Obstructive sleep apnoea in acromegaly: the role of craniofacial changes

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ABSTRACT: Obstructive sleep apnoea (OSA) is due to craniofacial changes and acromegaly. The question addressed by this study was whether growth hormone (GH) induced craniofacial changes might explain persisting OSA despite endocrine inactivity in acromegaly.

Nineteen patients treated for acromegaly were examined cephalometrically for craniofacial changes and polysomnographically for OSA. Twelve patients proved to have OSA with an apnoea/hypopnoea index >15; seven patients showed no evidence of OSA at all.

With respect to the endocrinological parameters, there were no differences between the two groups that would explain the presence or absence of OSA. Neither group differed with respect to sex, age, or body mass index. Craniofacial changes were predominantly found in the mandible. The group with OSA proved to have increased vertical, dolichofacial growth compared to those without OSA. Consecutively, in the OSA group the posterior airway space was narrowed, and the hyoid was displaced more caudally.

Thus, it seems that craniofacial structures of patients with acromegaly and persisting obstructive sleep apnoea are different from those without obstructive sleep apnoea. Surgical corrections of pertaining acromegaly-induced craniofacial changes should be performed with an awareness of the individual craniofacial condition so as not to enhance obstructive sleep apnoea.

Eur Respir J 1999; 14: 196–202.

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Keywords: Acromegaly
cephalometry
craniofacial surgery
sleep apnoea

Received: November 20 1997

Accepted after revision February 17 1999

Acromegaly leads to typical skeletal as well as soft tissue craniofacial changes, which have been well known for many years [1–5]. Whereas many of the clinical symptoms can be relieved by treatment of the primary condition, the bony and some of the soft tissue changes are permanent, despite growth hormone homeostasis [6–8]. Furthermore, many patients with acromegaly also have obstructive sleep apnoea (OSA) [9–11]. Even though sleep apnoea severity is often reduced after adequate treatment of the endocrine syndrome [12–17], relevant obstructive events remain in some cases [18, 19] and amelioration of symptoms is not sufficient. The reasons for OSA are heterogeneous and multifarious [20], whereas OSA in combination with acromegaly suggests a causal connection. Nevertheless, in one case macroglossia caused pharyngeal obstruction [21], whereas other investigations exclude the tongue as a reason for obstruction [22].

With respect to the pathophysiology of OSA [20], one of the main factors is the facial skeleton [23]. Thus, the questions arise as to whether or not some typical craniofacial changes, as a consequence of acromegaly, provoke OSA, and whether there are craniofacial differences between acromegalic patients with and without OSA.

A secondary aspect is that facial bone distortion, nasal growth and macroglossia due to acromegaly can be surgically corrected, not only for aesthetic but also for psychosocial and functional reasons, such as articulatory

speech defects [24–27]. Reduction of hyperplastic bone formation may result in pharyngeal obstruction and, thus, enhance OSA [28, 29]. With respect to OSA and the underlying craniofacial deformity, the surgical treatment plan may be different in those cases so as not to provoke or enhance OSA.

Methods

Patients

Nineteen consecutive acromegalic patients participated in this study after giving informed consent. They were examined cephalometrically for craniofacial changes and polysomnographically for OSA over a 2-yr period. At the time of the cephalometric evaluation, acromegaly had been diagnosed and treated for a period of 2 weeks to 6 months, but it was unknown whether or not the patient had OSA. Twelve patients proved to have severe OSA with an apnoea/hypopnoea index (AHI) >15 events·h sleep⁻¹ (table 1), and seven patients showed no evidence of OSA at all. The group with OSA consisted of three females and nine males; the group without OSA consisted of two females and five males. With respect to sex (Fisher's exact test $p=1.0$), age and body mass index (BMI), there were no statistically significant differences between the groups (table 1).

Table 1. – Anthropometric data of patients with and without obstructive sleep apnoea (OSA)

	Group with OSA (n=12)				Group without OSA (n=7)				p-value ⁺
	Mean	SD	Min	Max	Mean	SD	Min	Max	
Age yrs	54.0	13.4	25	72	49.6	10.2	34	62	0.290
BMI kg·m ⁻²	32.2	5.1	25.4	41.7	30.3	5.2	24.9	39.8	0.365
AI event·h sleep ⁻¹	32.0	19.1	7	63	0.3	0.8	0	2	0.000
AHI events·h sleep ⁻¹	39.7	19.3	15	68	0.9	1.6	0	4	0.000

⁺: Two-tailed U-tests. Min: minimum; Max: maximum; BMI: body mass index; AI: apnoea index; AHI: apnoea/hypopnoea index.

Endocrine status

Serum growth hormone (GH) and insulin-like growth factor-1 (IGF-1) levels were determined using a radio-immuneassay (RIA) method (normal range for GH <5 ng·mL⁻¹; normal range for IGF-1, age 25–39: 120–382 ng·mL⁻¹; age 40–54: 75–306 ng·mL⁻¹, age >55: 43–283 ng·mL⁻¹) (table 2). Sixteen patients had been treated by transsphenoidal resection of pituitary gland adenoma (10 with OSA, six without OSA). Three patients were treated conservatively with octreotide (two with OSA, one without OSA). In addition to pituitary adenoma resection, six patients with postoperatively increased and non-suppressible GH levels were consecutively treated by radiotherapy (four with OSA, two without OSA). Five patients were postoperatively treated with octreotide (three with OSA, two without OSA). At the time of evaluation, 10 patients had persistent elevated GH secretion (no suppression below 2 ng·mL⁻¹ after glucose load) and increased IGF-1 levels (five with OSA, five without OSA). Postoperatively, three patients developed complete pituitary insufficiency (one with OSA, two without OSA). At the time of the diagnosis of sleep apnoea, however, all patients were under adequate replacement therapy. Therefore, hypopituitarism particularly hypothyroidism did not play a role in sleep apnoea.

Cephalometrics

Cephalometric examination was carried out using standardized recording techniques [30] with remote radiographic tracing of the viscerocranium in profile view for the measurement of vertical and sagittal dimensions. The lateral radiograph was performed using a 4-m distance between the focal point and radiograph film. The distance between the patient and the radiography film was kept as small as possible. This method minimizes magnification

of the cephalometric measuring distance due to projection effects. The cephalometric analysis of patients with OSA must not only investigate skeletal landmarks but also pharyngeal soft tissue dimensions, as previously reported [23]. This initial analysis used for cephalometric investigation in OSA patients consists of more than 50 parameters, but only the major and most important are quoted in this investigation, as defined in tables 3 and 4 and illustrated in figure 1.

Of the skeletal parameters, the angulation of the skull base is described by the N-S-Ba angle and the saddle angle. SNA and SNB are measures for the sagittal dimension of the maxilla and mandible in relation to the skull base, NL-NSL, ML-NSL and ML-NL for their vertical dimension. The sum of the saddle, articulare, and gonion angle best describes the facial type [30]. Facial axis is a measure for sagittal, as well as vertical, facial growth; facial depth and maxillary depth are mere sagittal parameters; the mandibular plane angle describes the vertical dimension of the mandible in relation to the Frankfurt horizontal (FH) plane and the mandibular arc angle is a measure for the angulation and growth of the mandible itself.

Skeletal dimensions influence the upper airway. The most important parameter for pharyngeal soft tissue dimension is the measurement of the posterior airway space (PAS), the distance between the velum or the base of the tongue, and the posterior pharyngeal wall, measured at different levels. Velum length and thickness are measured, as well as the relation of the tongue base to skeletal landmarks and the two-dimensional sagittal and vertical size of the tongue. Finally, the position of the hyoid is of major importance.

Despite the fact that two-dimensional cephalometric measurements do not allow a final judgement of the three-dimensional pharyngeal structures, there is a close correlation between the cephalometric parameters and the three-dimensional measurements of the pharynx obtained from computer tomograms.

Table 2. – Endocrinological data of patients with and without obstructive sleep apnoea (OSA) before and after treatment of acromegaly by different surgical methods

	Group with OSA (n=12)				Group without OSA (n=7)				p-value ⁺
	Mean	SD	Min	Max	Mean	SD	Min	Max	
Before treatment									
GH ng·mL ⁻¹	31.3	37.3	3.2	145.0	37.9	38.2	7.6	120.5	0.526
IGF-1 ng·mL ⁻¹	799	408	358	1268	623	135	527	719	0.643
After treatment									
GH ng·mL ⁻¹	2.8	3.6	0.2	12.1	15.0	24.3	0.1	69.0	0.139
IGF-1 ng·mL ⁻¹	341	180	129	699	409	274	48	753	0.554

⁺: Two-tailed U-tests. Minimum; Max: maximum; GH: growth hormone; IGF-1: insulin-like growth factor-1. See text for normal ranges.

Table 3. – Definitions of cephalometric landmarks and reference lines

Landmarks	Definition
S	Sella, midpoint of fossa hypophysealis
N	Nasion, anterior point at nasofrontal suture
O	Orbitale, most inferior point of the orbit
ANS	Spina nasalis anterior, most anterior point of anterior nasal spine
PNS	Spina nasalis posterior, most posterior point of hard palate
A	A-Point, deepest anterior point in concavity of anterior maxilla
B	B-point, deepest anterior points in concavity of anterior mandible
Pg	Pogonion, Most anterior point of bony chin
Gn	Gnathion, most antero-inferior point of bony chin
Me	Menton, most inferior point of bony chin
Go	Gonion, a mid-planed point at the gonial angle located by bisecting the posterior and inferior borders of the mandible
Ar	Articulare, a mid-planed point at the intersection of posterior ramus with inferior cranial base
Pt	Pterygon, Inferior border of foramen rotundum bisecting posterior border of pterygomaxillary fissure
Ba	Basion, most inferior point on anterior foramen magnum
Po	Porion, most superior point of bony external auditory meatus
H	Hyoid, most antero-superior point of the hyoid
TB	Tonguebase, ML bisecting posterior margin of the tonguebase
TT	Tonguetip, most anterior point of the tip of the tongue
UT	Uvulatip, tip of uvula
NSL	Nasion-sella line, a line through N and S
NL	Nasal line, a line through ANS and OS
ML	Mandibular line, a line through Me and Go
FH	Frankfurt horizontal line, a line through O and Po

Polysomnography

The diagnosis for OSA was undertaken in several steps according to the recommendations of PETER *et al.* [31]. The first step for graduated polygraphic diagnosis was the nightly recording of heart rate, oxygen saturation and snoring as indirect parameters for OSA with a MESAM IVTM (Madaus-Schwarzer, München, Germany). MESAM IVTM is a mobile four-channel recorder, with a sensitivity of ~95% in the diagnosis of OSA [32]. Patients with suspicious findings underwent detailed overnight cardio-respiratory polygraphy, measuring the following parameters: electrooculogram (EOG), submental-(genio-glossus) and leg- (anterior tibialis) electromyogram (EMG) and electrocardiogram (ECG). Nasal airflow was monitored by a nasal airflow thermistor (Pro-Tech Services, Woddingville, WA, USA), and an uncalibrated inductive respiratory plethysmograph (RespitraceTM; Stimotron, Wendelstein, Germany) monitored rib cage and abdominal wall movements. Respiratory sounds were recorded *via* a microphone placed over the anterior surface of the neck (Zentrales Entwicklungslabor für Elektronik, Marburg, Germany). Oxygen saturation was continuously recorded by a pulse oximeter (Biox 3700TM; Ohmeda, Erlangen, Germany).

Table 4. – Cephalometric parameters and normal values

Parameter	Definition	Normal values
N-S-Ba°	Angle between N-S and S-Ba	130±5
SNA°	Angle between S-N and N-A	82±3
SNB°	Angle between S-N and N-B	80±3
NL-NSL°	Angle between NSL and NL	8.5±3
ML-NSL°	Angle between NSL and ML	32±5
ML-NL°	Angle between NL and ML	23.5±5
Saddle angle°	Angle between S-N and S-Ar	123±5
Articular angle°	Angle between S-Ar and Ar-Go	143±6
Gonion angle°	Angle between Ar-Go and Go-Me	130±7
Sum angle°	Sum of saddle, Ar and Go angle	396±3
Facial axis°	Angle between Pt-Gn and Ba-N	90±3
Facial depth°	Angle between FH and N-Pg	90±3
Maxillary depth°	Angle between FH and N-A	90±3
Mandibular plane°	Angle between FH and ML	2 3±4.5
Mandibular arc°	Angle between mandibular ramus axis and corpus axis	26±4
PAS-NL mm	Distance from posterior pharyngeal wall to TB at NL	28±3.5
PAS-UT mm	Distance from posterior pharyngeal wall to uvulatip	9.5±3
PAS-ML mm	Distance from posterior pharyngeal wall to TB at ML	13.53
Velum length mm	Length of the soft palate distance PNS-UT	45.8±5
Velum thickness mm	Thickness of the soft palate largest diameter	12±2
TB-B mm	Distance from TB to point B	73±5
TB-PNS mm	Distance from TB to posterior nasal spine	54±5.5
TB TT mm	Distance from TB to tonguetip	78±5.5
Tongue height mm	Largest diameter of the tongue perpendicular to TB-TT	39±5
H-ML mm	Shortest distance from H to mandibular plane	21±6
N-S-H°	Angle between N-S and S-H	90±4

For definitions see table 3.

Polygraphic data were recorded continuously on an eight-channel polygraph (UD210; Madaus-Schwarzer, München, Germany) at a paper speed of 1 mm·s⁻¹.

Respiratory parameters were scored visually from the polygraph recordings with each quantified respiratory disturbance requiring a minimum duration of 10 s to be scored. Apnoeas were scored as described previously [33]. Furthermore, an apnoea was scored as obstructive if respiratory efforts continued during the cessation of nasal airflow. A lack of respiratory efforts characterized a central apnoea. Hypopnoeas were scored if nasal airflow and/or thoracic and abdominal respiratory excursions were reduced to <50% in comparison to normal respiration and if this respiratory event was associated with an oxygen saturation drop >3%. Hypopnoeas were scored as obstructive when snoring sounds were recorded during reduced thoracic and abdominal respiratory excursions.

From the total number of apnoeas and hypopnoeas, the apnoea index (AI) and hypopnoea index (HI) (average numbers of each event per hour of sleep time) were calculated. The AHI was calculated by adding AI and HI.

Fig. 1. – Diagrammatic representation of cephalometric radiograph indicating landmarks and reference lines. For definitions see table 3 and 4.

All patients with OSA were treated with nasal continuous positive airway pressure (nCPAP). The individual nCPAP pressure required by each patient was titrated manually during a further two nights of study in the sleep laboratory.

Statistics

Statistical evaluation was performed with SPSSTM Release 6.13 (SPSS Inc., Chicago, IL, USA) for Windows (Version 3.1). Mean, median values and standard deviations were calculated for all parameters. Because normal probability plots indicated that the values were not normally distributed, a two-tailed U-test was used and nominal p-values were calculated for discrimination of the differences between the two groups with and without OSA. Fisher's exact test was used to prove differences between the two groups with respect to sex.

Results

Firstly, as previously mentioned, the two groups with and without OSA did not differ with respect to BMI, age and sex. The group with OSA consisted of three females and nine males, and the group without OSA consisted of two females and five males. Both groups did not differ with respect to sex ($p=1.0$ Fisher's exact test). Age and BMI were within a range of 25–72 yrs and 25.4–41.7 kg·m⁻², respectively for the group with OSA and 34–62 yrs and 24.9–39.8 kg·m⁻², respectively for the group without OSA (table 1). The median AHI for the acromegalic group with OSA was 42.5 events·h⁻¹ (median AI 38.0, median HI 6.5) compared to a median of 0.0 for AI, HI, and AHI in the group without OSA (table 1). In this group without OSA, five patients had an AHI of 0, one patient had an AI of 2 and one patient an HI of 4 events·h⁻¹.

Table 5. – Skeletal parameters of patients with and without obstructive sleep apnoea (OSA)

Parameter	With OSA (n=12)		Without OSA (n=7)		Nominal p-value
	Mean	SD	Mean	SD	
N-S-Ba°	126.4	5.6	129.6	4.2	0.122
SNA°	81.0	4.3	80.3	1.2	0.146
SNB°	78.9	2.7	81.5	4.2	0.373
NL-NSL°	8.8	3.5	9.5	3.0	0.426
ML-NSI°	34.3	5.0	26.5	8.3	0.031*
ML-NL°	25.5	4.8	16.9	9.0	0.019*
Saddle angle°	122.9	4.8	128.2	4.9	0.024*
Articular angle°	141.9	6.0	137.9	4.7	0.134
Gonion angle°	129.5	6.6	120.4	5.8	0.011*
Sum angle°	394.3	5.0	386.5	8.3	0.031*
Facial axis°	86.3	3.4	90.3	4.2	0.083
Facial depth°	87.7	2.5	90.3	4.5	0.223
Maxillary depth°	88.5	3.0	86.5	4.6	0.542
Mandibular plane°	26.9	5.0	20.2	6.7	0.019*
Mandibular arc°	34.8	5.0	43.8	7.0	0.014*

*: $p<0.05$, two-tailed U-test. For definitions see table 3 and 4.

With respect to the endocrinological parameters, the mode of treatment and replacement therapy did not differ enough between the two groups to explain the presence or absence of OSA (table 2).

With respect to skeletal parameters (table 5), no relevant differences could be found between the two groups for the angulation of the skull base (N-S-Ba angle), whereas the saddle angle was considerably larger in the group without OSA. The difference between the parameters is that one of the reference points for N-S-Ba is the skull base (basion (Ba)), whereas for the saddle angle this landmark is replaced by the articulare (Ar), a point at the posterior border of the mandibular ramus, indicating relevant changes of the mandible between both groups, as will be described later. No major differences could be found for the parameters SNA, SNB, facial depth and maxillary depth as measures for the sagittal dimension of maxilla and mandible indicating the same sagittal dimensions for acromegalic patients with and without OSA. All these parameters were within a normal range (table 4), even if the definition of "normal" is highly problematic. Major differences could be measured for vertical and pure mandibular dimensions. Whereas the maxillary plane proved to have just the same inclination in relation to the skull base (NL-NSL), the mandibular plane ML was found to be considerably more tilted in relation to NSL, NL and FH in the OSA group. ML-NSL, ML-NL and the mandibular plane angle are enlarged, which is called a vertical facial type or dolichofacial appearance. This vertical, dolichofacial type means dorso-caudal rotation of the mandible with consecutive reposition of the tongue ground. This situation can be found predominantly in patients with OSA [23]. The sum angle was also increased and supports these findings. Nevertheless, the increase of the sum angle was mainly due to a considerable increase of the gonion angle indicating predominant changes of the mandible. The clear decrease of the mandibular arc coincided with the above mentioned changes.

These skeletal changes influence the upper airway (table 6). While the PAS as a measure for pharyngeal soft tissue dimension was equal for both groups at the maxillary

Table 6. – Pharyngeal parameters of patients with and without obstructive sleep apnoea (OSA)

Parameter	With OSA (n=12)		Without OSA (n=7)		Nominal p-value
	Mean	SD	Mean	SD	
PAS-NL mm	26.4	3.7	25.1	1.4	0.261
PAS-UT mm	7.4	2.5	10.0	1.9	0.049*
PAS-ML mm	12.3	2.9	17.8	5.3	0.039*
Velum-length mm	53.7	4.9	50.8	5.9	0.303
Velum-thickness mm	13.9	2.5	15.1	2.4	0.325
TB-B mm	78.2	5.5	85.8	9.6	0.075
TB-PNS mm	56.5	11.2	66.8	8.7	0.061
TB-TT mm	83.4	8.1	89.3	11.9	0.189
Tongue-height mm	44.0	5.9	42.2	8.4	0.708
Hyoid- ML mm	27.6	7.5	19.7	6.8	0.015*
N-S-H°	91.8	4.0	91.9	5.5	0.963

*: $p < 0.05$, two-tailed U-test. For definitions see tables 3 and 4.

plane level (NL), there was a clear narrowing of the PAS at the level of the uvula tip (UT) and at the level of the mandibular plane (ML) within the group with OSA compared to the group without OSA. The space for the tongue in relation to skeletal landmarks (TB-B, TB-PNS) was reduced, at least in this two-dimensional vertical and sagittal measurement, although these soft tissue differences were not as clearly expressed in the small sample of patients. Sagittal and vertical dimensions of the velum and the tongue did not differ between the two groups; therefore, pharyngeal narrowing in the patients with OSA cannot be explained by soft tissue hyperplasia alone, although clinical signs of macroglossia were present in some cases. The position of the hyoid, which plays a major role in the aetiopathology of OSA, did not differ within the two groups in the sagittal dimension, but the distance to the mandibular plane was increased considerably in the group

Fig. 3. – Relationship between apnoea/hypopnoea-index (AHI) as a measure of the severity of obstructive sleep apnoea and ML-NSL as measure for the vertical facial dimension. Below horizontal line=no obstructive sleep apnoea (OSA); above horizontal line=OSA. For definitions see table 3.

with OSA. A deep hyoid position is another pathognomonic sign in patients with OSA and further enhances the effects of dorsocaudal rotation of the mandible. Figure 2 gives an example of the craniofacial situation for an acromegalic patient with OSA compared to one without OSA. Figure 3 demonstrates the relationship between AHI, as measure for the severity of OSA, and ML-NSL, as measure for the vertical facial dimension.

Discussion

Typical craniofacial changes of patients with acromegaly were systematically described in 1955 by KORKHAUS

Fig. 2. – Example of an acromegalic patient a) with obstructive sleep apnoea (OSA) and b) without OSA. Note the vertical facial growth with steep mandibular plane (ML) and pharyngeal narrowing in (a) as apposed to horizontal facial growth with flat ML, and no pharyngeal narrowing (b). For definitions see table 3.

[1]. The study predominantly found only hyperplasia of the mandible in a series of skulls, with great variability and macroglossia in a sample of patients. Later, cephalometric evaluations led to a more precise definition of these changes [3–5]. In accordance with the current findings, all of these cephalometric evaluations of acromegalic patients found relevant skeletal changes only in the mandible. In 27 patients with active acromegaly, predominantly vertical changes could be found (facial and mandibular height) which did not depend on disease duration [5]. All the bony and soft tissue changes are very heterogeneous. No further studies exist about pharyngeal changes or about bony and soft tissue changes with respect to pharyngeal obstruction and sleep apnoea.

Many patients with acromegaly also have OSA [9, 11]. The frequency of sleep apnoea in acromegaly has been documented in a large scale sleep study showing a frequency of 60% [10]. In many, but not all, OSA can be reduced by treatment of the endocrine syndrome and reduction of GH levels to normal [12–17]. The relationship between sleep apnoea and the biochemical activity of acromegaly is not clear, at least no correlation between GH level and severity of sleep apnoea appears to exist [10]. Many cases remain with relevant OSA despite endocrine inactivity [18, 19]. In this study, at the time of evaluation, 10 patients had persistent elevated GH secretion (no suppression below $2 \text{ ng}\cdot\text{mL}^{-1}$ after glucose load) and increased IGF-1 levels (five patients with OSA and five without OSA), therefore not explaining the occurrence of OSA. Obviously, a causal connection between OSA and acromegaly exists, but OSA in acromegaly exists with the same heterogeneous influences of many other parameters as does OSA without acromegaly.

As a result of pituitary gland resection, pituitary insufficiency may develop. This was the case in three patients with complete insufficiency (one with OSA and two without OSA). At the time of the diagnosis of OSA, however, all patients were under adequate replacement therapy. Therefore, hypopituitarism, particularly hypothyroidism, does not explain the occurrence of OSA.

Even though one third of cases are reported to have central apnoeas [10], none of the patients in this study had pure central apnoeas, they all demonstrated obstructive mixed apnoeas. With respect to craniofacial changes as a consequence of acromegaly, the reasons for obstructive apnoeas in acromegalic patients can include obstruction by tissue hypertrophy, macroglossia and jaw deformity [18]. Pharyngeal obstruction due to soft tissue changes [21] might help to explain why the treatment of the endocrine disease reduces obstructive apnoeas in some cases. Some of the soft tissue changes are reversible after GH homeostasis, but the thickening of the skin as a result of hypertrophy of collagen fibres is not fully reversible, for instance [7]. In some other cases, macroglossia cannot be observed or can be excluded as a reason for pharyngeal obstruction [22]. Skeletal craniofacial disorders (mainly retrognathic, dolichofacial appearance) are one of the main reasons for OSA, besides obesity [23]. Therefore, it was interesting to see whether similar predictions could be made in patients with acromegaly and OSA compared to those with acromegaly and without OSA. In congruence with previous cephalometric evaluations in acromegalic patients [4, 5] major skeletal changes could be measured only in the mandible. The groups with and

without OSA did not differ with respect to sagittal dimension, which means that patients with acromegaly and OSA were not more retrognathic than patients without OSA. Despite the small sample, however, the two groups differed considerably with respect to vertical dimensions, and all vertical parameters gave clear indications of a more vertical, dolichofacial growth pattern in the group with OSA. Vertical, dolichofacial growth means dorso-caudal development and rotation of the mandible with consecutive repositioning of the tongue ground, which moves even further dorsally during mouth opening. This facial type can be found predominantly in patients with OSA and contributes to pharyngeal obstruction [23]. Along with these skeletal findings, measurements of pharyngeal parameters demonstrated pharyngeal narrowing in the OSA patients, the PAS was considerably smaller at the mandibular and hypopharyngeal level. There were no differences between the two groups at a higher velopharyngeal level. Due to the vertical, dolichofacial development of the mandible the space for the tongue was narrowed, even though this is difficult to examine with these two-dimensional cephalometric measurements. Also, the hyoid was far more caudally positioned, with an increased distance to the mandibular plane in the acromegalic group with OSA.

Other possible influences could not be found. The BMI as an important factor in the aetiopathology of OSA was increased in both groups but to the same degree

Conclusion

These results, with the described differences of craniofacial appearance between patients with acromegaly and OSA and those without OSA, clearly support the concept of the multifarious pathophysiology of OSA [20]. As is the case for OSA patients without acromegaly, certain craniofacial changes are also of major importance in the aetiology of OSA in patients with acromegaly. In the acromegalic patient a vertical growth of the mandible leads to dorso-caudal rotation and consecutive pharyngeal obstruction. Some of the soft tissue changes owing to increased GH may recede after adequate endocrine inactivity, but skeletal changes remain. Therefore, persisting OSA after GH homeostasis might be due to skeletal changes, which could be treated by surgical skeletal corrections. Diagnosing OSA in acromegalic patients should also mean evaluation of the underlying craniofacial condition. Nevertheless, surgical reduction of hyperplastic bone formation in acromegalic patients may result in pharyngeal obstruction and thus enhance OSA [28, 29].

Depending on the cephalometric evaluation, especially with respect to the pharyngeal situation, maxillary advancement should be considered in preference to mandibular reduction when performing surgical facial corrections [25]. Pharyngeal soft tissue corrections such as uvulopalatopharyngoplasty should not be advised for acromegalic patients with obstructive sleep apnoea [34]. Uvulopalatopharyngoplasty is ineffective in most cases as a treatment for obstructive sleep apnoea [35] and addresses neither skeletal changes nor enlarges hypopharyngeal airway space, which seems to be the predominant site of obstruction in acromegalic patients.

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