Craniofacial Microsomia

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KEYWORDS

• Craniofacial microsomia • Hemifacial microsomia • Oculoauriculovertebral syndrome
• Distraction osteogenesis • Costochondral grafting

KEY POINTS

- There are several classification systems for craniofacial microsomia that group patients based on their degree of asymmetry. The most recent and comprehensive of these is the OMENS PLUS (Orbit, Mandible, Ear, Nerve, Soft tissue) system.
- Treatment of craniofacial microsomia is based on the severity of the deformity.
- Timing of surgical repair remains controversial.
- Mandibular distraction osteogenesis is a well-accepted method of correction of mandibular asymmetry but there is evidence of relapse if patients undergo distraction before completion of growth.
- Treatment includes not only correction of skeletal deformities but also soft tissue deficits (by means of free tissue flaps, fat grafting, and implants).

INTRODUCTION

Craniofacial microsomia (CFM) is a term used to describe a spectrum of craniofacial abnormalities caused by abnormal development of the first and second pharyngeal arch derivatives. The term CFM is often used interchangeably with several other terms, including otomandibular dysostosis, lateral facial dysplasia, malformation syndrome of the first and second arches, temporal oculoauricular dysplasia, and hemifacial microsomia (HFM). In addition, Goldenhar syndrome is considered a variant of CFM, which also includes epibulbar dermoids and vertebral anomalies. It is thought that the entities mentioned earlier represent several different phenotypical presentations that exist within a continuum, and thus the term oculoauriculovertebral spectrum (OAVS) was proposed by Cohen and colleagues[1] in 1989 to encompass all of these variants. Each of the variants includes some degree of developmental abnormality of the facial skeleton (mandible, maxilla, zygoma, and/or temporal bone), ear, and soft tissues.

EPIDEMIOLOGY

CFM is the second most common craniofacial birth defect after cleft lip and palate. It affects an estimated 1 in 3600 to 5600 live births in the United States each year. Literature reviews suggest that it is 50% more prevalent in boys (3:2 ratio). Ten percent of cases are bilateral, and most unilateral cases occur on the right.[2]

CAUSE/PATHOGENESIS

The mechanism behind CFM is thought to be related to the development of the pharyngeal arch structures. The pharyngeal arches start to form around the fourth week of embryologic development and are composed of mesenchymal cells that give rise to various facial structures (including skeletal, muscular, and neural elements). The morphogenesis of these structures depends on continuous and reciprocal tissue-tissue interactions, and any disruption of these interactions can lead to developmental abnormalities.[3,4] There

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are 2 leading theories to explain the pathogenesis of CFM:

1. Vascular disruption of the stapedial artery during development of the first and second pharyngeal arch derivatives leads to hematoma formation and subsequent abnormal growth and malformation of the mandible.[5]
2. Death, failure of development, or failure of migration of cells from the neural crest to the pharyngeal arches, causing dysmorphology of the arches.[6]

GENETICS

The causes of CFM include both extrinsic and genetic risk factors. Most documented cases are sporadic with no relevant family history. However, there is growing evidence for a genetic predisposition. Previously, a positive family history was documented in about 2% of patients who were within the OAVS spectrum. However, recent studies have shown significantly larger numbers of familial cases. It is also hypothesized that the reported percentage of familial involvement is underestimated given the broad phenotypic spectrum, with some family members having mild presentations that go undetected.[7,8] In a study by Kaye and colleagues,[9] 44% of cases of CFM had a positive family history of facial malformation, with an overall recurrence rate of 2% to 3% in first-degree relatives. Their data favored an autosomal dominant mode of inheritance with incomplete penetrance rather than a recessive or polygenetic mode of transmission.

Several chromosomal abnormalities have been identified in patients with CFM (**Table 1**). Studies reveal that the 22q11 locus may harbor genes important for regulation of craniofacial symmetry and first and second pharyngeal arch development, because craniofacial skeletal and soft tissue asymmetries have been observed in patients with genomic imbalances on the 22q11 locus.[40] The Crkl gene (in the 22q11 region) regulates signaling events in developing pharyngeal arches, again supporting its potential contribution to craniofacial dysmorphism.[41] The OTX2 gene was also identified as a very likely causal gene in CFM. This gene encodes a transcription factor that plays a critical role in craniofacial development and anterior brain morphogenesis. Zielinski and colleagues[13] investigated the largest CFM pedigree to date and found that a duplication in chromosome 14q22.3 (coding for OTX2) was present in all affected individuals.

Environmental factors are also thought to play a causative role in CFM. It is hypothesized that gestational diabetes, exposure to teratogens such as thalidomide, vasoactive drug use, smoking, and multiple gestation pregnancies cause disruption of embryonic blood flow during fetal development, leading to several structural congenital anomalies.[42–44]

PRESENTATION

There are no established criteria for diagnosis of CFM. However, several studies have indicated that either mandibular or auricular defects are mandatory for diagnosis. Cousley[45] proposed in his 1993 article the following minimum diagnostic criteria:

1. Ipsilateral mandibular and ear defects (external/middle)
2. Asymmetrical mandibular or ear defects (external/middle) in association with:
   a. Two or more indirectly associated anomalies, or
   b. A positive family history of HFM

There are varying degrees of severity within the spectrum of CFM. Mandibular deficiency can range from missing the condylar cartilage and disc to complete developmental failure of the ramus. The maxilla, temporal bone, and orbit can also be affected as a result of primary malformation. However, CFM is not characterized by bony dysmorphism alone, because there is soft tissue, neural, and muscular involvement as well. **Table 2** outlines the anomalies that are seen and their incidence.

CLASSIFICATION SYSTEMS

The heterogeneity of phenotypic presentations in CFM has led to difficulty developing a reproducible classification system to distinguish between varying degrees of deformity and to help aid in surgical planning.[49] The first accepted classification was proposed by Pruzansky[50] in 1969, and focused on the size and shape of the mandible and glenoid fossa. Kaban and colleagues[51,52] modified this classification system in 1988, proposing further stratification of the type II mandible based on the relationship of the mandibular condyle and glenoid fossa (**Fig. 1**). Another classification system described in the literature is the SAT (skeletal malformations, auricular involvement, and soft tissue defects) system, proposed by David and colleagues[53] in 1987. Vento and colleagues[46] took this one step further, defining the OMENS (Orbit, Mandible, Ear, Nerve, Soft tissue) classification system, which expanded the SAT system to include other affected structures: orbital distortion, mandibular hypoplasia, ear