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Case Report
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Hemifacial Microsomia: A Mini-Review and Case Report

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Objectives Hemifacial microsomia (HFM) is an asymmetric craniofacial malformation, which results from hypoplasia of the first and second branchial arch components and is characterized by a wide spectrum of phenotypic expressions, varying from the underdevelopment of the temporomandibular joint, mandible, facial and trigeminal nerves, masticatory muscles, ears, and hypoplastic maxillary, temporal, orbital, and zygomatic bones to conductive hearing loss due to external and middle ear deformities. Management of this developmental defect is multidisciplinary and associated with various phenotypic spectra and severities. A wide range of treatment protocols, such as surgical interventions, have been proposed, especially for mandibular hypoplasia, including rib or fibular bone grafting, distraction osteogenesis (DO), orthognathic surgery, and a combination of these procedures.
Case In this study, the treatment course and 17-year follow-up of a patient with HFM were described. The treatment included autogenous costochondral grafting, followed by full-time application of an asymmetric hybrid functional appliance, fixed orthodontic therapy, orthognathic surgery, and contour modification surgery to achieve optimal facial aesthetics.
Conclusion Patients can benefit from functional jaw orthopedics psychosocially and the consequent enhanced facial symmetry during childhood and adolescence is really advantageous.
Keywords Hemifacial microsomia; Facial asymmetry; Congenital anomalies; Unilateral hypoplasia

Introduction

Hemifacial microsomia (HFM), as the most common craniofacial birth anomaly following cleft lip and cleft palate, is one of the congenital abnormalities responsible for asymmetrical defects, with an estimated incidence of 1:3500 to 1:5600 live births. [1, 2] This anomaly appears to be less common in females than males (2:3) and is unilateral in 70% of cases. The right side is more commonly affected than the left side, and if it is bilateral (10% of cases), one side is more affected than the other. [3] Strong evidence suggests that genetics plays an important role in the multifactorial etiopathogenesis of HFM, and the majority of cases are sporadic, with no positive familial history. [2, 4]

Considering the wide spectrum of phenotypic expressions related to disturbed embryonic development of the first and second pharyngeal arches, patients often have various diagnoses, such as Goldenhar syndrome (with a triad of epibulbar dermoids or choristomas, preauricular skin appendages, and mandibular facial dysplasia), oculo-auriculo-vertebral spectrum, craniofacial microsomia, and some other disorders, such as lateral facial dysplasia, unilateral otomandibular dysostosis, first and second branchial arch syndrome, and facio-auriculo-vertebral sequence. [2, 4-8]

HFM is commonly characterized by the congenital underdevelopment of the temporomandibular joint (TMJ) (i.e., small glenoid fossa, malformed condyle, and ankylosis), mandible (i.e., shortened mandibular corpus and ramus, abnormal canting, and deviated chin), facial and masticatory muscles, trigeminal, facial, and hypoglossal nerves and the surrounding soft tissues, macrostomia, and ocular deformities (strabismus, anophthalmia, microphthalmia, eye asymmetry, exophthalmia, and upper eyelid coloboma). [3] Moreover, it is associated with the underdevelopment of the maxillary, temporal, zygomatic, and orbital bones, preauricular tags, microtia, and conductive hearing loss due to external and middle ear deformities (e.g., incus, malleus, and tympanic bone) with various severities, which result in facial asymmetry and adversely affect the patient's social and functional well-being. [2, 5-7, 9-11] Extracranial manifestations are primarily found in the kidneys, lungs, heart, gastrointestinal and skeletal systems, and cervical spine. [7, 8]

The prevalence of vertebral anomalies (hemivertebrae, block vertebrae, scoliosis/kyphoscoliosis, and spina bifida, mostly in the cervical and thoracic spines) ranges from 8% to 79% in HFM patients. [6, 7] Cranial nerve deficits can be found in nearly 25% of all HFM patients. The marginal mandibular branch of the facial nerve is most commonly affected, followed by the frontalis muscle dysfunction. [12] Retrusion and vertical morphology of both mandible and maxilla are more common in HFM patients compared to the general population. Besides the skeletal involvement of the jaws, malformation can lead to some problems in dentition, such as impaction, delayed eruption, agenesis, hypoplasia, microdontia, malocclusions, and delayed tooth development, with most alterations in posterior teeth, depending on the extent of mandibular deformity. Besides, some patients have cleft lip and/or cleft palate, velopharyngeal insufficiency, and obstructive sleep apnea. [2, 4, 7, 10]

Although the etiology of HFM is heterogeneous and has not been precisely identified, disruption of the first and

second branchial arches during the first six weeks of gestation and early loss of neural crest cells seem to be influential. [5, 6, 13] Different theories have been proposed regarding the pathogenesis of HFM, including the hemorrhage theory, which is assumed to be the most plausible one. [5, 6] Poswillo suggested that the cause of HFM is vascular disruption, causing hematoma during the embryologic development of the stapedial artery, accompanied by abnormal development of the first and second branchial arches. Another concept based on experimental evidence proposes that impaired secretion of vascular endothelial growth factor decreases the blood supply to the Meckel's cartilage, which plays a crucial role in the development of the mandible and middle ear. [6]

The environmental risk factors associated with pregnancy include drugs and chemicals, such as retinoic acid, triazene, primidone, thalidomide exposure, vasoactive medications (pseudoephedrine, phenylpropanolamine, aspirin, and ibuprofen), and cigarette smoking in the first trimester, vaginal bleeding in the second trimester, multiple gestations, use of assisted reproductive technology (age of the parents and donor may be cofounders), excessive alcohol consumption by the mother, and preexisting or gestational diabetes. [2, 4, 6, 7]

Regarding the role of genetics, although most cases are sporadic, some patients show an autosomal dominant genetic component (associated with chromosome 14), an autosomal recessive component, and alterations in chromosome 5 (5p deletion), chromosome 18 (trisomy), and chromosome 22 (22q11.2 deletion). [2]

Numerous classification systems have been proposed for HFM, based on clinical manifestations. [8] One of the most versatile, comprehensive, and objective classifications is the orbit, mandible and TMJ, ear, nerve, soft tissue deficiency (OMENS) classification proposed by Vento et al. (1999). [4, 5, 11] Management of this developmental defect is multidisciplinary, and given the variety of phenotypic spectra and severities, a wide range of treatment protocols, especially for mandibular hypoplasia, have been proposed, such as different surgical interventions, including rib or fibular bone grafting, distraction osteogenesis (DO), orthognathic surgery, and a combination of these procedures.

Generally, the type and scheduling of treatment depend on the patient's age and the severity of condition. Age can be divided into three periods: (1) neonatal, (2) childhood, and (3) skeletal maturity. [15] Vital functions should be assessed immediately after birth. In case of severe airway obstruction and dysphagia, instant tracheostomy and insertion of a gastrostomy feeding tube are essential. [15] Mild cases of mandibular hypoplasia can be potentially managed with orthodontic hybrid functional appliances during childhood. [6, 15] For severely hypoplastic mandibles (Pruzansky type III), costochondral rib graft is highly recommended in the age range of 6-12 years after eruption of the lower first molar. However, when the rib graft growth is insufficient, subsequent distraction of the construct should be performed within the mandible or rib graft, not at the rib graft-mandible interface. [16]

Although the psychological value of early DO (for grade I and II mandibular hypoplasia or after costochondral graft for grade III) must be considered, in the absence of major functional problems, such as airway obstruction, the advantages of mandibular DO remain debated. It has been also found that before skeletal maturity, the severity of hypoplasia may increase over time. [17] To correct skeletal deformities in most mature HFM patients, conventional three-phase management, consisting of presurgical orthodontics, orthognathic surgery, and postsurgical orthodontics, is the treatment of choice. [18]

The present study aimed to describe the treatment course and long-term follow-up of an HFM patient with right-sided mandibular hypoplasia and ear malformation.

Case Report

Patient's history

A five-year-old Iranian girl was referred to the Orthodontic Department of Shahid Beheshti Dental School (Tehran, Iran) according to the oral and maxillofacial surgeon's suggestion, with complaints of lower face asymmetry since the first months after birth (when she was six months old, as her mother recalled). The patient's mother reported a history of consanguineous marriage in the past two generations of her family (her parents were first cousins), as well as cesarean section. Her mother reported taking isoxsuprine since the second month of gestation to prevent premature labor, with adverse effects, such as severe palpitation. The patient had no familial history of specific diseases or syndromes, and no family member had a similar condition.

The ear, nose, and throat (ENT) consultation and audiogram performed at the age of four years revealed complete hearing loss in the right side and normal hearing of the left ear. No other disorders were identified in the medical examination, including cardiac evaluation using electrocardiography (ECG), assessment of kidneys and other internal organs via ultrasound, and blood sampling for autoimmune diseases or gene mutations. The patient had undergone surgery for autogenous costochondral grafting from the fifth rib to reconstruct the right mandibular condyle and ramus two months earlier; the operation was performed in October 2005 (Figure 1).

Examination

Based on the general examination, weight and height gain occurred at a slower rate compared to her peers, and she had no learning difficulties. The extraoral examination

revealed evident facial asymmetry, deviation of the lower jaw and chin toward the right side, convex profile, tense lips, obtuse nasolabial angle, absent mentolabial sulcus, incompetent lips at rest, unilateral macrostomia, asymmetric smile due to the upward inclination of lips to the right, skin tags, and grade III microtia of the right ear. Additionally, a smaller and higher right eye, less prominence of the right cheek, and elevated level of the right ala were evident.

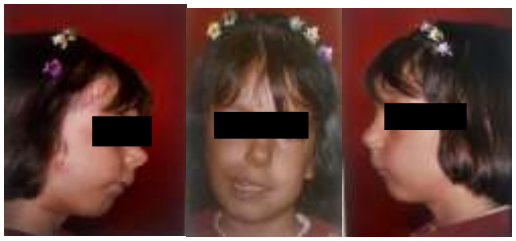

Figure 1: The patient's images six months after the costochondral graft

To evaluate the facial nerve, the patient was asked to raise her eyebrows, close her eyes and keep them closed against resistance, puff out her cheeks, and reveal her teeth. There was no evidence of right-sided facial paralysis. By asking the patient to stick out her tongue, the normality of hypoglossal nerve was ensured, as no deviation to either side was observed. On palpation, the right masseter muscle was deficient. The sternocleidomastoid muscle was prominent due to a depression, which was a scar from a previous costochondral graft surgery. The dental midlines were deviated to the right, and the lower midline shift was more than the upper midline shift.

The intraoral examination indicated a mesial step relationship in the primary molars in the left posterior region, a high-arched palate, and decreased overjet and anterolateral open bite and crossbite on the right side. There was a marked transverse canting of the maxillary occlusal plane upward toward the right side and clear yaw rotation of the mandible. In the mandibular right quadrant, primary molars were infra-positioned, there was increased mobility, and the gingiva was recessed and inflamed. The tongue size, position, and range of movement were normal.

In the functional analysis, an anterolateral tongue thrust swallowing pattern, combined oronasal respiration, decreased maximum mouth opening (23 mm) with deviation to the right on opening, and restricted excursive movement to the left side were observed. The panoramic radiograph revealed the proximity of surgical screws to the lower right first and second permanent molar follicles and severe root resorption of the adjacent primary molars. There was evident crowding in the area of succedaneous tooth buds in the deficient side of the mandible. The developmental stage of lower permanent teeth, except for the first molars, was identical in the two quadrants (Figure 2).

Figure 2: The costochondral graft fixed by rigid internal fixation (RIF)

On lateral cephalograms, severe mandibular deficiency (ANB=15°, Witt's=16 mm) and a vertical growth pattern were observed (Figure 2). The posteroanterior cephalogram indicated skeletal asymmetry, canting of the maxilla and floor of the nose, and chin deviation to the right side. Bilateral orbital and zygomatic bones were symmetrically developed contrary to the soft tissue examination. The radiographic examination indicated the shortened anterior arch of the fifth rib and an expansile fourth-rib lesion. There were no skeletal anomalies, affecting the vertebrae. Based on the aforementioned clinical and paraclinical examinations, a diagnosis of HFM was established and categorized as O2.M3.E3.N0.S2, according to the OMENS classification.

Treatment

In the first phase of orthodontic treatment, full-time wear of an asymmetric hybrid functional appliance with bilateral bite blocks (thickness of the right side lower than the left side) was prescribed to correct the transverse canting of the maxillary arch by differential eruption of the affected upper posterior side into the space provided in the costochondral graft surgery. Correction of chin deviation was also addressed by adjusting the appliance in a way that the patient would close the jaw in midline. Appointments were scheduled every four weeks. In each visit, 1 mm of the bite block was removed from the superior part of the appliance on the right side using acrylic burs to allow for the eruption of teeth and gradual maxillary compensation for occlusal canting. After 10 months, with the patient's compliance, the canted maxillary occlusal plane was approximately flattened, and chin deviation was partially corrected (Figure 3).

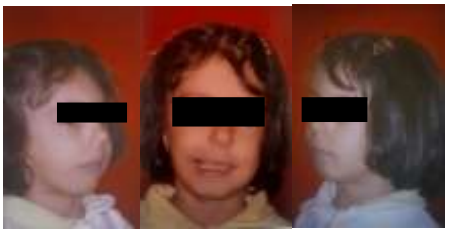

Figure 3: Images of the patient 10 months after fulltime wear of the appliance

The appliance was retained, and the patient was closely

followed-up until completion of growth (post-puberty). Besides regular clinical examination and appliance adjustment, periodic orthopantomographic and lateral and posteroanterior cephalometric evaluations were scheduled within two-year intervals. In the first follow-up panoramic image, the underdeveloped and infra-positioned lower-right permanent first molar and deficient contiguous alveolar bone were distinctly evident. After four years, the patient received a new appliance. Following consultation with her oral and maxillofacial surgeon, at the age of 12 years, the first and second lower right permanent molars were extracted due to their adverse effects on the development of the surrounding bone to prepare the recipient site for iliac crest autogenous bone grafting, which was performed six months later. After 12 years of fulltime wear of the hybrid functional appliance, combined with discussions with her oral and maxillofacial surgeon, a bimaxillary surgery was planned with presurgical and postsurgical orthodontics to achieve facial aesthetics and optimal functional occlusion (Figure 4).

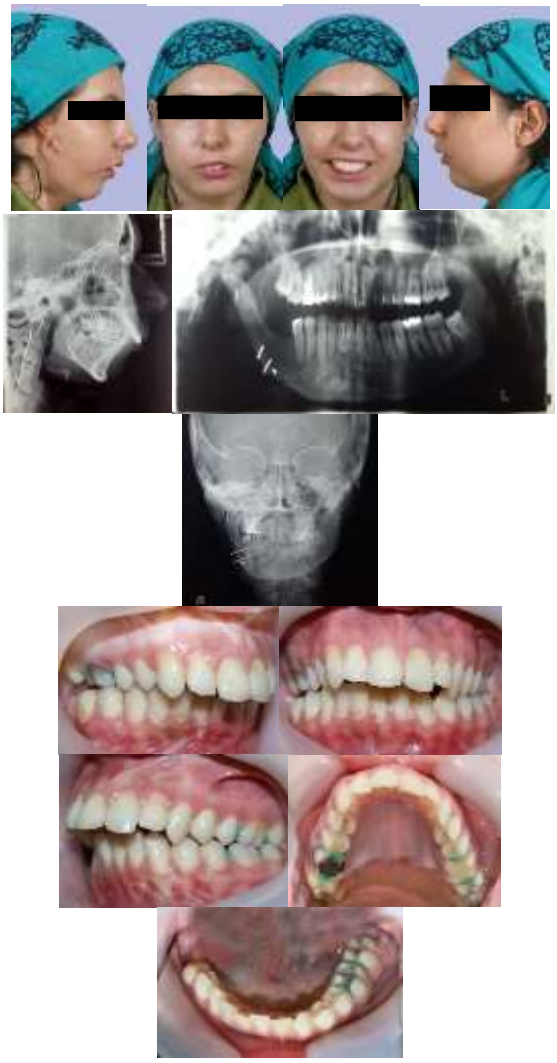

Figure 4: Extraoral photographs, lateral cephalogram, panoramic view, PA cephalogram and Intraoral photographs of the patient before presurgical orthodontics.

Preoperative fixed therapy using a pre-adjusted edgewise appliance (Roth appliance with a slot size of 0.022×0.028) was initiated when the patient was 17 years old; after 13 months, she was considered prepared for the bimaxillary surgery (i.e., asymmetric mandibular advancement with bilateral sagittal split osteotomy and LeFort I osteotomy, followed by ipsilateral maxillary vertical elongation with contralateral impaction). Additionally, advancement genioplasty was performed to improve the profile aesthetics. Rigid fixation was achieved with four miniplates in the maxilla and several screws in the mandible. For levelling, the orthodontist used asymmetric inter-arch elastics. Braces were debonded nine months after the surgical intervention, and a maxillary retainer with a lateral crib, contacting the acrylic base of the lower appliance on the left side, was delivered to the patient to prevent reposturing of the mandible to the previous shifted position (Figures 5 & 6).

Figure 5: photographs and radiographs of the patient after postsurgical orthodontics

Figure 6: The used maxillary retainer with a lateral crib on the left side

The patient was called every two months for the follow-up to monitor the stability of the results and adjust the removable retainer. Reconstructive and adjunctive procedures, including titanium prosthetic device insertion

and iliac bone graft and scar revision surgery, were postponed due to the emergence of COVID-19 pandemic and implemented at the age of 22 years (Figure 7).

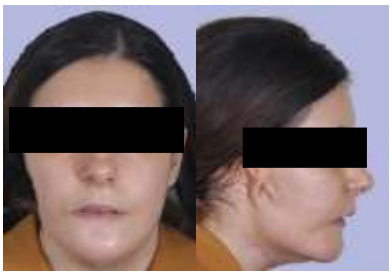

Figure 7: Patient's images six months after titanium prosthesis insertion and scar revision

Discussion

HFM is a complicated form of dysmorphogenesis, with a broad range of clinical manifestations, depending on its severity and extent of organ involvement. Mandibular hypoplasia is pathognomonic for this congenital anomaly (found in 89-100% of cases). [1, 18] Mandibular deformity consists of ramal and condylar underdevelopment, correlated with the surrounding soft tissue and dentoalveolar anomalies. The glenoid fossa may be also malformed in nearly one-fourth of the patients. [16] According to dichotomized Pruzansky- Kaban classification, our patient falls into grade III microsomia (absence of TMJ, ramus, and glenoid fossa). The second most common symptom is an ipsilateral hypoplastic ear (66-99% of cases). The present case showed severe malformation of external ear and malposition of the ear lobe (grade III microtia, atresia). Absence of middle ear and auricular labyrinth was confirmed by the ENT examination.

Generally, the etiology of HFM has not been clarified, and several theories have been proposed for its pathogenesis; however, the intake of vasoactive medications in the first trimester is associated with an increase in the risk of HFM. [2] In the present case, maternal isoxsuprine consumption was a plausible contributing factor for HFM. Although diagnosis is mainly established based on clinical assessments, a more comprehensive analysis of this pathology is feasible. Conventional 2D imaging methods, such as orthopantomography and posteroanterior and lateral cephalometry, are still very helpful in assessing the condylar anatomy and the extent of asymmetry. [12]

Panoramic radiography enables an initial assessment of mandibular and maxillofacial structures and dental development. Posteroanterior cephalogram was the gold standard for the assessment of facial asymmetry before the introduction and widespread application of cone-beam computed tomography (CBCT). This method is helpful for determining midline deviation in the maxilla and mandible, assessment of ramus height and occlusal canting, and comparison of facial bones on both sides. [3] Today, 3D imaging modalities, such as computed tomography (CT) scan and stereolithography, have enhanced the diagnosis of HFM and revolutionized the treatment of this disorder due to a much more precise quantification of soft and hard tissues compared to conventional 2D imaging techniques; they can also guide the application of surgical tools. [4]

Magnetic resonance imaging (MRI) can represent hypoplasia of facial muscles, subcutaneous fat, and bones and also aid in the assessment of facial nerves. Anomalies of the cardiovascular system associated with HFM (e.g., tetralogy of Fallot, ventricular septal defect, aortic coarctation, and patent ductus arteriosus) should be ruled out by electrocardiography. Additionally, renal ultrasonography needs to be performed for such patients in an early stage to detect urogenital anomalies (e.g., renal agenesis, ectopic kidney, multicystic dysplastic kidney, vesicoureteral reflux, and ureteropelvic junction obstruction). Besides, neurological examinations should be conducted, and if the results are abnormal, MRI of the brain and spine can be prescribed. Also, standard upright posteroanterior and lateral radiographs should be obtained if vertebral anomalies are suspected. [12, 19]

Our patient underwent a comprehensive examination, and no extra-craniofacial anomaly was detected. The differential diagnosis of HFM involves facial asymmetry as the prominent clinical characteristic, such as TMJ ankylosis and hemi-mandibular hypoplasia, where a glenoid fossa is present, and there is no soft tissue deficiency, except for chin deviation subsequent to condylar, coronoid, and ramus hypoplasia. Syndromes, such as Treacher-Collins syndrome (TCS), Pierre Robin syndrome, Nager syndrome, Miller-Dieker syndrome, Townes-Brocks syndrome, CHARGE syndrome, branchio-oto-renal syndrome, and Parry-Romberg syndrome, have similar features to HFM, such as mandibular disorders, coloboma or eyelid malformations, and abnormalities of the outer ear. [2]

Some findings of TCS patients, such as hypoplasia of facial bones, especially malar and mandibular bones, external, middle, and internal ear malformations, macrostomia, and high palatal arch, imitate the HFM features. However, TCS is symmetrical and does not affect the nerves. Also, coloboma is present in the upper eyelid of HFM patients and in the lower eyelid of TCS patients. [20] Besides, TCS patients do not have vertebral anomalies or epibulbar dermoids. [21] The bilateral presentation of HFM can be easily confused with TCS; however, discrimination is based on the mirror-image presentation of hypoplasia on both sides of the face in TCS. [4]

Pierre Robin syndrome is commonly characterized by symmetrical micrognathia, glossoptosis, and U-shaped

cleft palate [5, 12], which were not reported in our case. The majority of HFM patients do not have clinical manifestations, such as the upper limb or anal malformations, which are typical in Townes-Brocks syndrome. [6] The interdisciplinary treatment for HFM seeks to improve functionality, along with optimal facial aesthetics, and create a joint simulating the TMJ where it is absent. [6] It involves surgical and nonsurgical repair of skeletal asymmetry, as well as soft tissue defects and auricular anomalies. [7] Treatment for grade III mandibular deformities can be divided into three major phases, depending on age and the extent and severity of deformity: (1) early (neonatal); (2) intermediate (during growth); and (3) delayed (after completion of growth).

During the neonatal period, persistent airway obstruction necessitates early interventions. These procedures include early DO, tongue lip adhesion, or temporary tracheostomy; feeding concerns may dictate using nasogastric tubes or gastrotomy. [12] Following the eruption of the first permanent molar, the affected side of the mandible should be either reconstructed using a costochondral graft or lengthened by DO, depending on the bone sufficiency. [5, 16] Long-term follow-ups have shown that costochondral graft alone is not a suitable treatment. Complications, such as overgrowth of the rib and more frequently, inadequate growth or even graft resorption, have been observed. In case of growth insufficiency, DO may be considered. [16]

Some advantages of DO include minimal invasiveness, lack of donor site morbidity, improved control of progress vector, and simultaneous distraction of soft tissues. [22] However, recurrence of asymmetry over time is plausible following DO. [9] According to a study by Zhang et al., there was no significant difference in the rate of orthognathic surgery at the age of skeletal maturity between individuals who underwent DO during childhood and those who did not. [17] In the present case, a 6-cm costochondral graft, with about 9 mm of cartilage, was harvested from the 5th rib through a carefully placed anterolateral chest incision from the contralateral side (for better contouring). An inferiorly based, inter-positional, temporalis Fingerlike temporalis muscle and fascia flap was placed in the fossa before costochondral grafting of the joint.

After lengthening the mandible with a costochondral graft in our patient, the space between the maxillary and mandibular teeth on the affected side required orthodontic treatment to bring the maxillary and mandibular teeth in contact; therefore, an asymmetrical hybrid functional appliance with bilateral bite blocks was prescribed to guide differential tooth eruption. It should be noted that the child must have at least 20-mm mouth opening to ensure that adequate translation of condyles allows the functional appliance to stimulate mandibular growth. [16] In mild forms of HFM, external ear reconstruction can be accomplished at the age of 6-8 years, as the contralateral ear achieves full growth. However, in severely affected cases, correction of the jaw asymmetry and cheekbone contouring should be performed before ear reconstruction. [5] To reconstruct a deficient zygomatico-orbital region at the age of 7-9 years, a split calvarial graft is the graft of choice. [16]

Distraction is mainly indicated in mandibular deformity grades I and II [11]. However, Shakir et al. proposed that without prior distraction in grade III, adult patients undergoing orthognathic surgery may show insufficient bone volume to perform osteotomy and mandibular repositioning, which entail an avascular bone graft with subsequent caveat of infection and malunion; therefore, an interval DO leads to easier and more predictable outcomes of secondary two-jaw orthognathic surgery.

In the present case, considering the successful costochondral graft outcomes, patient's good cooperation in functional appliance use, and regular recall sessions, there was no need to perform intermediate DO, and periodic radiography provided sufficient bone for mandibular osteotomy. Also, the patient benefited from functional jaw orthopedics and the consequent enhanced facial symmetry psychosocially during her childhood and adolescence. Finally, it should be noted that written and verbal informed consent was obtained from the patient before case presentation.

Conclusion

Patient can benefit from functional jaw orthopedics psychosocially and the consequent enhanced facial symmetry during childhood and adolescence is really advantageous.

Conflict of Interest

No Conflict of Interest Declared ■

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