Int. J. Oral Maxillofac. Surg. 2017; xxx: xxx–xxx
http://dx.doi.org/10.1016/j.ijom.2017.04.025, available online at http://www.sciencedirect.com

International Journal of Oral & Maxillofacial Surgery

Systematic Review
Craniofacial Anomalies

Vertebral anomalies in craniofacial microsomia: a systematic review

R. W. Renkema[1], C. J. J. M. Caron[1], I. M. J. Mathijssen[2], E. B. Wolvius[1], D. J. Dunaway[3], C. R. Forrest[4], B. L. Padwa[5], M. J. Koudstaal[1,3,5]

[1]Department of Oral and Maxillofacial Surgery, The Dutch Craniofacial Centre, Erasmus MC, Sophia's Children's Hospital Rotterdam, Rotterdam, The Netherlands; [2]Department of Plastic and Reconstructive Surgery and Hand Surgery, The Dutch Craniofacial Centre, Erasmus MC, Sophia's Children's Hospital Rotterdam, Rotterdam, The Netherlands; [3]The Craniofacial Unit, Great Ormond Street Hospital, London, UK; [4]Division of Plastic and Reconstructive Surgery, Department of Surgery, The Hospital for Sick Children, Toronto, Canada; [5]Department of Plastic and Oral Surgery, Boston Children's Hospital, Boston, MA, USA

R. W. Renkema, C. J. J. M. Caron, I. M. J. Mathijssen, E. B. Wolvius, D. J. Dunaway, C. R. Forrest, B. L. Padwa, M. J. Koudstaal: Vertebral anomalies in craniofacial microsomia: a systematic review. Int. J. Oral Maxillofac. Surg. 2017; xxx: xxx–xxx.

Abstract. Craniofacial microsomia (CFM) is characterized by a heterogeneous underdevelopment of the facial structures arising from the first and second branchial arches, but extracraniofacial malformations such as vertebral anomalies also occur. This systematic review provides an overview of the literature on the types and prevalence of vertebral anomalies found in patients with CFM. A systematic search was conducted. Data on the number of patients, patient characteristics, types and prevalence of vertebral anomalies, and other associations between CFM and vertebral anomalies were extracted from the articles identified. Thirty-one articles were included. Seventeen articles described both the prevalence and types of vertebral anomalies in CFM, five articles described solely the types of vertebral anomalies in CFM, and nine articles reported solely the prevalence of vertebral anomalies in CFM. The vertebral anomalies most often reported in CFM are hemivertebrae, block vertebrae, scoliosis/kyphoscoliosis, and spina bifida. These anomalies are mostly present in the cervical and thoracic spine and ribs. The reported prevalence of vertebral anomalies in CFM varies from 8% to 79%. To diagnose vertebral anomalies early in patients with CFM, further research should focus on determining which patients with CFM are at risk of vertebral anomalies.

Key words: craniofacial microsomia; oculo-auriculo-vertebral spectrum; hemifacial microsomia; Goldenhar syndrome; vertebral anomalies; cervical anomalies; systematic review.

Accepted for publication 27 April 2017

Craniofacial microsomia (CFM) is a heterogeneous disorder, causing a wide variety of facial malformations ranging in severity[1–5]. After cleft lip and palate, CFM is the most common congenital craniofacial disorder, with an incidence of 1:3000 to 1:5000 live-births[1,6–8]. The craniofacial anomalies found in CFM are believed to be related to the first and second branchial arches[1–3]. In CFM, the mandible, zygoma, external and middle ear, facial musculature, facial nerve, and soft tissues can be affected. Although ear deformities are part of CFM, isolated microtia is generally not regarded as CFM[3,9]. However, it is still discussed whether isolated microtia might be a minor form of CFM[3,7].

CFM is primarily known for its craniofacial malformations, but extracranial manifestations, such as vertebral, renal, heart, central nervous system, lung, and gastrointestinal defects may also occur[5,9–15]. Goldenhar reported what he believed to be a specific variant of CFM; these patients have the clinical features of CFM in combination with epibulbar dermoids and

Please cite this article in press as: Renkema RW, et al. Vertebral anomalies in craniofacial microsomia: a systematic review, *Int J Oral Maxillofac Surg* (2017), http://dx.doi.org/10.1016/j.ijom.2017.04.025

vertebral anomalies[9,16]. However, Vento and colleagues documented no association between these anomalies and refuted the existence of this variant[14]. More recently Tuin et al. attempted to differentiate Goldenhar syndrome from CFM and concluded that the term Goldenhar syndrome was inconsequential[17]. The most frequently seen vertebral anomalies in patients with CFM are hemivertebrae, fusion of the vertebrae, scoliosis, accessory vertebrae, occipitalization of the atlas, and spina bifida[1,18].

Several terms are used for CFM, such as oculo-auriculo-vertebral spectrum, hemifacial microsomia, lateral facial dysplasia, and first and second branchial arch syndrome. Presumably, these conditions are part of the CFM spectrum[17,19–21]. In this article, the deformity is referred to as craniofacial microsomia (CFM), as this is currently the term most often used in the literature.

The exact origin of CFM is unknown. The most widely accepted theory is that CFM is the result of a disturbance in the embryological development of the first and second branchial arches during the first 6 weeks of gestation[4,9,11]. During these first 6 weeks of embryological development, both the skull and spine are formed[11]. Therefore, a common pathogenic mechanism is likely to be the basis of both craniofacial and vertebral malformations in patients with CFM.

Although the precise link between the facial and vertebral malformations has not been clarified, the deficiency presumably occurs during vertebral somite formation, resulting in incorrect formation of the vertebrae and the skull[22]. This may lead to congenital scoliosis or instability of the cervical spine[22–24]. Instability of the cervical spine may also be the result of abnormal development of the ligamentous structures and could cause compression of the spinal cord during movement[22]. The clinical presentation of vertebral instability is largely variable and may or may not be associated with signs or symptoms[22]. Symptoms of cervical spine instability include neck pain, torticollis, and limited neck movement, and neurological symptoms may occur if there is compression of the spinal column or vertebral artery[22,25]. The cerebellum and cranial nerves can be involved, which may lead to a wide range of neurological symptoms, including ataxia, coordination disturbances, and diplopia[22]. Basilar impression, which is associated with cervicovertebral anomalies, can cause similar symptoms[26,27]. Excessive cervical spine manipulation, which may be induced by sports activities, may result in spinal cord impingement in patients with unrecognized cervical instability[28]. Besides the possible neurological effects, fusion or underdevelopment of the vertebrae could also result in fractures of the ankylosed segments or in progressive scoliosis[29–34]. It is important to keep these, often asymptomatic, vertebral anomalies in mind when performing surgery, as cervical spine instability can put these patients at risk of spinal cord injury during intubation or surgical manipulation[35–38].

Since vertebral anomalies occur in CFM patients and may cause serious complications, it is important that clinicians are aware of the possible anomalies and their consequences. The aim of this systematic review was to study the available literature on vertebral anomalies and their respective prevalence rates in patients with CFM.

Methods

Search strategy

This study was guided by the PRISMA statement (Preferred Reporting Items for Systematic Reviews and Meta-Analyses)[39]. A systematic search of the literature was performed to identify papers focusing on CFM and its synonyms combined with synonyms for spinal and central nervous system anomalies. The search was conducted in Embase, Ovid MEDLINE, Cochrane Central, Web of Science, PubMed (articles not yet indexed in MEDLINE), and Google Scholar (most relevant articles) from inception until 21 June 2016. Results were limited to human studies written in English. No date limits were applied. Conference abstracts, letters, notes, and editorials were excluded. See the **Supplementary Material** online for the full search strategy.

The studies were selected independently by two researchers (R.W.R. and C.J.J. M.C.). Titles and abstracts were screened for relevance based on the inclusion and exclusion criteria. Studies concerning CFM in relation to vertebral anomalies were further reviewed. Those in which prevalence and/or the types of vertebral anomalies in CFM were mentioned were included. The articles had to report original studies. Case reports were excluded. Although there is still debate on whether isolated microtia is a form of CFM, this was considered to be a different entity for the purpose of this review. Therefore, studies describing solely patients with isolated microtia were not included. However, data concerning the CFM patients were extracted from papers describing both patients with microtia and patients with CFM.

Data extraction

A table with predetermined characteristics was constructed prior to the full-text review of the articles. All papers were graded on quality of evidence using the Oxford Centre for Evidence-Based Medicine (CEBM) criteria. The following information was extracted when available: the number of patients, inclusion criteria applied in the studies, prevalence of vertebral anomalies in CFM, types of vertebral anomalies, and other correlations between CFM and vertebral anomalies.

Results

Study selection

In total, 6034 articles were identified after the initial search and after including articles found through reference list searching. After removing duplicate articles, 3646 articles remained; these were examined based on title and abstract. A total 3467 articles were excluded at this stage as a result of not meeting the inclusion criteria. The full texts of the remaining 179 articles were reviewed. Finally, 31 articles were identified for inclusion in the review. Twenty-six articles described the prevalence of vertebral anomalies and 22 articles described the types of vertebral anomalies in their investigated population (Fig. 1).

Study characteristics

The characteristics of the studies included are described in Table 1. Several studies included patients diagnosed with isolated microtia[19,20,40–42]. These patients were extracted from the studies and not included in this literature review for further analysis. Patients with incomplete data were excluded from the analysis. Radiographs or computed tomography scans were used to evaluate the vertebral anomalies. Most studies were retrospective[11,12,14,17,18,28,40,41–52], although some prospective studies and case series were found[5,10,13,19,20,29,53–57]. The number of patients studied ranged from six to 259 per study[5,10–14,17–20,28,29,40–58].

Prevalence of vertebral anomalies in CFM

Details of the numbers of patients and level of spinal examination in articles on the prevalence of vertebral anomalies in CFM are reported in Table 2. The reported