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Hemifacial Microsomia: A Mini Review

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Hemifacial Microsomia (HFM) is a congenital anomaly involving embryological derivatives of the first and second branchial arches and characterized mainly by mandibular hypoplasia and unilateral or bilateral microtia; although, other facial structures may be affected. It may have long-term effects on psychological development and social well-being, due to unaesthetic facial appearance, functional disturbances and complex medical treatments.

Keywords: Hemifacial microsomia (HFM); omens classification; facial asymmetry/ hypoplasia.

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1. INTRODUCTION

Hemifacial microsomia (HFM) is a complex, variable, developmental malformation of the body involving asymmetrical hypoplasia of the face and ear. It is a relatively rare congenital anomaly that involves immature derivatives from the first and second branchial arches characterized by mandibular underdevelopment and unilateral or bilateral microtia; although, other facial structures may be affected. Disordered craniofacial development frequently results in definitive facial asymmetries that can significantly impact an individual's social and functional well-being.

2. INCIDENCE AND NOMENCLATURE: HEMIFACIAL MICROSOMIA

HFM is a facial anomaly or birth defect and ranks second in prevalence only behind facial clefting/ cleft lip and palate [1]. Microtia (hypoplasia of the external ear) affects approximately 0.03% of newborns, which is common feature of HFM [2]. An incidence study of HFM report as 1 of 3500 births, yet there has been little research on its risk factors and sequelae [3].

Nomenclatures such as first and second arch syndrome, Oral-mandibular-auricular syndrome, Oculoauriculovertebral dysplasia, Goldenhar syndrome, lateral facial dysplasia, unilateral craniofacial microsomia and otomandibular dysostosis have been applied to HFM assuming different etiologies for cases with or without epibulbar dermoid and/or vertebral anomalies. However, it is now understood that these various combinations of vertebral anomalies with HFM represent gradations in the severity of a similar morphogenic error [4,5,6].

Since HFM is defective formation of first and second branchial arches during development of face hence the term- first and second arch syndrome. Goldenhar first described the triad of epibulbar dermoids or choristomas, preauricular skin appendages and pretragal blind-ending fistulas in association with mandibular facial dysplasia [7]. However the diagnostic criteria of Goldenhar syndrome remain unclear, so this term is not used frequently [8]. Later patients with associated vertebral anomalies were given the classification of Oculoauriculovertebral dysplasia [9]. When the features of the Oculoauri-culovertebral dysplasia are predominantly unilateral and lack vertebral anomalies and epibulbar dermoids, the condition has been called HFM. There is increasing evidence that hemifacial microsomia, Goldenhar syndrome and oculoauriculovertebral dysplasia are part of a spectrum within a single entity. Frequency of cervical spine malformations in HFM and microsomia was greater than values for a normal population and this further supports the probable association between HFM, Goldenhar syndrome and Oculoauriculovertebral dysplasia [10].

3. ETIOPATHOGENESIS

The etiopathogenesis of this developmental disorder can be discussed in terms of its embryologic development that causes hypoplasia of structures derived from fetal tissues during the first six weeks of gestation [11,12]. Since the mandible plays a prominent role in defining symmetry of face and act as an active region of growth, so it commonly acquires asymmetric features [13]. HFM risk of an individual is related to maternal exposures affecting blood flow to particular fetal tissues and suggested that maternal use of vasoactive medications in the first trimester and associated cigarette smoking. Additional risk factors of HFM that might represent vascular events include multiple gestations, diabetes mellitus, bleeding during second trimester and heavy alcohol consumption by the mother [3].

HFM are generally thought to result from a combination of inadequate migration and formation of facial mesenchyma. Because many structures of the head and neck migrate during fetal development, an understanding of embryologic development helps determine the origin and nature of such congenital lesions [14].

Poswillo D suggested that hematoma might be involved in the development of HFM in rodents and primates [15]. A study suggested that hematoma at the site of the developing stapedial artery and mandibular hypoplasia were observed among the offspring of CS1 mice treated with triazene during gestation. There are clinical evidences suggesting reduced carotid flow on the affected side of HFM cases; further raising the possibility that it might result from a disruptive vascular pathogenesis (Robinson LK, et al. [16]). Hypodontia was found to be more prevalent in patients with HFM than in normal subjects, possibly indicating an etiologic link between the two conditions [17].

HFM encompasses a broad spectrum of phenotypes resulting from defective development

of facial structures and associated with anomalies of the mandible, facial bones, ears and overlying soft tissues. The cause of HFM is thought to involve both extrinsic and genetic risk factors [18].

Thus two or more anomalies may be interrelated with a similar etiopathologic link, suggesting an overlapping pathogenesis. Whether the cause is genetic or environmental, there may be a common pathway leading to a disturbance in neural crest cell migration in HFM who also have a concurrent cleft lip or palate [19].

4. GENETICS AND HEMIFACIAL MICROSOMIA

Since the knowledge of genetic basis of human disease and its effect on embryologic development has greatly expanded in recent years [14]. There is evidence that genetics play an important role in non-Mendelian-inherited type of HFM and concordance has been reported for both monozygotic and dizygotic twins, but the high level of discordance in monozygotic twins suggests that both genetic and environmental factors are important for the manifestation of this disorder. Based on families with inherited forms of HFM, the patterns of occurrence of both HFM and isolated microtia have suggested that either an autosomal recessive or autosomal dominant inheritance pattern is likely in such developmental anomalies [20,21,22]. It has been shown that HFM can be induced genetically through a mouse chromosome 10 mutation and sometimes there is no family history of HFM in most of the cases [23]. The risk is also studied using DNA collection and it showed that genetic variation is possible in pathways associated with vasculogenesis and hemostasis [3].

5. PSYCHOLOGICAL STATUS IN HEMIFACIAL MICROSOMIA

The psychological impact of the disorder hinders overall growth of the individual with HFM. The affected children are more inhibited, depressed, anxious, introverted and less socially adaptable [24]. They may have poor academic performance, peer rejection and higher levels of internalizing behavior problems than children unaffected by such craniofacial anomalies [3].

Studies and further analyses will determine whether they vary by HFM phenotype, parenting style or other indicators of social risk (e.g., level of education or socioeconomic status). Sometimes, neuropsychological development may be more directly compromised by underlying major or minor central nervous system malformations associated with some cases of HFM [25].

6. CLASSIFICATION OF HEMIFACIAL MICROSOMIA

Numerous classification systems have been devised to facilitate the individualized components of this complex condition and to help stratify patients based on the severity of their defects [26].

One of the most accepted classification systems, the OMENS system, scores five clinical manifestations of hemifacial microsomia according to dysmorphic severity on a scale from 0 to 3: orbital asymmetry, *m*andibular hypoplasia, *e*ar deformity, *n*erve dysfunction, and *s*oft-tissue deficiency. The OMENS classification represents the most comprehensive, versatile, objective and easily adaptable attempt at clinical categorization to aid in the evaluation of hemifacial microsomia patients and also to assist in data sharing amongst clinicians and surgeons [27]. The terms and systems of classification have been reviewed multiples times but OMENS (orbit, mandible, ear, cranial nerve and soft tissues) system has been proposed to classify the severity of each of the major craniofacial manifestations of HFM.

7. CLINICAL MANIFESTATIONS

HFM basically represents a spectrum of congenital malformations involving embryological derivatives of the first and second branchial arches. The multiple anomalies that may coexist in this disorder present considerable variability in patients with the diagnosis [26]. Males are more frequently affected than females and about 45% of patients have affected relatives and 5%–10% have affected siblings [21].

The clinical manifestations of HFM comprise a spectrum of disease that is both broad and complex, characterized by a heterogeneous underdevelopment of the facial structures [27]. The fundamental features include unilateral hypoplasia of the craniofacial skeleton and its overlying malformed soft tissues [28]. Further, the term hemifacial implies the defect is unilateral, but structures are often affected

bilaterally, though to different degrees, giving the face an asymmetric appearance [20]. There is often a unilateral deformity of the external ear ranging from isolated preauricular tags to atresia of the external auditory canal [6] The findings of study on 89 patients by Loevy HT and Shore SW suggest that the mandibular deformity associated with HFM does not have an effect on dental maturation compared with the corresponding non-affected side [29], although hypodontia may be present [17].

The tissues that are more commonly affected in HFM include the condyle and ramus of the mandible, zygomatic arch, malar bone, external ear, middle ear ossicles, temporal bone and muscles of facial expression. HFM may involve some or all of these structures. In fact, HFM is most notable for its vast array of craniofacial and extra-craniofacial manifestations, including associated malformations of other branchial arch derivatives such as the eye, vertebrae and heart, as well as malformations of non-arch derivatives also, such as the kidneys [30,12,4]. The vertebral anomalies most often present are hemivertebrae, block vertebrae, scoliosis/kyphoscoliosis and spina bifida mostly in the cervical and thoracic spine and ribs and the prevalence varies from 8% to 79% as discussed in systematic review by Renkema RW [28]. It is known to be etiologically heterogenous and phenotypic differentiation of the various subgroups remains a challenge. A review of 50 patients with HFM by Bassila MK et al has yielded data that may help explain different pathogenetic processes. There may be association of facial nerve palsy, sensorineural hearing loss or both in a higher percentage of patients than expected [31]. The incidence of obstructive sleep apnea in population of patients with hemifacial microsomia approaches 24 percent as discussed in study conducted by Cohen et al. So patients with hemifacial microsomia should undergo routine screening for obstructive sleep apnea: a positive history warrants polysomnographic and anatomic workup frequency and severity of airway disorders, especially those leading to upper airway obstruction [32]. Thus even hearing loss, mastication impairment, breathing problems, speech impediments and sleep disorders can occur as part of HFM [3].

8. DIAGNOSTIC CRITERIA

The diagnosis of Hemifacial microsomia (HFM) correlates with mandibular hypoplasia and unilateral or bilateral microtia; although, other facial structures may be affected [33]. The phenotype is highly variable and there may be cardiac, vertebral and central nervous system defects, in addition to craniofacial anomalies. So familiarity with craniofacial embryology and its associated effects on resultant anatomy leads to a better understanding of the pathophysiologic basis of such developmental craniofacial disorders which in turn aids in formulation of precise diagnoses and differential diagnostic considerations. Additionally, it helps to establish a search pattern for characteristic radiologic features of many of these anomalies. Ear deformities predominantly occur along a spectrum of this disorder from the distorted size and shape of the external auricle to anotia [14]. A coloboma of the upper eyelid is frequently encountered and may be seen radiographically on soft-tissue windows. A detailed examination of the temporal bone should be performed to evaluate associated, though uncommon, malformations of the middle ear and an aberrant course of the facial nerve [6].

Radiographic evaluation of HFM reveals asymmetric hypoplasia of the maxilla and mandible where one side of the face may be underdeveloped or distorted in shape. There are variable degrees of malformation involving the TMJ, including hypoplasia of the condyle and coronoid. A large variation in the TMJ has been observed on the more affected side; however, the degree of TMJ disc dysplasia does not appear to correlate with the degree of mandibular dysplasia [34]. Patients with HFM have more retruded mandibles and maxillae and a more vertical morphology compared to the reference population [33]. The cranial base axis is not deviated in the patients with HFM compared with the age-matched controls and there exists little difference in endocranial morphologic measurements with increasing severity of HFM. These data are interesting, given the role of the cranial base in facial growth and the varying hypotheses regarding the mechanism of disease in HFM [35]. Also there are studies which shows that in persons with hemifacial microsomia, certain neuromuscular patterns may differ from the norm because of missing or underdeveloped muscles and because of the different relationship between the mandible, its attached muscles and adjacent structures [36].

9. DIFFERENTIAL DIAGNOSIS

Differential diagnoses include unilateral bony ankylosis of temporomandibular joint, Treacher

Collins syndrome, hemifacial hyperplasia and branchio-oto-renal syndrome [37].

10. MANAGEMENT

Hemifacial microsomia present diagnostic and treatment challenge to medical and dental professionals and multidisciplinary approach is advised. New therapeutic and clinical management techniques offer promising interventions that can allow many young patients to have more normal childhoods. Due to a unilateral deficiency of the mandible and lower face, patients have specific dental needs that require not only restorative and orthodontic treatment but also surgical correction of facial tissues. Treatment of patients includes repair of bony asymmetry as well as soft tissue defects and auricular anomalies. Surgical intervention is individualized based on each patient's deficits [18]. The growth curves showed very high inter-variability among patients, further strengthening the need for individualized treatment plans that consider all three dimensions and the severity of the condition [33]. Although surgical reconstruction is the treatment of choice for auricular deformities that result from hemifacial microsomia, the implant-retained auricular prosthesis must be considered when surgery is not possible [38].

Distraction osteogenesis is an alternative treatment option resulting in new bone formation between incrementally separated bony segments for patients with facial asymmetry and mandibular hypoplasia [39,40]. Even with this treatment procedure, it is sometimes difficult to obtain the horizontal occlusal plane and facial symmetry in HFM patients [41].

Correction of the skeletal deformity in children with HFM has been advised to improve growth potential and reduce secondary deformity. Though some authors suggest that facial asymmetry in HFM does not increase with age, a study conducted by Kearns et al demonstrate that HFM is progressive and underscores the importance of early surgical correction of mandibular asymmetry in this disorder [42]. Treatments and rehabilitation procedures can occur over many years to improve function of mastication, speech and hearing which can undoubtedly disrupt both child and family. HFM may have long-term effects on emotional development and social well-being, so psychological counseling is recommended due to unusual facial appearance, functional problems and prolonged medical treatments [3].

11. CONCLUSION

Hemifacial microsomia is a complex craniofacial anomaly causing unilateral facial hypoplasia with a spectrum of phenotypic differentiation and varied nomenclature. Since there has been little research on its risk factors and sequelae, several studies and the subsequent genetic and follow-up studies, are each groundbreaking in terms of their multi-disciplinary approach and their potential impact on affected families. As it results in definitive facial asymmetries, multidisciplinary approach is appreciable as it can significantly impact an individual's social and functional well-being.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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