightly narrowed EAC, conductive hearing loss ear, short neck, shortened sternocleidomastoid, divarication of recti, Pilonidal dimple. Macrostomia was present. There was elevation of scapula and mild scoliosis. Presence of epicanthal folds and microphthalmia. |
| Mahore et al [5]   | 2010              | Lower motor neuron facial nerve paresis, bilateral microtia, inferiorly situated ears, torticollis, left hemifacial hypoplasia. Ectopic kidneys, |

Stringer et al [24], reported portal vein cavernoma in association with Goldenhar syndrome. They presented 3 cases with Goldenhar syndrome and portal vein cavernoma. Maan and others [25] reported a case of two siblings with Goldenhar syndrome. They presented with clinical features suggestive of Goldenhar syndrome with no systemic abnormality. Gajre et al [26] reported Goldenhar in association with agenesis of septum pellucidum.

Vinay and others [4] reported Goldenhar syndrome based on clinical and radiographic findings with no systemic involvement.

**Conclusion**

Severe cases of GS can affect the routine and social life of the patient. Early detection can help avoid complications at a later stage of life. Such patients will have an increased risk for psychosocial difficulties.

The study of this condition is still controversial because the symptoms and the physical features may vary greatly in range and severity from case to case.

**Declaration of patient consent:** The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published, and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.
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