Available online at www.sciencedirect.com

SciVerse ScienceDirect

British Journal of Oral and Maxillofacial Surgery 51 (2013) 902–907

BRITISH Journal of Oral and Maxillofacial Surgery
www.bjoms.com

Craniofacial morphology in unilateral hemifacial microsomia

E.M. Ongkosuwito [a,*], J.W. van Neck [b], E. Wattel [c], L.N. van Adrichem [b], A.M. Kuijpers-Jagtman [d]

[a] *Department of Orthodontics, Erasmus MC-Sophia, University Medical Center, P.O. Box 2060, 3000 CB Rotterdam, The Netherlands*
[b] *Department of Plastic and Reconstructive Surgery, Erasmus MC, University Medical Center, P.O. Box 2040, 3000 CA Rotterdam, The Netherlands*
[c] *Section Geometry, Department of Sciences, Vrije Universiteit, De Boelelaan 1081, 1081 HV Amsterdam, The Netherlands*
[d] *Department of Orthodontics and Craniofacial Biology, Radboud University Nijmegen Medical Center, P.O. Box 9101, 6500 HB Nijmegen, The Netherlands*

Accepted 21 October 2012
Available online 30 November 2012

Abstract

Hemifacial microsomia (HFM) is a complex three-dimensional congenital condition that is characterized by mandibular hypoplasia and unilateral or bilateral microtia; although, other facial structures may be affected. Little is known about craniofacial growth and morphology in patients with HFM; therefore, we examined 75 HFM patients by means of a cephalometric analysis in a longitudinal study on serial lateral cephalograms. We hypothesized that the growth of several facial structures on both sides of HFM patients would be different compared to Dutch controls. We determined patients with HFM had more retruded mandibles and maxillae and a more vertical morphology compared to the reference population. In addition, there was a more retruded and vertical pattern on the affected side compared to the unaffected side and in patients with a severe condition compared to those with a mild condition. 'Mild' HFM patients were more similar to the Dutch reference population than the 'severe' HFM patients. Individual HFM growth curves showed very high inter-variability, further strengthening the need for individualized treatment plans that consider all three dimensions and the severity of the condition.

Keywords: Facial asymmetry; Alveolar process; Neural crest; Cephalometry

Introduction

Hemifacial microsomia is a craniofacial condition that changes over time.[1] The most obvious clinical presentation is mandibular hypoplasia combined with unilateral or bilateral microtia.[2,3] Both musculature and the facial skeleton are involved, but the degree of bony and muscular malformation seem unrelated.[4] However, closer inspection showed that there was asymmetry of the soft tissue and facial skeleton that involved the maxilla and the orbit.[5] There is downward growth of the nasomaxillary region on the affected side, which is probably restricted or influenced secondarily by the small mandible.[6] This has not been directly associated with any known aetiological factor or any defect in gene regulation that directly affects the maxilla.

The etiology of hemifacial microsomia is still not clear, although it is heterogeneous and has been primarily associated with vascular perturbation, or neural crestopathy, or both.[7] Skeletal mandibular defects develop early, probably within the first 10 or 12 weeks of gestation.[7] Muscular defects may also originate from an event in early embryonic development, and derive from a defect in the communication between the cranial neural crest and cephalic myogenic mesodermal

* Corresponding author at: Erasmus MC-Sophia, Room Sp 1408, Dr Molewaterplein 60, 3015 GJ Rotterdam, The Netherlands. Tel.: +31 10 7036425; fax: +31 10 7036810.
E-mail address: e.ongkosuwito@erasmusmc.nl (E.M. Ongkosuwito).

0266-4356/$ – see front matter
http://dx.doi.org/10.1016/j.bjoms.2012.10.011

cells.[8] Recently, studies in mice showed inactivation or the allelic reduction of *Edn1*, *Ednra*, *Dlx5*, *Dlx6*, *Gsc*, *Pitx1*, and *Gbx2*, all of which result in a proximal defect of the developing mandible or of the middle and external ear,[9] which is also characteristic of hemifacial microsomia. However, combined maxillary and mandibular conditions are rarely associated, and might correspond to earlier defects in the differentiation of cephalic neural crest cells.[9]

From a clinical perspective the phenotype is highly variable in the extent of the deformity.[6] Patients with a milder form may show more normal craniofacial growth, while there may be limited growth in patients who have a severe form. It is not clear whether the mandibular growth condition worsens over time, which is likely to be a result of the variability.[1,6,10] Even less is known about maxillary growth, so it is still uncertain if early or late surgical treatment is best.[11]

Further insight into the growth and most appropriate time of treatment is needed, so in this study we aimed to design craniofacial linear growth curves for the non-operated mandible in children with unilateral disease and for Dutch controls. The hypotheses to be tested were: there is no difference in craniofacial growth between patients and normal Dutch children, and no difference between the mild and severe types of hemifacial microsomia.

Patients and methods

Patients

Between 1980 and 2005, 75 consecutive patients (39 girls and 36 boys) diagnosed with unilateral hemifacial microsomia or Goldenhar syndrome were seen at the Department of Orthodontics, Erasmus Medical Center, Rotterdam, The Netherlands, and were included in this study. Patients were classified into 4 grades based on the Pruzansky/Kaban classification[12] by a maxillofacial surgeon, a plastic surgeon, and an orthodontist. A consensus was reached in cases of disagreement. The patients were then divided into a mild group (I and IIa, 24 and 22 patients, respectively) and a severe group (IIb and III, 23 and 6 patients, respectively). Patients with types I and IIa are functionally similar because they have an adequate temporomandibular joint, while patients with types IIB and III are also similar in that a new temporomandibular joint and ramus must be constructed.[2] The distribution of girls over the four grades was 9 (I), 12 (IIa), 14 (IIb), and 4 (III). The distribution of boys was 15 (I), 10 (IIa), 9 (IIb), and 2 (III). Patients were diagnosed early, had their first follow up around 4 years of age, and were treated (or operated on) at various ages. The number of lateral cephalograms varied from 1 to 7/patient, with a mean of 2.7 preoperative cephalograms/patient (age range 4–29 years, mean (SD) 10 (5) years). This study of human subjects followed an approved protocol and satisfied the requirements of our institutional review board (approval number MEC 2008-258).

Controls

The records of 232 boys and 254 girls with no signs of hemifacial microsomia from the Nijmegen Growth Study (NGS), a five-year mixed longitudinal study of 482 children, were chosen to act as controls. We used cephalograms taken at the ages of 4–14 years. The mean (SD) age was 12 (3) years for boys and 11 (3) years for girls. A total of 2524 cephalograms were used.[13]

Craniofacial measurements

Cephalograms of growing patients were included unless they had been operated on, as surgical intervention may influence growth. Digitized cephalograms from film (before 2003) and digital cephalograms (from 2003 to 2010) were imported into a cephalometric measurement program (Viewbox version 3.1.1.12, DHAL software, Kifissia, Greece).

Thirteen measurements (Table 1) were made by one experienced observer.[14] In patients, the landmarks articulare and gonion cannot always be found on the affected side. In those cases, the angle between the ramus and the body of the mandible (Ar–Go–Me) cannot be established, so the most distal and upper point (*Z*) and the most distal and lower point (*Q*) on the affected side of the mandible were used to construct the angle (*Z*–*Q*–Me).

Statistics

To calculate the intra-examiner reliability, 20 randomly selected lateral cephalograms from patients with hemimandibular microsomia were measured twice by the same experienced observer. Intra-examiner reliability was assessed with the intraclass correlation coefficient (ICC) for the level of measured distances.[15] ICC values range from 0 to 1; ICC values of 0.61–0.8 are interpreted as substantial agreement and values of 0.81–1.0 indicate almost perfect agreement.

The measurements for patients were compared with those from the control group using a procedure that started with the creation of individual curves. Subsequently, these individual curves were combined by a curve-fitting procedure into one combined curve. If too much individual variation existed no combined curve was created, but values for a certain point in time were estimated using these individual curves. The linear function used for the individual patient data was $Y = AX + B$, in which A indicates the increment (mean length over time) and B the intercept (length at age zero). The procedure was used for the control subjects from the NGS (boys and girls together), the affected or unaffected side in patients, and in patients in the mild (I, IIa) and severe (IIb, III) groups. The results were then compared using a 2-tailed Student's *t*-test. The Statistical Package for the Social Sciences version 18.0 (SPSS Inc., Chicago, IL, USA) was used to aid statistical analysis.