True hemifacial microsomia and hemimandibular hypoplasia with condylar-coronoid collapse: Diagnostic and prognostic differences

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Introduction: Long-term results after orthopedic or surgical treatment of hemifacial microsomia (HFM) have shown a tendency toward recurrence of the facial asymmetry. However, the literature contains a number of successful case reports that show surprising changes in the morphology of the condyles. In addition, patients with similar mandibular asymmetries, treated early with surgery, have excellent long-term follow-ups, especially those who have little or no soft-tissue involvement, but only severe mandibular ramal deformities. The phenotypes of these cases are unexpectedly similar, with a consistent collapse of the condyle against the coronoid and a deep sigmoid notch. The objectives of this article were to help distinguish true HFM from this peculiar type of hemimandibular asymmetry morphologically and to quantify their differences before treatment and in the long term. Methods: Panoramic radiographs taken at pretreatment and the long-term follow-up of 9 patients with hemimandibular hypoplasia, characterized by the collapse of the condyle against the coronoid, were compared with those of 8 patients with severe type I and type II HFM; these records were collected before and at least 10 years after distraction osteogenesis. Results: Ratios and angular measurements before and after treatment differed significantly between the 2 groups. Conclusions: Perhaps these patients were misdiagnosed and actually had secondary injuries of the condyle, which have a normal functional matrix. Therefore, with growth and functional stimulation, they would tend to grow toward the original symmetry. To make a differential diagnosis between true HFM and this peculiar type of hemimandibular hypoplasia, the collaboration between not only orthodontists and surgeons, but also geneticists and dysmorphologists, is of great importance because of the different prognoses. (Am J Orthod Dentofacial Orthop 2011;139:e435-e447)

Etiologic diagnosis is possibly the most difficult, but also the most important, step in orthodontic treatment. Facial asymmetries are certainly a challenging chapter for both the orthodontist and the maxillofacial surgeon. Hemifacial microsomia (HFM), the best known of the branchial arch syndromes, is a relatively common craniofacial anomaly with a birth prevalence of at least 1 in 5600, characterized by asymmetric underdevelopment of the structures originating from the first and second branchial arches. Deformities can involve the ear, the mandible, the maxilla, the zygomatic arch, the temporal bone, the fifth and eighth cranial nerves, the cervical spine, and the facial muscles. The degree of ear involvement is markedly variable. Ear tags and pits might be present. The condition is etiologically heterogeneous. Many chromosome abnormalities have been recorded, but also environmental causes including thalidomide, primidione, and retinoic acid administered during the organogenesis. A recent model, based on a mutation of a locus on chromosome...
10, appears to support the hypothesis that HFM anomalies have partly a genetic cause.\(^2\)\(^,\)\(^3\) Most cases are sporadic, but rare familial instances with autosomal dominant inheritance have also been observed.\(^4\)\(^,\)\(^5\) HFM is 1 of 4 conditions defined as otofacial malformations, which are neurocristopathies, sharing a major involvement of neural crest cells, together with DiGeorge syndrome, retinoic acid syndrome, and

### Table I. Differential diagnosis between true HFM and hemimandibular hypoplasia with CCC

<table>
<thead>
<tr>
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<th>HFM</th>
<th>CCC</th>
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<tr>
<td><strong>History</strong></td>
<td>Generally diagnosed at birth</td>
<td>Usually not diagnosed at birth</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Seldom history of trauma</td>
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<tr>
<td><strong>Clinical examination</strong></td>
<td>Soft-tissue defects (may be very mild)</td>
<td>No soft-tissue defects</td>
</tr>
<tr>
<td></td>
<td>Ear defects, preauricular tags</td>
<td>Normal ears, no preauricular tags</td>
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<tr>
<td></td>
<td>Facial nerve asymmetries</td>
<td>No nerve deficit</td>
</tr>
<tr>
<td></td>
<td>Masseter muscle hypoplasia</td>
<td>Well-developed masseter</td>
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<tr>
<td></td>
<td>Deviation of the chin on the affected side, associated with flatness on the affected cheek</td>
<td>Deviation of the chin on the affected side, associated with fullness on the affected cheek</td>
</tr>
<tr>
<td></td>
<td>Mild deviation to the affected side during opening</td>
<td>Significant deviation to the affected side during opening</td>
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<tr>
<td><strong>Panoramic x-ray (or computed tomograph)</strong></td>
<td>Hypoplasia of the ramus and condyle and coronoid processes up to absence of the condyle and temporal fossa</td>
<td>Hypoplasia of the ramus and condyle and coronoid processes, which are typically collapsed one on the other; the temporal fossa is always present</td>
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</table>

**Fig 1.** A-C, Type II Pruzansky HFM ramal deformity (note the associated ear deformity); D-F, misdiagnosed ramal deformity.
Treacher Collins syndrome. A condition analogous to HFM has been induced in mice by causing a local hemorrhage from the embryonic stapedial artery between the 30th and 40th days of fetal development, a critical period of neural crest cell migration.

Neural crest cells are a migratory cell population. Just before the neural fold fuses to form the neural tube, neuroectodermal cells adjacent to the neural plate migrate into the facial region, where they form the skeletal and connective tissues of the face: bone cartilage, fibrous connective tissue, and all dental tissues except enamel. Thus, facial mesenchyme is of neural crest origin; this in turn guides the formation of vascular endothelium and skeletal muscles, which are of mesodermal origin. Thus, a craniofacial malformation can be the consequence of a disruption in the migration or proliferation of neural crest cells, but the primary defect might have a genetic origin.

What is more important than the etiology, in view of the aim of this article, is that the neural crest cells that migrate into the first branchial arch carry the pattern of information needed for proper morphogenesis of mesodermal derivatives such as cranial muscles. Extirpation of the mandibular neural crest stream leads to severe alterations of mandibular-muscle patterning. Whereas Meckel’s, palatoquadrate, suprarosstral, and infrarostral cartilages can be severely malformed or missing, all muscles of the levator mandibulae group will also be similarly affected. Therefore, although HFM can be variable in terms of phenotype, mandibular deformity is always proportionate to the associated muscular deformity.

As stated before, under the diagnosis of HFM, there is much variability; thus, treatment varies. Patients with HFM with minor mandibular and soft-tissue involvement can be treated by using
A conservative approach, obtaining good dentoalveolar correction and some mild improvement in the skeletal asymmetry. Orthodontic functional appliance therapy during growth has been suggested even in moderate to severe cases, but there is no consensus about the value and the true effect of such treatment.

At present, the timing of treatment and the optimal treatment protocol are still controversial. Therapy includes orthodontic and surgical measures for the correction of the skeletal asymmetry. Preoperative and postoperative treatment with functional appliances has been recommended to improve muscle function and to stimulate growth of the soft and hard tissues. Vargervik et al demonstrated that functional appliances improved the short-term results after costochondral grafting, but, nevertheless, in most cases, the asymmetry returned during subsequent growth. Likewise, it was recently shown that functional therapy associated with distraction osteogenesis only slows down the return to the original asymmetry of HFM. In contrast, the literature includes many case reports describing successful orthopedic treatment in patients diagnosed with severe forms of HFM. Asymmetrical mandibular growth is also seen in patients who have suffered postnatal trauma or infection in the condylar region. This deformity differs from HFM in that it is limited to the jaw, without affecting the ear, soft tissues, or other organs. Therefore, mandibular asymmetry can be part of many conditions with different causes. According to the time of their onset, they might be related to (1) abnormality of early embryonic development (lack of neural crest cell migration) such as HFM or micrognathia (in these conditions, some alteration of growth patterns is observed as a consequence of the developmental abnormality. Usually orthopedic treatment has little probability of changing the pattern) or (2) abnormality of late fetal or postnatal growth, where it is presumed that the abnormal process becomes

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Fig 3. Male patient misdiagnosed with HFM and treated with unilateral mandibular DO: A and B, before DO, the ear, although normal in structure, is abnormally positioned due to the skeletal deformity; it is lateral and more prominent on the affected side; C and D, immediately after DO; E and F, 8 years after DO.
causative after the embryonic period. This group includes abnormalities due to trauma, infection, or surgical iatrogenic deformities. Often these patients have involvement of only the bony structures of the mandible, but usually the soft tissues or the neuromuscular pattern is not affected. Therefore, these conditions are more likely to show good responses to functional stimulation.

The aim of this article was to describe a peculiar type of mandibular asymmetry, frequently misdiagnosed as HFM. The patients shown share 2 main characteristics that distinguish them from more traditional HFM patients (Table I, Fig 1). (1) There is no soft-tissue involvement, the external ear is present and well-formed, and the musculature seems to be well developed. Although the chin point deviates to the affected side, there is not the typical flatness of the gonial area seen in HFM patients (Fig 1, A–C). On the contrary, there is more fullness on the affected side than on the unaffected side (Fig 1, D–F). (2) The shape of the hypoplastic ramus is peculiar and extremely similar in all patients. The condyle is short and collapsed against the coronoid process (Fig 1, D–F). Figures 2 through 5 show 4 patients who were treated surgically with excellent long-term results; Figures 6 through 10 show 5 patients who were treated orthodontically, with a similar remarkable ramal deformity correction. All had been erroneously diagnosed as having HFM by a surgeon or an orthodontist. Other patients with almost identical phenotypes misdiagnosed as having HFM can be found in the literature, and others already identified as without HFM can be also found. All of these, whether treated surgically or orthopedically, had successful long-term follow-ups. In contrast, we also followed for over 10 years (range, 10–13 years) a sample of patients affected by HFM and treated with unilateral mandibular distraction osteogenesis (DO) during early childhood (Figs 11 and 12). The 5-year follow up of these patients was previously reported. The objective of this study was to clearly define, not only in

Fig 4. Male patient misdiagnosed with HFM and treated with unilateral mandibular DO: A and B, before DO, the ear, although normal in structure, is abnormally positioned due to the skeletal deformity; it is lateral and more prominent on the affected side; C and D, immediately after DO; E and F, 6 years after DO.
Fig 5. Female patient misdiagnosed with HFM and treated with unilateral mandibular DO: A and B, before DO; C and D, immediately after DO; E and F, 10 years after DO.

Fig 6. Male patient misdiagnosed with HFM and treated with an Andreasen modified appliance: A and B, pretreatment; C and D, 11-year follow-up. Note the normal ear and the fullness of the soft tissues on the affected side, even fuller than the contralateral side.
terms of morphology, but also quantitatively in terms of initial differences and posttreatment long-term follow-ups, the differences between patients with HFM and those with hemimandibular asymmetries with a peculiar ramal morphology consisting of the collapse of the condyle against the coronoid process (CCC).

Fig 7. Female patient misdiagnosed with HFM and treated with a Class II bionator: A and B, at pretreatment, the ear, although normal in structure, is abnormally positioned due to the skeletal deformity; it is lateral and more prominent on the affected side; C and D, at the 12-year follow up, note the typical pretreatment shape of the condyle-coronoid relationship, similar in all of these patients. Note the integrity of the ears and the fullness of the soft tissues on the side of the mandibular deviation (in true HFM, there is usually flatness of the gonial area).

Fig 8. Male patient misdiagnosed with HFM and treated with an asymmetrical functional activator: A and B, at pretreatment, the ear, although normal in structure, is abnormally positioned due to the skeletal deformity; it is lateral and more prominent on the affected side; C and D, at the 9-year follow up, note the fullness of the soft tissues on the affected side before treatment and the excessive fullness after treatment. In the posttreatment panoramic x-ray, there is an evident tendency toward overgrowth on the affected side (pattern similar to a hemimandibular hypertrophy). Overgrowth is an uncommon, but reported, effect of trauma.25
MATERIAL AND METHODS

One sample consisted of panoramic radiographs of 9 patients with unilateral mandibular hypoplasia with CCC, who had all been previously misdiagnosed as having HFM, at pretreatment (Tpre) and long-term follow-up (Tlt) (range, 8–29 years) after DO (Figs 2–5) and after functional treatment (Figs 6–10). These patients were selected from several centers based on the similarity of their pretreatment condylar-coronoid morphology. The other sample included panoramic radiographs of 8 consecutively treated patients affected by HFM from 2 centers (confirmed by a dysmorphologist) at Tpre and Tlt.

Fig 9. Male patient misdiagnosed with HFM and treated with a “morpho-correcting” functional appliance: A and B, pretreatment; C and D, 12-year follow-up.

Fig 10. Female patient misdiagnosed with HFM and treated with an asymmetric functional activator23: A and B, pretreatment; C and D, 10-year follow-up.
Measurements considered on the panoramic x-rays are described in Figure 13.

The use of panoramic x-rays in the diagnosis of mandibular deformities, in particular for gonial angle measurements and vertical ratios, has been previously demonstrated to be reliable. An unpaired Student t test was used to check for significant differences in the HFM sample at Tpre and Tlt and between the HFM and the pseudo-HFM sample at each time point.

RESULTS

The results of the comparisons at Tpre and Tlt in the true HFM patients and the CCC patients are listed in Table II.

The gonial angle was significantly smaller on the affected side in the CCC patients at Tpre, whereas at Tlt there was no difference between the affected and unaffected sides. The angle increased an average of 24.7° from Tpre to Tlt (P < 0.01). In the HFM patients, both affected and unaffected gonial angles were reduced, but not significantly.

The condylar-coronoid process angle was negative at Tpre in the CCC patients and increased an average of 31° at Tlt, justifying the stunning morphologic change of the ramus (P < 0.01). In the HFM patients, both sides increased, but not significantly.

The ratio between the affected and unaffected ramus increased significantly by 27% from Tpre to Tlt in the CCC patients. On the contrary, the true HFM patients returned to the same ratio from the Tpre to the Tlt records (Figs 11 and 12).

The ratio between the affected and unaffected sigmoid notch depths decreased significantly from Tpre to Tlt in the CCC patients. Conversely, the true HFM patients had no significant difference from the Tpre to the Tlt records.

Fig 11. Male patient affected by left HFM (type II mandibular deformity), treated with unilateral mandibular DO: A and B, before DO; C and D, immediately after DO; E and F, 13 years after DO.
DISCUSSION

In 2005, the American Association of Orthodontists Council on Scientific Affairs concluded that “there is no evidence that functional appliances significantly increase mandibular growth when evaluated in the long term.”

Functional appliances certainly induce major dentoalveolar changes, but the actual mandibular bony changes are 1 to 2 mm according to the literature. This is even more true for vertical lengthening of the ramus.

This aspect must be carefully considered when treating any mandibular asymmetry, but even more so when treating syndromic patients. Although minor soft-tissue and skeletal asymmetries in HFM patients can be treated with satisfactory results with functional treatment and good dentoalveolar compensations are obtained with some mild skeletal improvement, it is still controversial whether it is appropriate to subject children affected by more severe forms of HFM to long functional orthopedic treatments.

Unilateral surgical lengthening of the ramus in growing patients through distraction osteogenesis is successful in the short term but has been disappointing in the long term. Asymmetry recurs with time, together with a consistent tendency toward a return to the original phenotype and facial proportion. The 8 HFM patients evaluated and measured over 10 years postdistraction showed returns to the original ratio between the affected and unaffected ramus heights (Table II, Figs 11 and 12). The reappearance of the asymmetry is linked to the involvement not only of the bony segments, but especially of the neuromuscular pattern, which slowly returns the bony proportions to the original architecture. The 4 CCC patients who were surgically treated, on the contrary, have gained and maintained symmetry in the long term (Table II, Figs 2-10). The similarity of the phenotype of these patients and the entity of the response to functional stimulation are certainly of great interest. The long-term changes of the gonial angle, the angle formed by the condylar and coronoid processes and the alveolar processes, are of great interest. These changes are linked to the involvement not only of the bony segments, but especially of the neuromuscular pattern, which slowly returns the bony proportions to the original architecture. The 4 CCC patients who were surgically treated, on the contrary, have gained and maintained symmetry in the long term (Table II, Figs 2-10). The similarity of the phenotype of these patients and the entity of the response to functional stimulation are certainly of great interest. The long-term changes of the gonial angle, the angle formed by the condylar and coronoid processes, are of great interest. These changes are linked to the involvement not only of the bony segments, but especially of the neuromuscular pattern, which slowly returns the bony proportions to the original architecture. The 4 CCC patients who were surgically treated, on the contrary, have gained and maintained symmetry in the long term (Table II, Figs 2-10). The similarity of the phenotype of these patients and the entity of the response to functional stimulation are certainly of great interest. The long-term changes of the gonial angle, the angle formed by the condylar and coronoid processes, are of great interest. 

Fig 12. Female patient affected by left HFM (severe type I mandibular deformity) and treated with unilateral mandibular distraction DO: A and B, before DO; C and D, immediately after DO; E and F, 13 years after DO.
processes, and the ratio of ramal height between the affected and unaffected sides in these patients compared with true HFM patients are not only visually evident, but also quantitatively and statistically significant (Table II).

Getting back to the results of functional treatment, Harkness and Thorburn24 questioned Kaplan’s orthopedic results suggesting that the shape of the mandibular hypoplastic side could be related to a mandibular fracture instead of HFM. Several long-term studies on mandibular condylar fractures show the ability to self-correct35 or successful correction with orthopedics.36 These authors suggested that all the patients described might have had undiagnosed early traumas. These patients had a bony defect, but a normal neuromuscular pattern, which can remodel the damaged bony structure into a new condyle-coronoid complex, with the help of functional stimulation or early mandibular surgery. However, early trauma does not always cause a condylar-coronoid deformity such as the one described and measured here, nor does it have the same prognosis. In some instances, even with a positive history of trauma, the prognosis is not as good because of secondary scarring that can severely disturb the functional matrix. These patients often show some hypomobility of the affected side, and the ramal morphology is not as disrupted as in the CCC patients shown. Other types of acquired mandibular hypoplasia, such as rheumatoid arthritis and Parry-Romberg syndrome, have a different clinical history and aspect, especially radiologically, and should not be as difficult to differentiate.

Long-term results of both functional and surgical treatment of hemimandibular hypoplasia with CCC are successful, compared with those of true HFM, which are poor in the long term, as shown in this study.

Because of the great heterogeneity of the HFM phenotype and the little genetic knowledge on the syndrome, the differences between these 2 types of hemimandibular hypoplasia are not always obvious. We have attempted to summarize the most important clinical and radiologic differences qualitatively and quantitatively (Tables I and II, Fig 1) to aid in differential diagnosis.

We believe that it is crucial to correctly recognize patients often misdiagnosed as having HFM, who might have a great benefit from functional stimulation. True HFM patients, on the other hand, because of the early onset of the pathology, are more likely to have bony and neuromuscular deficits, which orthopedics might improve, but certainly not correct.

CONCLUSIONS

Cooperation between not only surgeons and orthodontists, but also geneticists and dysmorphologists, is crucial in the treatment of craniofacial anomalies. It is embryologically unlikely that a congenital disease such as HFM, which occurs between the 30th and 40th days in utero, could cause no deficit in the neuromuscular pattern and the soft tissues. The neuromuscular pattern drives craniofacial growth,16 and, although orthopedic treatment has been proposed,57 orthodontists might not have the proper tools at this time.15

However, some patients with a recognizable condylar deformity, such as those we have described, might benefit from functional stimulation. It is important to identify patients eligible for this approach and distinguish them from true HFM patients, in order not to impose ineffective orthopedic therapy or surgical treatment with a poor prognosis on those with a clear embryologic deficit.

Fig 13. Tracing of a panoramic radiograph of a patient with CCC before treatment. Co (condyion), uppermost point of the condyle; Cor (coronoid), uppermost point of the coronoid process; Syg, deepest point of the sigmoid notch; Go (gonion), most inferior and posterior point of the mandibular ramus where it intersects the tangent to the lower border of the mandible. A tangent to the proximal segment of the coronoid process is traced. A tangent to the posterior border of the ramus is also traced. The angle formed by these 2 lines defines the condylar-coronoid angle. The angle formed by the tangent to the posterior border of the ramus and the tangent to the lower border of the mandible defines the gonial angle. The height of the ramus is defined by the distance Go-Co. The depth of the sigmoid notch is defined by the perpendicular distance of Syg to the line connecting Co and Cor.
Table II. Measurements on panoramic radiographs of patients with HFM and with hemimandibular hypoplasia characterized CCC

<table>
<thead>
<tr>
<th>CCC</th>
<th>Difference</th>
<th>T1</th>
<th>T2</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>RHa/RHna</td>
<td>0.71 ± 0.05</td>
<td>0.98 ± 0.07</td>
<td>0.27*</td>
<td>0.67 ± 0.09</td>
</tr>
<tr>
<td>CC angle (°)</td>
<td>a</td>
<td>−21.2 ± 6.8</td>
<td>10.1 ± 4.6</td>
<td>31.3</td>
</tr>
<tr>
<td>Gonial angle</td>
<td>a</td>
<td>13.7 ± 3.2</td>
<td>15.2 ± 5.1</td>
<td>1.5</td>
</tr>
<tr>
<td>SigNa/SigNna</td>
<td>128.8 ± 6.4</td>
<td>124 ± 5.6</td>
<td>−4.8</td>
<td>131.5 ± 5.1</td>
</tr>
</tbody>
</table>

*RHa/RHna, Ratio of the height of the affected ramus and unaffected ramus; CC angle, angle formed by the tangent to the posterior border of the mandible and the tangent to the coronoid process; Gonial angle, formed by the tangent to the posterior border of the mandible and the tangent to the inferior border; SigNa/SigNna, ratio of the depth of the sigmoid notch on the affected and unaffected sides; a, affected; na, unaffected. *P <0.05; | P <0.001.

REFERENCES


