Hemifacial microsomia: skeletal abnormalities evaluation using CBCT (case report)

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ABSTRACT

The article presents a case report and literature review of hemifacial microsomia with cervical vertebral anomalies. Unilateral hypoplasia of the mandible, congenital anomalies of the external ear and cervical spine pathology identified in this case are common major signs/symptoms of Goldenhar (Goldenhar-Gorlin) syndrome. Complete fusion of bodies and spinous processes of the second and third cervical vertebrae as well as atlantooccipital assimilation and anterior cleft of the atlas were also found. All abnormalities were accidentally identified and not accompanied by clinical symptoms.

CASE REPORT

CASE REPORT

An 18-year-old Caucasian male was referred by the medical board of the Military Registration and Recruitment Office to the oral and maxillofacial surgeon with the chief complaint of having facial deformity since childhood. Supposedly, unilateral (left side) mandibular hypoplasia and left and right ear skin tags were noticed at birth with no other anomalies detected. The patient underwent surgery for ear malformation at 1 year of age. Signed informed consent regarding radiological images and data publication was obtained.

Cone beam computed tomography performed on Galileos GAX5 (Germany) revealed the following findings:

- Facial skull asymmetry due to a relatively smaller size of the left half of the face mainly expressed in the region of the mandible (Figure 1).
- Elongated left styloid complex including the styloid process and ossified stylohyoid ligament measuring 41.38 mm (Figure 2).
- Shortening of the left mandibular ramus with medial and anterior shift and the condyle size reduction. Articular tubercle was located laterally from condylar head (Figure 3).
- Complete fusion of C2-C3 vertebral bodies and spinous processes; the parasagittal slit-like defect of the anterior arch of the atlas (Figure 4); atlantooccipital assimilation (fusion of the left lateral masses of the atlas with the occipital condyle (Figure 5).
- Absence of visible pathology of the external, middle and inner ear.
- Absence of the pneumatization of the mastoid processes on both sides.

DISCUSSION

Hemifacial microsomia (HFM) is an asymmetric craniofacial malformation, variably affecting structures derived from the first and second pharyngeal arches [1, 2, 3, 4]. Many terms have been used for this malformation, thus indicating a wide spectrum of anomalies observed and emphasized by the authors from various disciplines. In addition to HFM, the malformation has been called *craniofacial microsomia* (some authors believe, that currently this is the most accepted term to mention this pathology), *oculo-auriculo-vertebral dysplasia, first and second branchial arch syndrome, lateral facial dysplasia, unilateral oto-mandibular dysostosis, facio-auriculo-vertebral sequence* and *oculo-auriculo-vertebral spectrum* [5].

HFM is characterized by unilateral hypoplasia of a mandible and ear, including a shortened mandibular ramus, small glenoid fossa, malformed condyle, hypoplastic coronoid process and preauricular tags [6]. As many as 55% of patients with HFM also have extracranial anomalies including central nervous system, skeletal, cardiac, lung, gastrointestinal and kidney defects [1, 7, 8]. The reported prevalence of vertebral anomalies in HFM varied from 8% to 79% and the most often reported anomalies without the specified location were hemivertebrae, block vertebrae, scoliosis/kyphoscoliosis and spina bifida [9].

Goldenhar syndrome was considered to be a variant of HFM [4]. It was first described by the Swiss ophthalmologist Maurice Goldenhar in 1952 as a syndrome by the presence of the same classic triad of eye, ear and vertebral changes.

Etiology & demographics

The estimated prevalence of HFM ranges from 1/ 3,500 to 1/ 26,550 in live births making this malformation the second most common craniofacial abnormality after cleft lip and palate [2, 3, 10, 11]. In Europe the prevalence of oculo-auriculo-vertebral spectrum defined as microtia/ear anomalies and at least one major characteristic anomaly was 3,8 per 100 000 births [11]. The major discrepancy in the literature on the incidence of HFM may be due to the lack of information on fetal deaths and terminated pregnancies, and the inclusion or exclusion of mild or extreme cases that are given a different diagnosis [12]. The documented prevalence of vertebral anomalies in HFM varied from 8% to 79% [9].

While the majority of cases are sporadic and appear to have a multifactorial etiology, cases with chromosomal abnormalities (mainly in chromosomes 5 [5p deletion], 18 [trisomy] and 22 [22q11.2 deletion]), mosaicism and families with autosomal recessive and autosomal dominant inheritance have been reported [11, 13, 14]. Despite previous efforts to reveal a genomic etiology of Goldenhar syndrome (GS), investigators have not been able to identify a causative gene [12].

Within the environmental causes of HFM there are various risk factors associated with pregnancy, such as vasoactive medications, vaginal bleeding during the second quarter, multiple gestations, the use of assisted reproductive technology by the mother and preexisting or gestational diabetes [3].

Although the precise etiology of hemifacial microsomia is unknown, disruption of the first and second branchial arches during the first 6 weeks of gestation is thought to be causative [15].

The most plausible hypothesis on the pathogenesis of HFM is the vascular abnormality and hemorrhage theory [6]. Between 1973 and 1975, Poswillo proposed that the pathogenetic makeup of hemifacial microsomia was based on an embryonic hematoma formation arising from the anastomosis that precedes the formation of the stapedial artery [16]. Eseonu and Vieira [16] considered the severity, variation, and heterogeneity of the symptoms of hemifacial microsomia to be a direct result of the size and amount of hematoma collection and expansion, where small hematomas cause less damage than their larger counterparts in regard to branchial arch growth.

Meckel's cartilage plays a crucial role in development of the mandible and middle ear, and damage to Meckel's cartilage may secondarily lead to its abnormal development, which can partially account for the skeletal defects of HFM [6]. Direct experimental evidence, based on surgical interference of mandibular development in the chick embryo confirms the latter concept [17]. Asymmetrical perturbation of Meckel's cartilage has been shown to result in asymmetry of the mandible. This hypothesis focused mainly on the HFM-type skeletal defects and was independent of any single pathogenic factor. The perturbation of the auriculofacial cartilage model may involve either of the fundamental processes of growth and morphogenesis and can be interfered by vascular events, teratogens and genetic defects among other factors. For example, hemorrhage in the vicinity of Meckel's cartilage is responsible for the disruption of normal chondrogenesis giving rise to malformed auditory ossicles and mandible. It was also revealed that impaired secretion of vascular endothelial growth factor is responsible for the reduced blood supply to Meckel's cartilage ultimately generating mandibular hypoplasia [18].

The presence of an elongated styloid complex indicates abnormal morphogenesis of simultaneous first and second branchial arch derivatives. This justifies the use of the term "first and second branchial arch syndrome" as a synonym for Goldenhar syndrome.

The crucial role in craniofacial development is played by cranial neural crest cells (CNCCs). Given that most craniofacial structures involved in HFM are derivatives of CNCCs, direct disturbances of the migration, proliferation and differentiation of CNCCs due to chromosomal abnormalities or a single gene mutation were then proposed as a possible mechanism for HFM [19].

Vertebral anomalies may be a result of unilateral defects of formation and segmentation of primitive vertebrae at the mesenchymal stage of development or are thought to be due to

the localized failure of vascularization of the developing cartilaginous centrum [20].

Clinical & imaging findings

Reports focused mainly on the craniofacial dysmorphic features and limited attention was paid to the vertebral abnormalities in patients with Goldenhar syndrome [20].

In the present case report radiological manifestation of hemifacial macrosomia and vertebral anomalies in cervical spine were detected using CBCT. Unilateral mandibular hypoplasia, congenital anomalies of the external ear and pathology of the cervical spine identified in this case are common major findings in Goldenhar (Goldenhar-Gorlin) syndrome. By the degree of hypoplasia of the mandibular ramus and the shape and location of the articular head they correspond to Type IIB of hemifacial microsomia according to the classification of Pruzansky-Kaban [21] shown in Table 1. Nevertheless, the patient could function with both temporomandibular joints and did not complain of any deficiency in chewing.

Vertebral anomalies in HFM are most common in the cervical spine, followed by the thoracic spine and ribs [9]. In our case it was possible to observe only the cervical part of the vertebral column where a number of radiographic signs were detected including complete fusion of C2-C3 vertebral bodies and spinous processes, atlantooccipital assimilation, the parasagittal slit-like defect of the anterior arch of atlas and fusion of C2 and C3 spinous processes. All these abnormalities were identified accidentally and were not accompanied by clinical symptoms.

Treatment & Prognosis

Treatment of HFM varies with age and according to systemic associations [22]. Reconstructive surgery is usually necessary in these patients. The treatment seeks to improve functionality along with optimum facial symmetry in order to increase the size of the affected mandibular side and its associated soft tissue and create a joint simulating the temporomandibular joint (TMJ) in cases where it is absent [3]. Patients with mandibular hypoplasia can be submitted to reconstructive surgery using rib bone grafts [22]. Mild cases can be potentially managed with orthodontic appliances alone [23]. Orthodontic treatment usually involves the use of a specialized type of functional appliance, hybrid appliances.

Depending on the individual's stage of development and severity of the vertebral defect different options exist for treatment. In order to prevent severe scoliosis it is best to take action early. Non-surgical options include bracing and physical therapy [15]. Depending on the defect surgical intervention such as spinal fusion or stabilizing growing rods may be necessary [24]. Prognosis is guarded in cases with systemic involvement, but is good in otherwise uncomplicated cases without any systemic associations [22].

Differential Diagnoses

The differential diagnosis is broad and includes other conditions in which facial asymmetry is a prominent clinical feature, for instance, like Parry Romberg syndrome (PRS) and Townes-Brocks syndrome. In Goldenhar syndrome unilateral facial asymmetry is usually seen, unlike in PRS, that condition is typically congenital and nonprogressive [25]. The majority of individuals with Goldenhar syndrome do not have such clinical manifestations as upper-limb or anal malformations which are typical for Townes-Brocks syndrome [26]. Vertebral abnormalities have been not included as a precise index to differentiate between these clinical entities from Goldenhar syndrome [20].

Table 2 provides a comparison of HFM (Goldenhar syndrome) with similar disorders [12].

Brachio-oto-rental syndrome, mandibulofacial dysostosis (Treacher Collins syndrome), maxillofacial dysostosis, Nager acrofacial dysostosis, and axial mesodermal dysplasia complex are also included in the differential diagnosis of HFM. Unlike HFM, individuals with the conditions listed above typically have symmetric facial malformations. Additional information about the phenotypic differences between HFM and rare genetic disorders could be found in the review published by Heike et al. [27].

TEACHING POINT

Serious structural abnormalities of the temporomandibular joint and the cervical spine can remain compensated for a long time not forcing a patient to seek for medical care. Abnormalities of the first and second branchial arches are often combined with a congenital defect of the cervical spine and can be detected using cone beam computed tomography.

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FIGURES

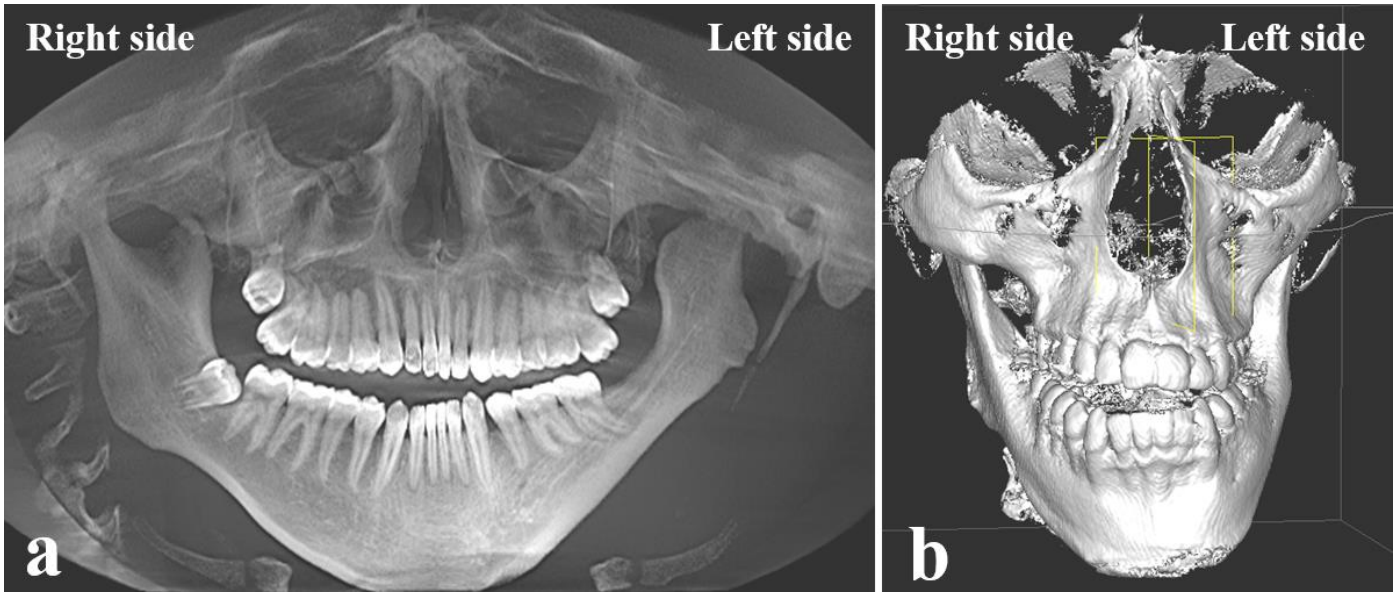

Figure 1: 18-year-old male adolescent with hemifacial microsomia

Findings: Facial skull asymmetry due to unilateral hypoplasia of the mandible (the left side is hypoplastic).

Technique: Cone beam computed tomography - panoramic view (a) and cone beam computed tomography volumetric rendering technique image (b), 85 kV; tube current 5-7 mA; acquisition period 14 s; effective radiation time 2-6 s; voxel size 0.3 × 0.3 × 0.3 mm

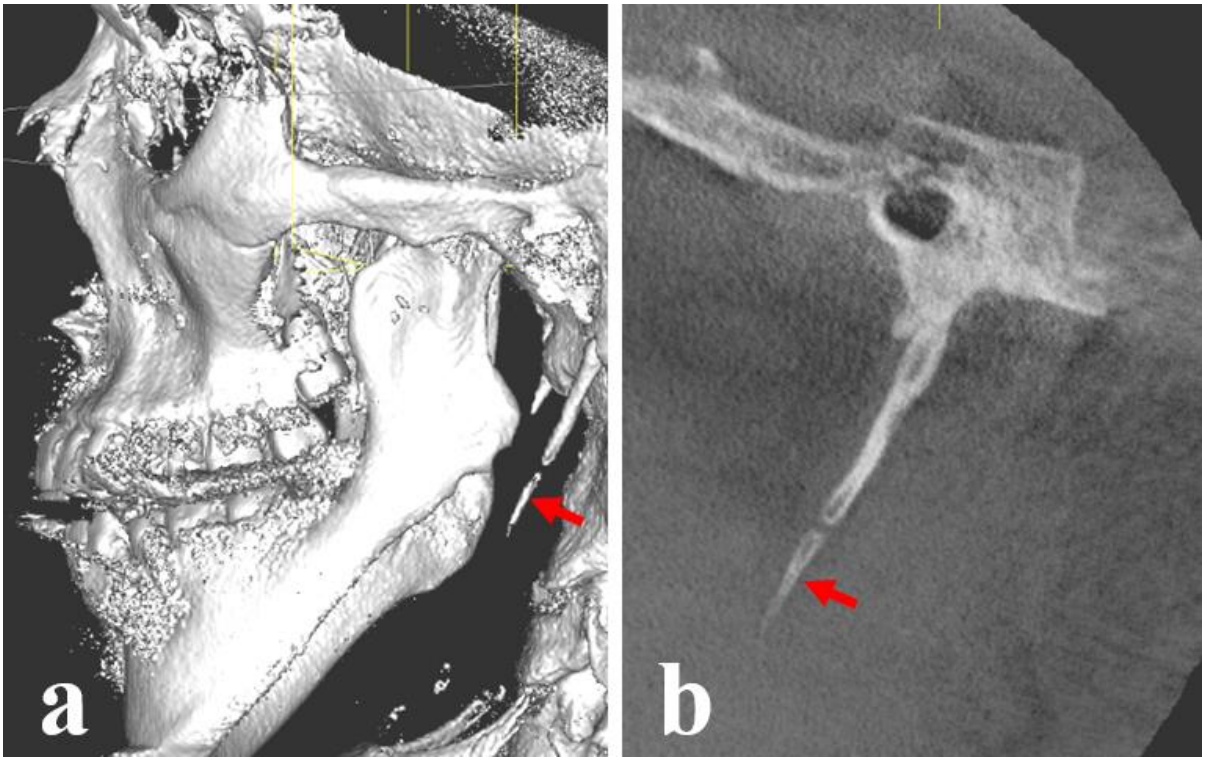

Figure 2: 18-year-old male adolescent with hemifacial microsomia

Findings: Calcified left stylohyoid ligament (red arrow).

Technique: Cone beam computed tomography - 3D reconstruction (a) and CBCT sagittal slice by drawing perpendicular lines to the long axis of the stylohyoid complex (b), 85 kV; tube current 5-7 mA; acquisition period 14 s; effective radiation time 2-6 s; voxel size 0.3 × 0.3 × 0.3 mm

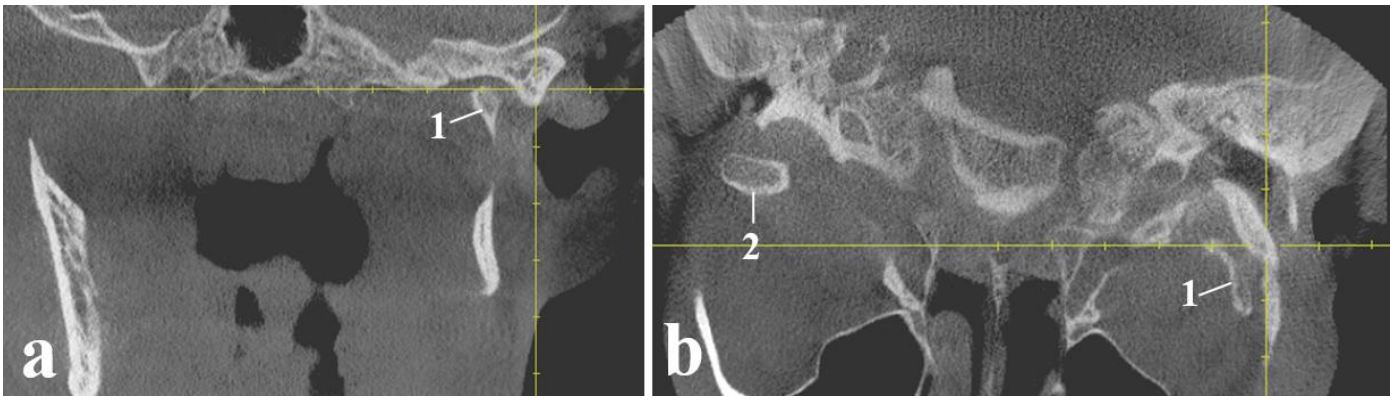

Figure 3: 18-year-old male adolescent with hemifacial microsomia

Findings: CBCT is showing relationships of articular surfaces of left temporomandibular joint. Yellow crosshair represents the apex of the articular tubercle located laterally from the head of mandible. 1 - the left head of the mandible; 2 - the right head of the mandible.

Technique: Cone beam computed tomography - coronal (a) and axial (b) view; 85 kV; tube current 5-7 mA; acquisition period 14 s; effective radiation time 2-6 s; voxel size 0.3 × 0.3 × 0.3 mm

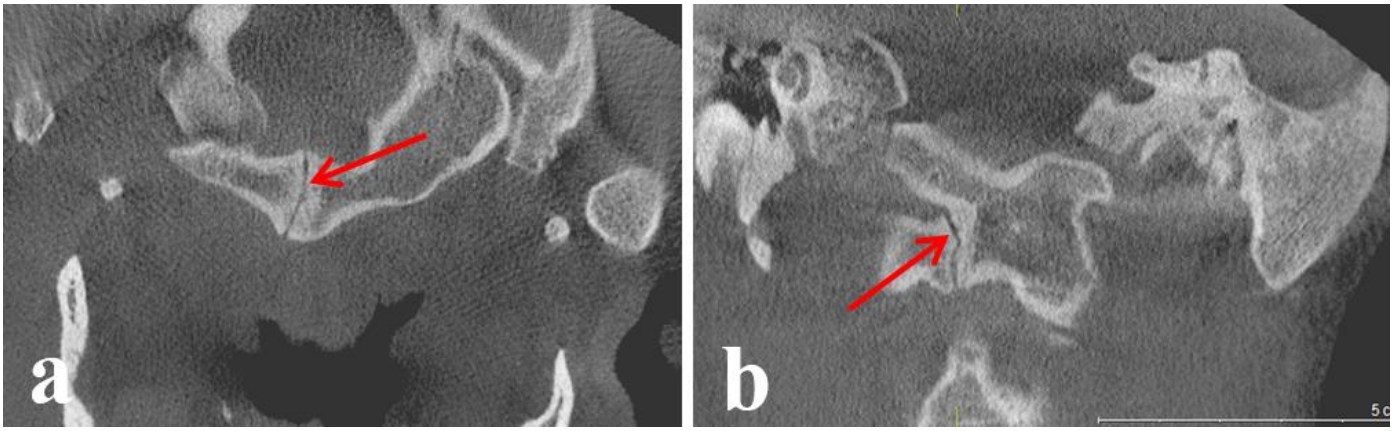

Figure 4: 18-year-old male adolescent with hemifacial microsomia

Findings: Parasagittal slit-like defect of the anterior arch on the right (red arrow).

Technique: Cone beam computed tomography - axial (a) and coronal (b) view; 85 kV; tube current 5-7 mA; acquisition period 14 s; effective radiation time 2-6 s; voxel size 0.3 × 0.3 × 0.3 mm

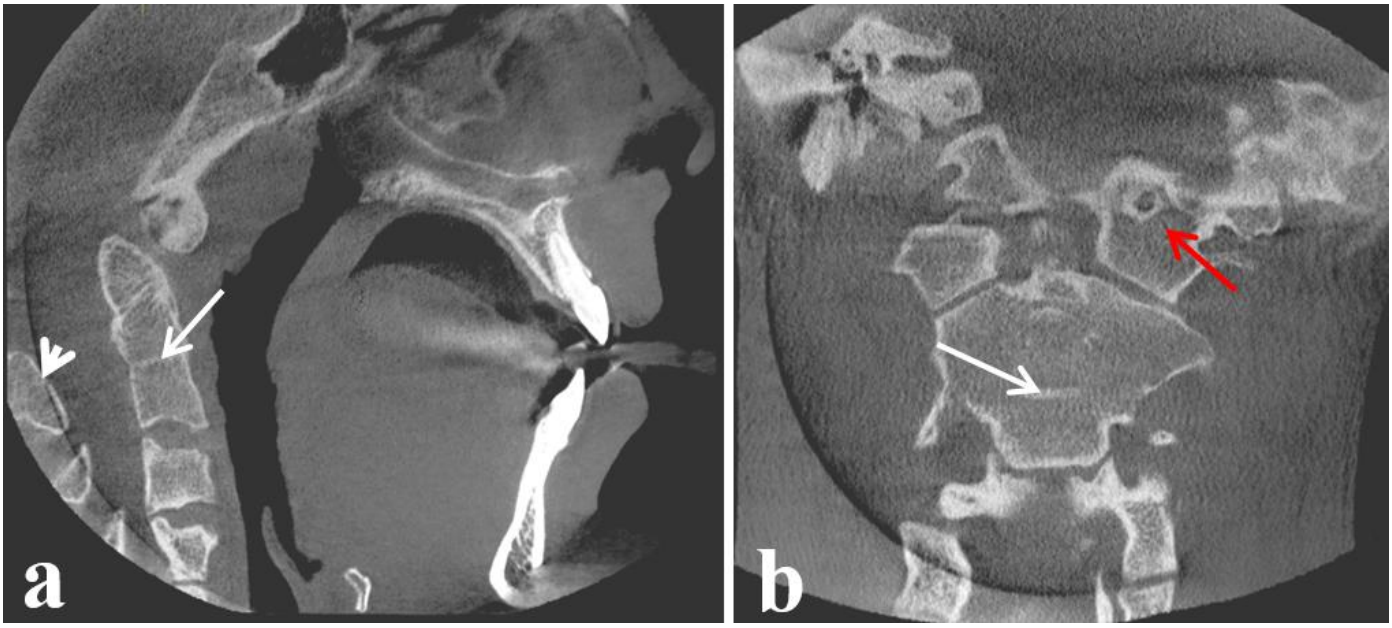

Figure 5: 18-year-old male adolescent with hemifacial microsomia

Findings: Complete fusion of C2-C3 vertebral bodies and spinous processes (white arrows indicate the site of the fusion of the vertebral bodies, white arrowhead shows the fusion of C2-C3 spinous processes) and atlantooccipital fusion (the red arrow).

Technique: Cone beam computed tomography - sagittal (a) and coronal (b) view; 85 kV; tube current 5-7 mA; acquisition period 14 s; effective radiation time 2-6 s; voxel size 0.3 × 0.3 × 0.3 mm

Type	Anatomy of the mandible and temporomandibular joint
I	Small mandible
IIA	Short mandibular ramus of abnormal shape; glenoid fossa in satisfactory position
IIB	TMJ abnormally placed inferiorly, medially and anteriorly
III	Absent TMJ

Table 1: Classification of the skeletal deformity by Pruzansky modified by Kaban [21]

	Goldenhar syndrome	**Hemifacial microsomia**	**Treacher Collins syndrome**	**Branchio-oto-renal syndrome**
Incidence	1/3,500–1/26,550	1/3,500–1/26,550	1/50,000	1/40,000
Etiology	Multifactorial	Multifactorial	AD: loss of function mutation of *TCOF1* gene on chromosome 5	AD: -*EYA1*: most frequently mutated -*SIX1* and *SIX5*mutations reported
Unilateral or bilateral facial deformity	Usually unilateral	Usually unilateral	Usually bilateral	Not applicable
Type of hearing loss	Usually conductive	Usually conductive	Usually conductive	Conductive, sensorineural, or mixed
Ocular anomalies	Epibulbar dermoids, upper lid colobomas, microphthalmia, anophthalmia, palpebral ptosis	Anomalies similar to GS but without epibulbar dermoids	Lower lid colobomas, absent medial lower eyelashes, downward slanting of palpebral fissures, affected vision, skeletal dysmorphism of the orbits	None
Auricular anomalies	Microtia, preauricular skin tags, atresia/stenosis of external auditory canal, absence of auricle, anotia, preauricular pits/sinus, malformation of middle ear and inner ear are less common	Anomalies similar to GS, and occur in 65–99% of patients	Deformed external ear, microtia or anotia, stenosis or atresia of external auditory canal, misshaped tympanic membrane	Preauricular pits (75–85% of cases), preauricular tags, lop or bat ears, microtia, atretic external auditory canal; some cases of abnormal ossicles, facial nerve, and fallopian canals; some cases of hypoplastic cochlea and absent or hypoplastic semicircular canals
Craniofacial anomalies	Mandibular hypoplasia, also mandibular ramus asymmetry, maxillary and malar hypoplasia, TMJ abnormalities, micrognathia, cleft palate with or without cleft lip	Anomalies similar to GS	Malar hypoplasia is most common, mandibular and maxillary hypoplasia, micrognathia, retrognathia, cleft palate	High arched or cleft palate, deep overbite
Other musculoskeletal anomalies	Vertebral defects, may have clubbing, polydactyly, clinodactyly, camptodactyly, or single palmar crease	No vertebral defects	Vertebral defects rare	None
Additional defining anomalies				Renal dysplasia in more than 2/3 of cases, branchial fistulae (usually bilaterally in lower part of the neck)
Associated anomalies	Cardiac, renal, genital, gastrointestinal, may have some cognitive disability	Anomalies similar to GS	Cardiac, renal, cryptorchidism, airway abnormalities	Aplasia or stenosis of the lacrimal ducts

Table 2: Differential diagnosis table for HFM (Goldenhar syndrome) [12]

ABBREVIATIONS

AD = Autosomal dominant
CBCT = Cone beam computed tomography
CFM = Craniofacial microsomia
CNCCs = Cranial neural crest cells
GS = Goldenhar syndrome
HFM = Hemifacial microsomia
TMJ = Temporomandibular joint

KEYWORDS

Hemifacial microsomia; Goldenhar (Goldenhar-Gorlin) syndrome; craniofacial microsomia; oculo-auriculo-vertebral dysplasia; first and second branchial arch syndrome; lateral facial dysplasia; unilateral oto-mandibular dysostosis; facio-auriculo-vertebral sequence; oculo-auriculo-vertebral spectrum; vertebral anomalies; temporomandibular joint abnormalities; cone beam computed tomography