Case Report

Goldenhar Syndrome in a 6-Year-Old Patient: a Case Report and Review of Literature

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KEY WORDS
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ABSTRACT

Goldenhar syndrome (GHS) is a complex syndrome characterized by relation of mandibular hypoplasia, abnormality of the ear, ocular dermoid and vertebral disorders and hemi facial macrosomia. Treatment protocol depends on the patient's age and systemic clinical presentations, with a multidisciplinary method often being required. This case report describes a typical 6-year-old female patient who presented to the Department of Pediatric Dentistry, Faculty of Dentistry, University of Medical Sciences, Kerman, Iran with mandibular hypoplasia, facial asymmetry, ear tags and ocular dermoid after plastic surgery. Diagnosis was based on clinical aspects, radiology and laboratory findings. GHS is a developmental complaint that can disturb many aspects of the patient's life; therefore, immediate treatment from birth is necessary.

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Introduction

Goldenhar syndrome (GHS), facio-auriculo-vertebral dysplasia or oculo-auriculo-vertebral syndrome, first reported in 1981 by German physician Carl Ferdinand Von Arlt [1]. In 1952, Goldenhar classified its clinical variations [1]. This is a rare growing defect. MSX homeobox genes play a central role in pathogenesis. GHS incidence is between 1:3500 and 1:5600. Male to female proportion is 3 to 2. In 85% of patients, only one side of face is affected, right side involvement is more common [1]. In 10-33% of cases, the involvement is bilateral. Most cases are infrequent. Multifactorial, autosomal dominant and autosomal recessive are the methods of heritage [2].

Precise etiology is yet unknown. First and second bronchial arches are implicated in GHS. The exposure to synthetic drugs or different viruses during pregnancy is expected as the etiology of GHS. Development of this syndrome is related to intake of some drugs, such as cocaine, thalidomide, tamoxifen, and retinoic acid by mother in gestation period. Maternal diabetes, influenza, and rubella have also been suggested as the causative factor [3].

The diagnosis of GHS must be based on radiologic, laboratory results and the clinical findings [3]. In a classic GHS, characteristic clinical findings include eyes anomalies, ears abnormalities, facial defects, heart syndromes, kidney and gastrointestinal defects, trachea and lungs malformations, central nervous system (CNS) involvement, dental and oral problems, and skeletal alterations.

The eyes anomalies include colomas of the iris, upper eyelid, and retina. The other eye malformations are microphthalmia, astigmatism, cataracts, and blepharophimosis. Epidermoid tumors present in 35% of patients, which 50% are unilateral and 25% are bilateral. These tumors are ovoid with color of yellowish or pinkish white. Their size is different from 8-10 mm. They have commonly fine hairs and their surfaces are smooth [4]. The ears abnormalities include blind fistulas or preauricular skin tags. Other ear malformations are aplasia and atresia of the external auditory meatus. The

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GHS with hereditary deafness was observed in 1 to 1000 children [5]. The facial defect includes unilateral facial hypoplasia. In few patients, mild pneumatization of the mastoid part can be observed. Hypoplasia of the mandibular ramus and condyle may cause a reduction in the size of temporal and malar bones. The heart problems include ventricular septal defects and tetralogy of Fallot with or without right aortic arch. The hypoplasia of the external carotid artery and tubular hypoplasia of the aortic arch are also reported [6].

The kidney and gastrointestinal defects include absence of kidney or kidney with double ureters, impaired blood supply to the kidney, and hydronephrosis [7].

In trachea and lungs malformations, the tracheoesophageal fistula is predominant. Pulmonary malformations vary from incomplete lobulation, hypoplasia to complete agenesis [7]. Concerning CNS involvement, mental retardation is observed. Seventh cranial nerve is involved and unilateral aplasia of the trigeminal nuclei and trigeminal anesthesia is reported [7].

The oral manifestations of GHS include cleft lip and palate, unilateral tongue hypoplasia, hypoplasia of the maxillary and mandibular arches, micrognathia, gingival hypertrophy, micrognathia, delayed tooth development, supernumerary teeth, enamel and dentin abnormalities are the main disorders [8-9].

Considering craniofacial abnormalities, skull anomalies like microcephaly and dolichocephaly have been detected. On the affected part, facial vertical and anteroposterior dimensions are reduced. Cervical vertebral unions may happen in 60% of cases. It is reported that spina bifida, hemi vertebrae, butterfly, Klippel- Feil anomaly, occur in most of the patients [3].

Lisbôa *et al.* [10] stated when there are two or more diagnostic features in the oro-cranium facial, ocular, auricular and vertebral areas, GHS is definitive. It is reported that at least two of the following findings must be present for diagnosis of GHS including unilateral micrognatia, unilateral mandibular hypoplasia, epibulbardermoid cysts or vertebral malformations [11-12]. The present study reports a case of GHS in a 6-year-old female, with no family history; where about some of the classic features of the syndrome were present. Early diagnosis and management of GHS by pediatric dentists can have a specific impact on the health of these children.

Case Report

A 6-year-old girl was referred to the Department of Pediatric Dentistry, Faculty of Dentistry, University of Medical Sciences, Kerman, Iran with the chief complaint of pain in tooth #51 and #61. Her mother had a full-term normal delivery and there was history of kidney stone in the third month of pregnancy and because of that, she took Rowatinex capsule for a week, 3 times a day before meal.

The age of the father and mother was respectively 26 and 28 years at pregnancy. There was no history of genetic or dental anomalies in the familial history. The parents had not the consanguineous marriage. The child had been born by natural birth and was the first child of the family. The child's height was normal but her weight was under normal curve. The patient had normal skin and hair. The girl had a younger brother with no sign of congenital anomalies.

On general examination, she was conscious and had normal learning skills. Vital signs were within normal limits. On extra oral examination, the patient had obvious left mandible hypoplasia with the chin slightly deflected to the affected side. Facial profile was convex (Figure 1a and b). Ear tags have been removed surgically when the child was 2 years old.

Figure 2 shows the post-surgical scars resulting from removal of ear tags and atresia of external auditory meatus after surgery. Ocular changes show dermoids in the conjunctiva of left eye; these dermoids were particularly large and interfere with vision, so they were surgically removed when she was 3 years old (Figure 3).

The results of complete blood count (CBC), alkaline phosphatase, Ca, P, ferritin and fasting blood sugar (FBS) tests were within normal range. The pretreatment panoramic view (Figure 4a) is not obvious as the patient was very uncooperative.

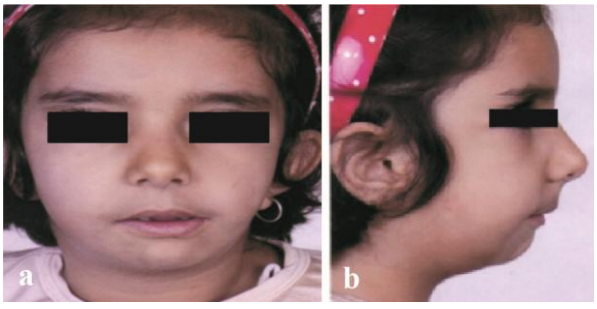

Figure 1a: Frontal view demonstrating unilateral deviation of mandible and left eye dermoid and **b:** Front view demonstrating convexity of the face

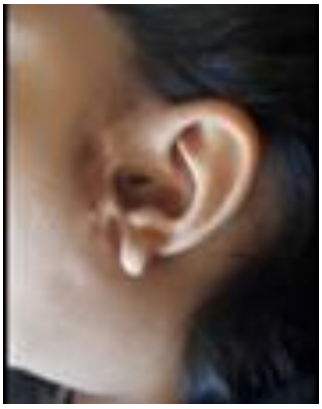

Figure 2: Scars resulting from surgical removal of ear tags and atresia of external auditory meatus

The post treatment view has been taken about one year later when the child was 7 years and more cooperative (Figure 4b). In post- treatment panoramic radiography, sequence of teeth eruption was normal, most of teeth germs were in developing phase, but the development of tooth bud of second premolar on the left mandible has not been started yet. Lack of development of the left ramus of mandible, imperfect development of the left coronoid process and condyle, lack of temporomandibular joint development, incomplete development and hypoplasia of zygomatic bone, maxillary zygomatic arc and ear bones on the same side were detected (Figure 4a and b).

Periapical radiographs show anterior mandibular and maxillary teeth before extraction (Figure 5a and b).

Intraoral examinations did not show any oral lesions. Examination of the teeth revealed deep caries of the deciduous teeth on the maxillary and mandibular teeth #51, #53, #61, #63, #74 and, #85. The oral hygiene was fair and periodontal tissues had a natural color and consistency (Figure 6a and b). The maxillary arch was normal, but the mandibular arch was asymmetric. The midline was off to the right side. The overjet was reverse. Canine relationship was class III on the both sides (Figure 7).

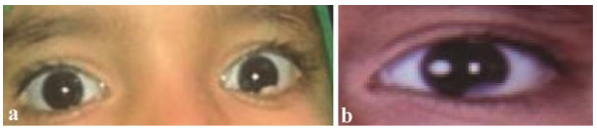

Figure 3: View demonstrating left eye dermoid **a:** before and **b:** after surgery

The primary teeth #51, # 61, #71, #72, #81 and #82 on the maxilla and mandibular arch were extracted due to the pain and exposed roots. The teeth #52, #54, #62, #64 on the maxillary arch and #75, #84 and #85 on the mandibular arch were extracted. Pulpectomy treatment with Metapex was done for teeth #53 and #63, and then restored with composite buildup technique. The tooth #73 was veneered with composite. Pulpectomy treatment with zinc oxide eugenol (ZOE) and placement of stainless steel crown (SSC) was undertaken for the teeth #55, #65 and #74. Ultimately, a Hollywood prosthetic appliance and a removable acrylic appliance were fabricated to upper and lower arch respectively in order to provide esthetic and chewing function until adolescent stage (Figure 8).

Other body organs are still under follow up. Cervical and lumbar vertebrae and kidneys show no problems in computed tomography (CT) scan imaging. Other bones are also normal in image (Figure 9). Hearing of child is normal but she is under precise monitoring of specialist. Oral hygiene instructions and dietary counseling were performed. The patient was kept under follow up visits every 6 months. A total of 5 ml whole blood from patient brachial vein in tubes containing 200µl of ethylene diamine tetra-acetic acid (EDTA) were collected, genomic DNA was isolated from leukocytes of the whole blood using salt-saturation method [13].

Discussion

GHS is a rare hereditary disorder with unknown etiology and is described as a triad of ocular dermoids, accessory

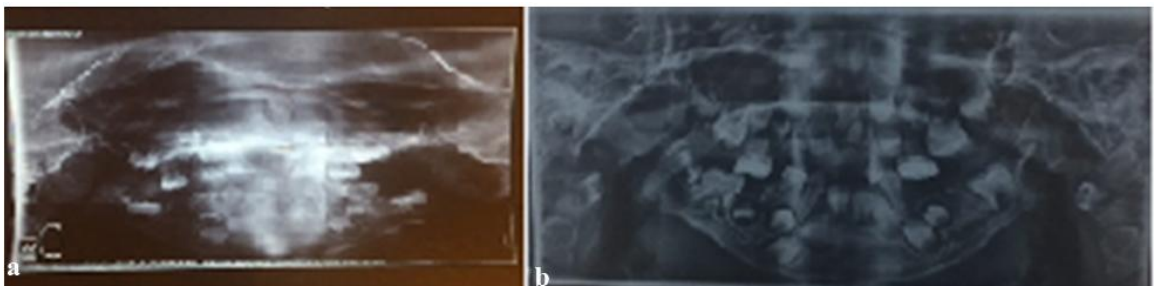

Figure 4: Panoramic radiograph reveals lack of development of mandible, zygomatic bone, zygomatic arc **a:** Pretreatment panoramic radiograph and **b:** Post treatment radiograph revealed under developed bone ears

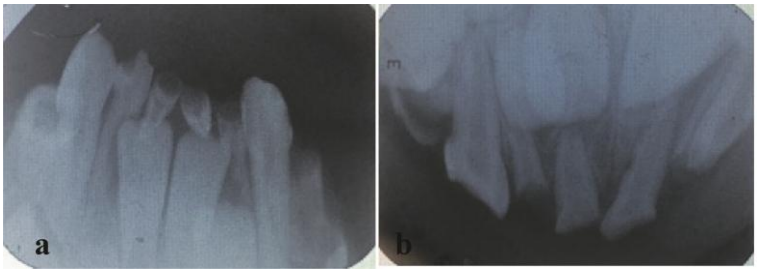

Figure 5a: Anterior mandibular periapical radiography and **b:** Anterior maxillary periapical radiography

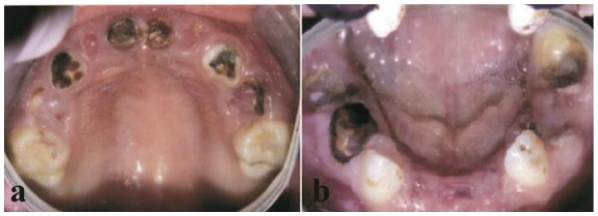

Figure 6a: Oclussal view of upper jaw showing deep caries and **b:** Oclussal view of lower jaw showing deep caries

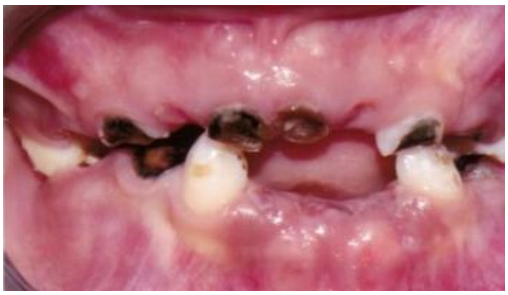

Figure 7: Class III relationship of canines in left and right side

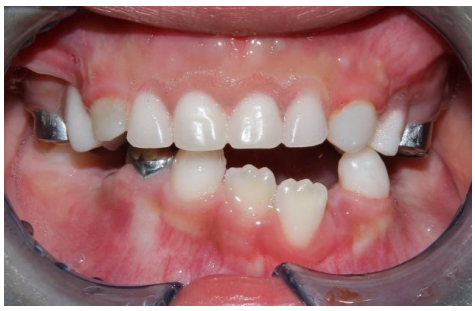

Figure 8: A Hollywood prosthetic appliance and a removable acrylic appliance fabricate to upper and lower arch

tragic and mandibular hypoplasia. This syndrome is different in severity in each patient [14-15]. Macrostomia forms in the second month of embryonic development, which is usually related to skin tags and pits between tragus and the comer of the mouth [16]. This syndrome is characterized by various anomalies affecting the first and second bronchial arches of the first pharyngeal pouch, the primordia of the temporal bone and the first branchial cleft [8, 17]. The occurrence of this syndrome is before the end of 7th or 8th week of embryonic life [18].

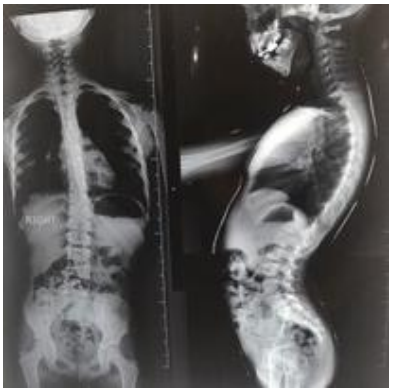

Figure 9: Frontal and lateral view of kidneys, cervical and lumbar spines in cervicothoracodorsolumbar radiography

Numerous possibilities have been proposed to explain the etiology of this syndrome, for example, Baum and Feingold [19] and De Golovine *et al.* [20] stated that GHS might be a sporadic anomaly that occurs early in embryogenesis, which is showed reduced penetrance, somatic mosaicism or epigenetic changes. Moreover, there are familial cases in families with history of consanguineous marriage [9]. Some etiologic factors consist of maternal medication use especially in relation with smoking in the first 2.5 months of gestation, primidone, retinoic acid and thalidomide and maternal diabetes [21]. There is no chromosomal or genetic test to diagnosis GHS. A specialist makes a diagnosis by identifying the symptoms of GHS [22]. When it is identified, the child usually needs to have further tests, such as hearing and vision tests and the examination of heart or kidney. A clinician may order ultrasound imaging for these checkups or X-ray of the spine to check for problems with vertebrae [22]. A total of 80 to 99% of patients with GHS have facial asymmetry, hearing impairment, hypoplasia of the maxilla, malar flattening, preauricular skin tag, which are diagnostic for GHS [23]. These features were observed in our presented case. In the present case, the mother took Rowatinex capsule for a week, 3 times a day in the third month of

pregnancy for her kidney stone. This drug may be the cause of this syndrome; however, it has not been mentioned in the literatures up to now.

The great prevalence of hereditary heart syndromes in GHS was reported by Friedman and Saraclar [24]. Abe *et al.* [25] described a case of GHS related to cardiac disorders such as single ventricle and patent ductus arteriosus. Mahore *et al.* [26] reported a patient of GHS with crossed ectopic kidneys in relation with other clinical findings. Our patient did not have a history of kidney and heart disease. The effect of GHS on developing of the patient is clear. Breathing problems are due to lack of development of the jaws, which need multidisciplinary approach in these patients [27].

Damage of differentiating tissue in the region of the jaw and ear by hematoma will produce arch disorder. Severity of the dysplasia is related to the extent of local damage. GHS is associated with sensorineural loss of hearing, vertebral anomalies, central nervous system, and renal malformations. Other syndromes related to multiple preauricular tragi are Treacher-Collins syndrome, Wildervanck syndrome, and Townes-Brocks anomaly [28]. Hypoplasia of maxilla and mandible are associated with Treacher Collins anomaly [15].

The treatment for GHS depends on age and systemic relations. Timing of the reconstruction has a major role in the treatment. In uncomplicated cases, cosmetic is a basic concern. Cleft repair, corrections of colobomas, ear anomalies at the age of 6 to 8 years and removal of dermoids and preauricular tags at the age of 5 are principal reconstructions [29]. In our case, preauricular tags of left ear were surgically reconstructed at age of five. In patients with mandibular hypoplasia, rib grafts can be used and a bone distraction device can extend an underdeveloped maxilla. Jaw reconstruction surgeries can be done in the early teens, in patients with milder involvement, epibulbar dermoids should be excised by surgery. Structural abnormalities of the eyes and ears are correctable by plastic surgery; in our patient helix, plastic surgery was done when she was 6 months as her mother was concerned about beauty of her ears. In uncomplicated cases, without any systemic complications, the disease prognosis is good [14, 30-31]. The complex treatment is focused on dental care, talking, hearing, prevention, and treatment of the psychosocial problems of the syndrome. In our case, due to providing esthetic and masticatory function, prosthetic devices were fabricated for upper and lower jaw until adolescent stage. Treatment needs constant follow-up and subsequently, we put our patient in 6-month follow-ups. Informed consent was obtained from the patient for publishing her clinical photography and radiography.

Conclusion

GHS is a developmental syndrome that can disturb many aspects of the patient's life. This syndrome does not have exact treatment. It needs multidisciplinary approach. In this patient, consultation with surgeon and orthodontist was performed. Distraction osteogenesis along with functional orthodontics was supposed to be used at older age. A long-term follow-up is necessary to observe the child growth.

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Conflict of Interest

The authors of this manuscript certify that they have no financial or other competing interest concerning this article.

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